Continence

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ICS

WEDNESDAY 7TH SEPTEMBER

07:30 - 09:00 **WORKSHOP 1 - INTERACTION BETWEEN BLADDER AND SEX IN SPINAL CORD DISEASE**
Hall K
Chair: Michele Spinelli (Italy),
Speakers: Marcalee Alexander (United States), Gianluca Sampogna (Italy), Melina Longoni (Argentina)

07:30 - 09:00 **WORKSHOP 2 - ARTIFICIAL URINARY SPHINCTERS IN MALES AND FEMALES AND NEUROGENIC PATIENTS, TECHNIQUE AND INDICATIONS**
Hall G
Chair: Wilhelm Hübner (Austria),
Speakers: Emmanuel Chartier-Kastler (France), Ralf Anding (Switzerland), Frank Van der Aa (Belgium), Ervin Kocjancic (United States)

07:30 - 10:30 **WORKSHOP 3 - THE PELVIC FLOOR LAPAROSCOPIC SURGERY WORKSHOP**
Hall N
Chair: Rufus Cartwright (United Kingdom),
Speakers: Joan Melendez-Munoz (Spain), Elisabetta Costantini (Italy), David Atallah (Lebanon), Bruno Deval (France), Arvind Vashisht (United Kingdom), Natalia Price (United Kingdom), Jerome Melon (Australia)

07:30 - 10:30 **WORKSHOP 4 - BEYOND SACROCOLPOPEXY: NEW ALTERNATIVES FOR PROLAPSE REPAIR**
Hall M
Chair: John Heusinkveld (United States),
Speakers: Christian Twiss (United States), addis ilana (United States)

08:00 - 10:00 **SCIENTIFIC COMMITTEE**
Meeting Room 1
Chair: Mr Laurence Stewart (United Kingdom)
Members: Prof Adrian Stuart Wagg (Canada), Dr Chantale L Dumoulin (Canada), Dr Lori A Birder (United States), Dr Elise Jaques Billings De (United States), Dr Kathleen Frances Hunter (Canada), Dr Alex Digesu (United Kingdom), Prof Wilhelm A. Hübner (Austria), Prof Christopher Henry Fry (United Kingdom), Dr Jennifer Kruger (New Zealand), Prof Kari A O Tikkinen (Finland), Mrs Elisabeth Udier (Austria), Prof Barbara Bodner-Adler (Austria)

08:00 - 11:00 **EDUCATION COMMITTEE**
Meeting Room 2
Chair: Dr Elise Jaques Billings De (United States)
Members: Prof David Castro-Diaz (Spain), Paula Igualada Martinez (Spain), Dr Ruwan Janaka Fernando (United Kingdom), Dr Howard B Goldman (United States), Miss Angie Rantell (United Kingdom), Dr Giulio A. Santoro (Italy), Dr Matthew Oliver Fraser (United States), Dr Mikolaj Przydacz (Poland), Miss Alison Hainsworth (United Kingdom), Prof Amy D. Dobberfuhl, MD, MS (United States), Marilena Gubbiotti (Italy), Dr Shannon Leigh Wallace (United States)

09:00 - 10:30 **WORKSHOP 5 - LEVERAGING NONINVASIVE IMAGING AND COMPUTATIONAL ANALYSES TO IMPROVE OUR UNDERSTANDING OF PELVIC ANATOMY AND FUNCTION**
Hall K
Chair: Marianna Alperin (United States),
Speakers: Milena Weinstein (United States), Paul Hodges (Australia), Megan Routzong (United States)

09:00 - 10:30 **WORKSHOP 6 - CURRENT SURGICAL MANAGEMENT OF POSTPROSTATECTOMY INCONTINENCE – WORKUP, OPTIONS AND DECISION MAKING**
Hall G
Chair: Ralf Anding (Switzerland),
Speakers: Vincent Tse (Australia), Craig Comiter (United States), Wilhelm Hübner (Austria)

10:30 - 12:30 **PHYSIOTHERAPY COMMITTEE**
Meeting Room 1
Chair: Dr Heather Lynn Moky (United States)
Members: Dr Chong-He Jiang (China), Mrs Frankie Bates (Canada), Prof Paul Hodges (Australia), Mrs Heidi FA Moossdorff-Steinhauser (Netherlands), Nelly Faghani (Canada), Mrs Ceren Gursen (Turkey), Miss Jenniffer Voelkl (Colombia), Dr Magdaléna Hagovská (Slovakia), Ms Marie-Pierre Cyr (Canada)

10:30 - 12:30 **STANDARDISATION STEERING COMMITTEE**
Meeting Room 3
Chair: Prof Matthias Oelke (Germany)
Members: Prof Donna Zimmaro Bliss (United States), Dr Roger Roman Dmochowski (United States), Prof Philip Edward Van Kerrebroeck (Belgium), Prof Yat-Ching Tong (Taiwan), Giovanni Mosiello (Italy), Mr Arun Sahai (United Kingdom), Prof Marcio Augusto Averbeck (Brazil), Mr Joan Melendez-Munoz (Spain), Dr Liliana Bordeianou (United States)

10:30 - 11:00 **COFFEE BREAK**

11:00 - 12:30 **WORKSHOP 7 - CASE BASED PEARLS IN PELVIC PAIN - A TUTORIAL ANCHORED IN CLINICAL SCENARIOS TO BRING TO YOUR PRACTICE**
Hall K
Chair: Elise De (United States),
Speakers: Alex Digesu (United Kingdom), Elizabeth Shelly (United States), Charles Argoff (United States)

11:00 - 12:30 **WORKSHOP 8 - NOVEL BPH THERAPIES – REVIEW OF MALES LUTS, TECHNOLOGIES AND PRACTICAL INSTRUCTION**
Hall G
Chair: Dean Elterman (Canada),
Speakers: Enrique Rijo (Spain), Vincent Misrai (France), Dmitry Enikeev (Russian Federation)

11:00 - 12:30 **WORKSHOP 9 - ICS CORE CURRICULUM (FREE): NURSING COMMITTEE WORKSHOP: SELF-MANAGEMENT IN CONTINENCE CARE**
Hall N
Chair: Tamara Dickinson (United States),
Speakers: Lori Saiki (United States), Bodil Rasmussen (Australia), E Jean C Hay-Smith (New Zealand), Donna Bliss (United States), Katie Thompson (United Kingdom)

11:00 - 14:30 **WORKSHOP 10 - ICS INSTITUTE MODERN TECHNOLOGY: ADVANCES IN NEUROSTIMULATION: TECHNOLOGY-BASED APPROACH- HANDS-ON TRAINING WITH 3D PRINTED MODELS**
Hall M
Chair: Emre HURI (Turkey),
Speakers: Stefan de Wachter (Belgium), David Castro-Diaz (Spain), John Heesakkers (Netherlands)

12:00 - 14:00 NEUROUROLOGY PROMOTION COMMITTEE
Meeting Room 2
Chair: Mr Rizwan Hamid (United Kingdom)
Members: Mr Marcus John Drake (United Kingdom), Dr Sanjay Sinha (India), Giulio Del Popolo (Italy), Dr Cristiano M Gomes (Brazil), Dr Ryuji Sakakibara (Japan), Prof Stefan de Wachter (Belgium), Dr Charalampos Konstantinidis (Greece), Dr Blayne Welk (Canada), Ms desiree vrijens (Netherlands), Mrs Collette Haslam (United Kingdom)

12:30 - 13:30 LUNCH BREAK

13:00 - 14:00 DEVELOPING WORLD COMMITTEE
Meeting Room 3
Chair: Prof Sherif Mourad (Egypt)
Members: Dr Ajay Singla (United States), Dr Raheela Mohsin Rizvi (Pakistan), Dr Margaret McDougald (United Kingdom), Sakineh Hajebrahimi (Iran), Prof Enrico Finazzi Agrò (Italy), Prof Harrina Erlianti Rahardjo (Indonesia), Prof Fasnéwindé ARISTIDE KABORE (Burkina Faso), Prof Cristiane Carboni (Brazil), Dr David Hernández Hernández (Spain), Dr Ahmed Maher Higazy (Egypt)

13:30 - 15:00 WORKSHOP 11 - AUTONOMIC DYSREFLEXIA (AD): A SERIOUS, RATHER UNDERESTIMATED CONDITION
Hall K
Chair: Charalampos Konstantinidis (Greece),
Speakers: Pierre Denys (France), Michael Kennelly (United States), Andrei Krassioukov (Canada)

13:30 - 15:00 WORKSHOP 12 - HOW TO PERFORM AND INTERPRET ANORECTAL MANOMETRY
Hall G
Chair: Alexis Schizas (United Kingdom),
Speakers: Linda Ferrari (United Kingdom), Ugo Grossi (Italy)

13:30 - 15:00 WORKSHOP 13 - MANAGEMENT OF COMPLICATIONS OF MESH SLING SURGERY - DEMONSTRATION THROUGH SURGICAL VIDEO CASES
Hall N
Chair: Howard Goldman (United States),
Speakers: karen guerrero (United Kingdom), Sandip Vasavada (United States)

14:00 - 15:00 CHILDRENS AND YOUNG ADULTS COMMITTEE
Meeting Room 1
Chair: Ms Ashani Couchman (Australia)
Members: Prof Rien Johan Marien Nijman (Netherlands), Mr Marcus John Drake (United Kingdom), Giuseppe Masnata (Italy), Miss Jenniffer Voelkl (Colombia), Mrs Dragana Dragan Zivkovic (Serbia), Israel Franco (United States), Dr Jennifer Dart Yin Sihoe (Hong Kong), Dr Beulah Jebakani (India)

14:00 - 15:30 ETHICS COMMITTEE
Meeting Room 3
Chair: Dr Anne M Suskind (United States)
Members: Mrs Ina DW Elving (Netherlands), Ms Tamara Dickinson (United States), Antonella Giannantoni (Italy), Prof Jian Guo Wen (China), Dr William Robert Gibson (Canada), Dr Martha Spencer (Canada), Dr Yahir Santiago-Lastra (United States), Miss Manjula Annappa (United Kingdom), Marilena Gubbiotti (Italy), Dr Shannon Leigh Wallace (United States)

15:00 - 16:00 URODYNAMICS COMMITTEE
Meeting Room 2
Chair: Mr Tufan Tarcan (Turkey)
Members: Prof Carlos Levi D'Ancona (Brazil), Dr John PFA Heesakkers (Netherlands), Dr Sanjay Sinha (India), Dr Alexandre Fornari (Brazil), Mr Christopher Harding (United Kingdom), Prof Enrico Finazzi Agrò (Italy), Dr Luis Miguel Abranches-Monteiro (Portugal), Mr Andrew R Gammie (United Kingdom), Prof Jian Guo Wen (China), Dr Christian Hector Cobreros (Argentina), Prof Maurizio Serati (Italy), Mr Eskinder Solomon (United Kingdom)

15:00 - 15:30 COFFEE BREAK

15:30 - 17:00 WORKSHOP 14 - ICS CORE CURRICULUM (FREE): THE INVESTIGATION OF POSTERIOR COMPARTMENT DISORDERS: AN INTEGRATED APPROACH
Hall K
Chair: Alison Hainsworth (United Kingdom),
Speakers: Giulio Santoro (Italy), Anders Mellgren (United States), Emma Breslin (United Kingdom)

15:30 - 17:00 WORKSHOP 15 - ICS CORE CURRICULUM (FREE): NEUROUROLOGY PROMOTION COMMITTEE: UPDATES ON TREATMENT OF NEUROGENIC BLADDER DYSFUNCTION
Hall G
Chair: desiree vrijens (Netherlands),
Speakers: Stefan de Wachter (Belgium), Charalampos Konstantinidis (Greece), Cristiano Gomes (Brazil)

15:30 - 16:30 WORKSHOP 16 - BOWEL CONSIDERATIONS FOR OPTIMAL CARE OF URINARY CONTINENCE
Hall N
Chair: Carina Siracusa (United States),
Speakers: Michelle Lyons (Ireland), Lori Mize (United States)

15:30 - 17:00 EARLY CAREER PROFESSIONAL SESSION
Hall M

15:30 - 17:30 NURSING COMMITTEE
Meeting Room 1
Chair: Ms Tamara Dickinson (United States)
Members: Dr Joanne Patterson Robinson (United States), Mrs Frankie Bates (Canada), Miss Angie Rantell (United Kingdom), Dr Kristine Marie Carlson Talley (United States), Dr Ka Lok Gilbert Lui (Hong Kong), Ms Joanne Dean (Australia), Mrs Janie Thompson (Australia), Lisa Krabbenhoft (United States), Mrs Juliana Neves da Costa (Brazil), Lori S. Saiki (United States)

17:00 - 19:00 WELCOME RECEPTION IN EXHIBITION HALL

19:00 - 23:00 EARLY CAREER PROFESSIONALS NIGHT OUT

THURSDAY 8TH SEPTEMBER

07:30 - 09:00 **WORKSHOP 17 - TARGETING NEUROTROPHIN AND NITRIC OXIDE SIGNALING TO PROMOTE RECOVERY AND AMELIORATE NEUROGENIC BLADDER DYSFUNCTION FOLLOWING SPINAL CORD INJURY—MECHANISTIC CONCEPTS AND CLINICAL IMPLICATIONS**
Hall K
Chair: Anthony Kanai (United States),
Speakers: Karl-Erik Andersson (United States), Christopher Fry (United Kingdom), Naoki Yoshimura (United States)

07:30 - 09:00 **WORKSHOP 18 - FEMALE VOIDING DYSFUNCTION: APPROACH TO DIAGNOSIS AND MANAGEMENT**
Hall G
Chair: Sanjay Sinha (India),
Speakers: Howard Goldman (United States), Salvador Arlandis (Spain), Claire Yang (United States)

07:35 - 10:35 **WORKSHOP 19 - BASIC URODYNAMICS - AN INTERACTIVE WORKSHOP**
Hall N
Chair: Hashim Hashim (United Kingdom),
Speakers: Andrew Gammie (United Kingdom), Arturo Garcia-Mora (Mexico), Laura Thomas (United Kingdom), Connie Chew (United Kingdom)

08:15 - 08:30 **WELCOME AND OPENING WORDS**
Hall D

08:30 - 09:00 **STATE OF THE ART LECTURE 1 - HOW DO WE KNOW ANYTHING? STEINAR HUNSKAAR**
Hall D
Chair: Prof Steinar Hunskaar (Norway)

09:05 - 10:35 **SESSION 1 - BEST UROLOGY**
Abstracts 1-6
Hall D
Chairs: Prof David Castro-Diaz (Spain), Prof Helmut Madersbacher (Austria)

09:05 - 10:35 **SESSION 2 - PRODUCTS, DEVICES AND INNOVATIVE THERAPIES**
Abstracts 7-18
Hall K
Chairs: Mrs Frankie Bates (Canada), Ms Karin Müller (Austria)

09:05 - 10:35 **SESSION 3 - PHARMACOLOGY AND LUTS**
Abstracts 19-30
Hall G
Chair: Prof Christopher Henry Fry (United Kingdom)

10:35 - 11:00 **SESSION 4 - OPEN DISCUSSION EPOSTERS**
Abstracts 31-52
Exhibition Hall

10:35 - 11:00 **COFFEE BREAK + EXHIBITION + S4 OPEN DISCUSSION EPOSTERS**

11:00 - 12:30 **SESSION 5 - MALE LOWER URINARY TRACT SYMPTOMS**
Abstracts 53-64
Hall D
Chair: Dr John PFA Heesakkers (Netherlands)

11:00 - 12:30 **SESSION 6 - PELVIC ORGAN PROLAPSE**
Abstracts 65-76
Hall K
Chair: Dr Heidi Wendell Brown (United States)

11:00 - 12:30 **SPOTLIGHT ON 1 - SINUG SOCIETY SESSION**
Hall G
Chairs: Francisco Cruz Miranda Rodrigues (Portugal), Montserrat Espuña Pons (Spain), Prof Salvador Arlandis (Spain)
Speakers: Mrs (Mary) Lynne Van Poelgeest-Pomfret (Netherlands), Alicia Martín Martínez (Spain), Bárbara Yolanda Padilla Fernández (Spain), Carlos Müller Arteaga (Spain), Isabel Paz Montes Posada (Spain), J. Roberto Martínez García (Spain), Luis López-Fando Lavalle (Spain), Pedro Blasco Hernández (Spain)

11:00 - 12:30 **NURSES FORUM**
Hall N
Chair: Ms Tamara Dickinson (United States)
Speakers: Miss Angie Rantell (United Kingdom), Mrs Frankie Bates (Canada), Prof Donna Zimmaro Bliss (United States)

12:30 - 13:30 **SESSION 7 - OPEN DISCUSSION EPOSTERS**
Abstracts 77-132
Exhibition Hall

12:30 - 14:30 **ICS BOARD OF TRUSTEES & COMMITTEE CHAIRS**
Meeting Room 1

12:30 - 13:30 **BREAK + EXHIBITION + S7 OPEN DISCUSSION EPOSTERS**

13:00 - 14:00 **PELVIC FLOOR EXERCISE CLASS**
Hall N
Chair: Prof Kari Bø (Norway)
Expert: Prof Siv Morkved (Norway)

13:30 - 14:30 **ROUND TABLE DISCUSSION 1 - ADDRESSING CONTINENCE TO KEEP PEOPLE LIVING WITH DEMENTIA AT HOME**
Hall D
Chair: Dr Joan Ostaszkiewicz (Australia)
Speakers: Dr Paul van Houten (Netherlands), Mrs Anita Francis (Australia), Mrs Heidi FA Moossdorff-Steinhauser (Netherlands)

13:30 - 14:30 **ROUND TABLE DISCUSSION 2 - INNOVATION IN RESEARCH METHODS AND MODELS**
Hall K
Chair: Dr Jennifer Kruger (New Zealand)
Speakers: Dr Heidi Wendell Brown (United States), Dr E Jean C Hay-Smith (New Zealand), Dr John Eric Jelovsek (United States)

13:30 - 14:30 **ROUND TABLE DISCUSSION 3 - PRACTICAL MANAGEMENT OF NOCTURIA IN OLDER COMMUNITY DWELLING PERSONS**
Hall G
Chair: Dr Wendy F Bower (Australia)
Speakers: Prof Karel CMM Everaert (Belgium), Prof Adrian Stuart Wagg (Canada), Dr Kathleen Frances Hunter (Canada)

14:35 - 16:05 **SESSION 8 - URODYNAMICS**
Abstracts 133-144
Hall D
Chair: Prof Enrico Finazzi Agrò (Italy)

14:35 - 16:05 **SESSION 9 - FEMALE LOWER URINARY TRACT SYMPTOMS**
Abstracts 145-156
Hall K
Chair: Dr Anna Rosamilia (Australia)

14:35 - 16:05 **SESSION 10 - GERIATRICS/GERONTOLOGY**
Abstracts 157-168
Hall G
Chair: Prof Adrian Stuart Wagg (Canada)

14:35 - 19:00 **21ST PHYSIOTHERAPY FORUM**
Hall N

16:05 - 16:30 **SESSION 11 - OPEN DISCUSSION EPOSTERS**
Abstracts 169-191
Exhibition Hall

16:05 - 16:30 **COFFEE BREAK + EXHIBITION + S11 OPEN DISCUSSION EPOSTERS**

16:30 - 18:00 **SESSION 12 - BIOMECHANICS AND APPLIED SCIENCE**
Abstracts 192-203
Hall D
Chair: Dr Jennifer Kruger (New Zealand)

16:30 - 18:00 **SESSION 13 - IMAGING**
Abstracts 204-215
Hall K
Chair: Miss Manjula Annappa (United Kingdom)

16:30 - 18:00 **SESSION 14 - PRIZE VIDEO, PROLAPSE, URETHROPLASTY, TRANSGENDER**
Abstracts 216-225
Hall G
Chair: Mr Laurence Stewart (United Kingdom)

18:15 - 19:30 **INDUSTRY SPONSORED SESSION**
Hall K

18:15 - 19:30 **INDUSTRY SPONSORED SESSION**
Hall G

FRIDAY 9TH SEPTEMBER

07:00 - 08:30 **INDUSTRY SPONSORED SESSION**
Hall K

07:00 - 08:30 **INDUSTRY SPONSORED SESSION**
Hall G

08:35 - 11:05 **WORKSHOP 20 - 'HANDS ON' WORKSHOP ON TRANSANAL IRRIGATION (TAI) IN THE MANAGEMENT OF ANORECTAL DYSFUNCTION**
Hall N
Chair: Paula Igualada Martinez (Spain),
Speakers: Katherine Pearson (United Kingdom), Carlene Igbedioh (United Kingdom), Emily Hoile (United Kingdom)

09:00 - 09:30 **STATE OF THE ART LECTURE 2 - THE DEVASTATED BLADDER**
Hall D
Chair: Prof Christopher R Chapple (United Kingdom)

09:35 - 11:05 **SESSION 15 - BEST BASIC SCIENCE**
Abstracts 226-231
Hall D
Chair: Dr Lori A Birder (United States)

09:35 - 11:05 **SESSION 16 - BEST CONSERVATIVE MANAGEMENT 1**
Abstracts 232-237
Hall K
Chairs: Dr Chantale L Dumoulin (Canada), Mrs Elisabeth Udier (Austria)

09:35 - 11:05 **SESSION 17 - NOCTURIA**
Abstracts 238-249
Hall G
Chair: Prof Philip Edward Van Kerrebroeck (Belgium)

11:05 - 11:30 **SESSION 18 - OPEN DISCUSSION EPOSTERS**
Abstracts 250-272
Exhibition Hall

11:05 - 11:30 **COFFEE BREAK + EXHIBITION + S18 OPEN DISCUSSION EPOSTERS**

11:30 - 13:00 **SESSION 19 - FEMALE STRESS URINARY INCONTINENCE**
Abstracts 273-284
Hall D
Chair: Dr Rufus Cartwright (United Kingdom)

11:30 - 13:00 **SESSION 20 - BEST CONSERVATIVE MANAGEMENT 2**
Abstracts 285-290
Hall K
Chairs: Dr Kathleen Frances Hunter (Canada), Mrs Barbara Goedl-Purrer (Austria)

11:30 - 13:00 **SESSION 21 - OVERACTIVE BLADDER**
Abstracts 291-302
Hall G
Chair: Mr Marcus John Drake (United Kingdom)

11:30 - 12:00 **SPOTLIGHT ON 2 - IUGA**
Hall N

12:30 - 13:00 **ICS AGM OPEN**
Hall N

13:00 - 14:00 **ICS AGM**
Hall N

13:00 - 14:00 **SESSION 22 - OPEN DISCUSSION EPOSTERS**
Abstracts 303-364
Exhibition Hall

13:00 - 14:00 **LUNCH + EXHIBITION + S22 OPEN DISCUSSION EPOSTERS**

14:00 - 15:00 **ROUND TABLE DISCUSSION 4 - RECONSTRUCTION OF THE DEVASTATED LOWER URINARY TRACT**
Hall D
Chair: Prof Christopher R Chapple (United Kingdom)
Speakers: Prof Hashim Hashim (United Kingdom), Mr Nadir Osman (United Kingdom), Prof Jean-Nicolas L CORNU (France)

14:00 - 15:00 **ROUND TABLE DISCUSSION 5 - CONSERVATIVE MANAGEMENT OF GENITOURINARY SYNDROME OF MENOPAUSE**
Hall K
Chair: Mrs Elisabeth Udier (Austria)
Speakers: Mrs Barbara Goedl-Purrer (Austria), Joanie Mercier (Canada), Dr Chantale L Dumoulin (Canada), Prof Cristine Homsi (Brazil)

14:00 - 15:00 **ROUND TABLE DISCUSSION 6 - MASTERCLASS IN POST-PROSTATECTOMY INCONTINENCE**
Hall G
Chair: Prof Frank Van der Aa (Belgium)
Speakers: Prof Vincent Tse (Australia), Dr Heather Lynn Moky (United States), Prof Wilhelm A. Hübner (Austria)

14:30 - 15:00 **SPOTLIGHT ON 3 - SUFU**
Hall N
Speaker: Dr Benjamin M Brucker (United States)

15:00 - 15:30 **SESSION 23 - OPEN DISCUSSION EPOSTERS**
Abstracts 365-394
Exhibition Hall

15:00 - 15:30 **COFFEE BREAK + EXHIBITION + S23 OPEN DISCUSSION EPOSTERS**

15:30 - 17:00 **SESSION 24 - BOWEL DYSFUNCTION**
Abstracts 395-406
Hall D
Chair: Mr Alexis M P Schizas (United Kingdom)

15:30 - 17:00 **SESSION 25 - TRANSGENDER HEALTH & SEXUAL DYSFUNCTION**
Abstracts 407-418
Hall K
Chair: Prof Ervin Kocjancic (United States)

15:30 - 17:00 **SESSION 26 - FISTULA, DIVERTICULUM AND WILD CARD**
Abstracts 419-428
Hall G
Chairs: Dr Elise Jaques Billings De (United States), Dr Milena M Weinstein (United States)

15:30 - 16:30 **SPOTLIGHT ON 4 - PACS**
Hall N

16:30 - 17:00 **SPOTLIGHT ON 5 - INUS**
Hall N
Chair: Prof Thomas M. Kessler (Switzerland)
Speakers: Dr Stefania Musco (Italy), Bárbara Yolanda Padilla Fernández (Spain)

17:15 - 18:15 **INDUSTRY SPONSORED SESSION**
Hall K

17:15 - 18:15 **INDUSTRY SPONSORED SESSION**
Hall G

20:00 - 23:00 **ANNUAL DINNER**

SATURDAY 10TH SEPTEMBER

08:00 - 09:30 **WORKSHOP 21 - MULTIDISCIPLINARY TEAM (MDT) APPROACH TO PELVIC FLOOR DISORDERS**
Hall N
Chair: Linda Ferrari (United Kingdom),
Speakers: Liliana Bordeianou (United States), Arun Sahai (United Kingdom), Alison Hainsworth (United Kingdom), Paula Igualada Martinez (Spain)

08:00 - 09:30 **WORKSHOP 22 - ICS CORE CURRICULUM (FREE): THE ETHICS OF WOMEN'S SEXUALITY AND THEIR PELVIC HEALTH: TWO WINGS OF THE SAME BIRD**
Hall M
Chair: Yahir Santiago-Lastra (United States),
Speakers: Maria Uloko (United States), Amir Lastra De Leon (Puerto Rico), Unwanaobong Nseyo (United States), TBD TBD (Sweden)

09:00 - 09:30 **STATE OF THE ART LECTURE 3 - THE REJUVENATED BLADDER**
Hall K
Chair: Dr Lori A Birder (United States)

09:00 - 09:30 **SPOTLIGHT ON 6 - SINGLE-INCISION MINI-SLINGS FOR STRESS URINARY INCONTINENCE IN WOMEN**
Hall G
Speaker: Dr Mohamed Abdel-fattah (United Kingdom)

09:35 - 11:05 **SESSION 27 - BEST UROGYNAECOLOGY AND FEMALE & FUNCTIONAL UROLOGY**
Abstracts 429-434
Hall K
Chair: Dr Alex Digesu (United Kingdom)

09:35 - 11:05 **SESSION 28 - PROSTATE & URETHRA**
Abstracts 435-446
Hall G
Chair: Prof Kari A O Tikkinen (Finland)

09:35 - 11:05 **SESSION 29 - CONSERVATIVE MANAGEMENT**
Abstracts 447-458
Hall N
Chairs: Paula Igualada Martinez (Spain), Katharina Meller (Austria)

09:35 - 12:30 **WORKSHOP 23 - INTEGRATED TOTAL PELVIC FLOOR ULTRASOUND IN PELVIC FLOOR DYSFUNCTION**
Hall M
Chair: Alison Hainsworth (United Kingdom),
Speakers: Giulio Santoro (Italy), Anders Mellgren (United States), Abbas Seyed Shobeiri (United States)

11:05 - 11:30 **SESSION 30 - OPEN DISCUSSION EPOSTERS**
Abstracts 459-481
Exhibition Hall

11:05 - 11:30 **COFFEE BREAK + EXHIBITION + S30 OPEN DISCUSSION EPOSTERS**

11:30 - 13:00 **SESSION 31 - CHILDREN & TRANSITIONAL CARE**
Abstracts 482-493
Hall K
Chair: Ms Ashani Couchman (Australia)

11:30 - 13:00 **SESSION 32 - SEXUAL FUNCTION AND UROGENITAL PAIN**
Abstracts 494-505
Hall G
Chair: Dr Marie-Eve Clermont (Canada)

11:30 - 13:00 **SESSION 33 - THE BEST OF THE REST IN SCIENCE**
Abstracts 506-517
Hall N
Chair: Prof Karl-Erik Andersson (United States)

13:00 - 14:00 **SESSION 34 - OPEN DISCUSSION EPOSTERS**
Abstracts 518-579
Exhibition Hall

13:00 - 14:00 **LUNCH + EXHIBITION + S34 OPEN DISCUSSION EPOSTERS**

14:00 - 15:00 **ROUND TABLE DISCUSSION 7 - REJUVENATING THE BLADDER - TREATING OXIDATIVE STRESS AND MITOCHONDRIAL DYSFUNCTION**
Hall K
Chair: Dr Lori A Birder (United States)
Speakers: Prof Karl-Erik Andersson (United States), Jennifer Southgate (United Kingdom), Pradeep Tyagi (United States), Prof Adrian Stuart Wagg (Canada)

14:00 - 15:00 **ROUND TABLE DISCUSSION 8 - ADVANCE PRACTICE MODELS OF CARE INVOLVING ALLIED HEALTH PROFESSIONALS**
Hall G
Chair: Dr Chantale L Dumoulin (Canada)
Speakers: Monika Siller (Austria), Paula Igualada Martinez (Spain), Dr Marie-Eve Clermont (Canada), Mrs Robyn L'Estelle Brennen (Australia)

14:00 - 15:00 **ROUND TABLE DISCUSSION 7 - MANAGEMENT OF COMPLICATIONS FOLLOWING MESH AUGMENTED PROLAPSE/ CONTINENCE SURGERY?**
Hall N
Chairs: Dr Anna Rosamilia (Australia), Dr Karl Tamussino (Austria)
Speakers: Prof Christl Reisenauer (Germany), Mr Roland Morley (United Kingdom), Prof Christopher F Maher (Australia)

14:00 - 14:30 **SPOTLIGHT ON 7 - MESH COMPLICATIONS**
Hall M

14:30 - 15:00 **SPOTLIGHT ON 8 - ESSIC**
Hall M

15:05 - 16:35 **SESSION 35 - CONSERVATIVE MANAGEMENT**
Abstracts 580-591
Hall K
Chair: Ms Tamara Dickinson (United States)

15:05 - 16:35 **SESSION 36 - ROBOTIC BLADDER NECK, ARTIFICIAL URINARY SPHINCTER, RECONSTRUCTIVE, PEDIATRIC AND TAPES**
Abstracts 592-601
Hall G
Chair: Mr Rizwan Hamid (United Kingdom)

15:05 - 16:35 **SPOTLIGHT ON 9 - TURKISH CONTINENCE SOCIETY**
Hall N

16:35 - 17:00 **CLOSING CEREMONY**
Hall G

THURSDAY 8TH SEPTEMBER

SESSION 1 - BEST UROLOGY

Abstracts 1-6
09:05 - 10:35, Hall D
Chairs: Prof David Castro-Diaz (Spain), Prof Helmut Madersbacher (Austria)

1 | www.ics.org/2022/abstract/1

BEST IN CATEGORY PRIZE: MALE STRESS URINARY INCONTINENCE (POST PROSTATECTOMY INCONTINENCE)

PROSPECTIVE MULTI CENTER REGISTRY FOR PATIENTS UNDERGOING SURGERY FOR MALE STRESS URINARY INCONTINENCE (SATURN): 1 YEAR FOLLOW-UP IN 500 PATIENTS

Martens F[1], Van der Aa F[2], Heesakkers J[3], Nilsen O[4], Zachoval R[5], Romero-Otero J[6], Kort de L[7], Renthergem van K[8], Martinez-Salamanca J[9], Castro-Díaz D[10], Thiruchelvam N[11], Everaert K[12], Gago J[13], Arlandis S[14], Sacco E[15], Bruwaene van S[16], Queissert F[17], Puche-Sanz I[18], Hüsch T[19], Lledó E[20], Kats J[21], Caris C[21], Wim W[21], Hamid R[22]
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HYPOTHESIS / AIMS OF STUDY

Artificial urinary sphincter (AUS) implantation has been the standard of care for male stress urinary incontinence (SUI) refractory to conservative treatment. Other devices are increasingly used. There are no clear recommendations on the patient characteristics that determine the best treatment option for male SUI. Therefore, EAU Research Foundation has initiated the prospective registry SATURN (Surgery for mAle incontinence with arTificial Urinary sphincters and slings). The reason for a registry as compared to an RCT is that for surgical treatments it is easier to attain equipoise. The objectives of the registry are to assess efficacy of male SUI surgery in daily life practice.

STUDY DESIGN, MATERIALS AND METHODS

SATURN aims to analyze 1000 patients undergoing male SUI surgery with 10 year follow-up. Inclusion is closed (n = 1000, 29 implanting centers in 9 European countries). Absence of pad use or only 1 security pad are considered “cured”. Patient related outcome measures (quality of life EQ-5D-5L, incontinence ICIQ-UI-SF) and data regarding complications are collected at baseline, around surgery, after 6 weeks (for devices that require activation), 12 weeks and yearly thereafter.

This abstract concerns data of the initial 500 patients who reached one year follow up.

RESULTS

Twenty centers included 500 patients. Mean age was 69 (SD 8.1) years. Mean age, age adjusted Charlson Comorbidity Index score and BMI didn't differ significantly per implant type.

Patients were suffering from incontinence after radical prostatectomy in 88% of whom 48% underwent a robot assisted laparoscopic prostatectomy. Radiotherapy (primary or salvage) was applied in 31% of all patients.

Preoperative urodynamic investigation was done in 67%, showing mainly pure SUI in 77% and mixed incontinence in 22%. Pure urgency incontinence and a hypocontractile detrusor were noticed in one patient. Cystoscopy preoperatively was performed in 92% of patients.

Devices implanted were: 332 AMS800, 85 Advance XP, 24 ATOMS, 21 VICTO (plus), 18 ProACT, 12 Argus, 3 ZSI375, 3 Virtue, 1 Remeex and 1 TI-LOOP. Of these patients 76% didn’t have a surgical previous treatment for SUI before the device implant that was registered into SATURN, 17% underwent one surgical previous treatment and 6% had two or more previous surgical treatments.

Pre-operative application of antibiotics, shaving or antiseptic washing at home were applied in respectively 7%, 25% and 12%. Perioperative antibiotics were administered in 98%. Shaving was done in the OR in 65% of patients.

A transurethral catheter was inserted in 79% and a suprapubic catheter in 12%. Nine percent of patients didn’t get a catheter. If a transurethral catheter was used, this was removed within 24 hours after surgery in 61%. In case of a suprapubic catheter this was done in 74%.

Complications during the first 12 postoperative weeks occurred mainly in AMS800, including mechanical failure, mispositioning of components, erosion, infection and retention. Whereas other devices reported much lower complication rates up to one year follow up. Surgical revision rates of complications are shown in Table 1.

Cure rate for all devices at one year was 63% (n = 400). Particularly in the ProACT group the increase in number of patients that became continent between 12 weeks and one year follow up was high (56%) as the device needs a period of outpatient adjustments before continence is reached. The majority of patients receiving other devices reached continence and remained so from the beginning. Eleven percent of all patients became incontinent again within one year, whereas 27% never became dry. Table 2 shows the pad weights at baseline before device implant surgery and at one year follow-up of the patients who became incontinent again or remained incontinent throughout the first year follow-up (n = 147).

INTERPRETATION OF RESULTS

To our view a registry better reflects routine clinical practice than a RCT. The drawback of SATURN is that results need to be interpreted more carefully, as SATURN is not a randomized clinical trial. Data are generally not suitable for statistical analysis or direct comparison between implants on clinical outcomes, for example results of implanted devices that are only done in a few participating centers. Moreover, not all centers included patients at an even rate, which means that a learning curves, availability of alternatives and other results are biased by center specific influences.

Despite these limitations, SATURN registry provides us an opportunity to get a better insight in daily clinical practice of these devices.

Patients were suffering from prostatectomy for prostate cancer in 88%. Radiotherapy (primary or salvage) was applied in 31% of all patients. However, only in 5% radiotherapy was the main cause of stress urinary incontinence.

Preoperatively, we do not know how many patients were withheld from surgery based on urodynamics as patients were included if they went for surgery. Therefore from this registry , we cannot deduct whether urodynamic outcome defines the type of chosen device. Moreover, SATURN doesn’t give us the final answer about the necessity of performing urodynamics in males with SUI opting for surgery.

Complication rates need to be interpreted carefully as specific asked complications in SATURN refer more to AMS800 and other complications might be underreported. The high amount of AMS800 as compared to other devices may cause bias. Selection of device type is not randomized, but based on patient and/or surgeon preference. For example, in 300 patients the result of the pre-operative 24-hour pad test performed was higher for AMS800 as compared to the other alternatives. So, more severe incontinence is treated with a more voluminous device, which is consequently most likely more

prone to complications. If a complication occurred, it was more likely to be approached surgically in patients with an AMS800 (Table 1).

As mentioned, preoperative 24-hours pad weight test was significantly higher for the AMS800 compared to other devices. However, if patients remained incontinent or noticed incontinence again after a postoperative period of continence, the remaining mean pad weight was relatively low (Table 2).

CONCLUDING MESSAGE

The first results of the SATURN registry in male stress urinary incontinence provide an impression of daily clinical practice and performance of implant devices. Longer follow up in a higher number of patients are into progress as the registry is still running.

FIGURE 1

	Advance XP	Other slings	ProACT	AMS800	Other artificial urinary sphincter
< 12 weeks	0%	25%	0%	51%	N/A
< 1 year	33%	33%	0%	52%	N/A

Percentage of complications that needs surgical revision.

N/A Not applicable as no complications were noticed.

Table 1

FIGURE 2

Pad weight test Gram Mean (95% CI)	Advance XP	Other slings	ProACT	AMS800	Other artificial urinary sphincter
Baseline Whole group (n=300)	176 (141 - 212)	393 (266 - 519)	186 (96 - 277)	698 (613 - 783)	738 (559 - 917)
Baseline Patients who remained or became incontinent (n=61)	313 (93 - 719)	582 (286 - 878)	408 (-24 - 841)	795 (581 - 1009)	636 (487 - 784)
1 year follow up Patients who remained or became incontinent (n=61)	111 (-196 - 418)	204 (35 - 372)	50 (-129 - 229)	56 (16 - 96)	188 (124 - 252)
1 year follow up Improvement in patients who remained or became incontinent (n=61)	64%	65%	88%	93%	70%

Pad weight tests results of patients that became or remained incontinent during the first year of follow up after surgery.

Table 2

Funding Funded with a restricted grant from Boston Scientific Group plc. **Clinical Trial** No **Subjects** Human **Ethics Committee Ethics Committee** of every participating centre as mentioned in the references **Helsinki** Yes **Informed Consent** Yes

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SINGLE INTRASPHINCTERIC INJECTION OF AUTOLOGOUS ADIPOSE-DERIVED STEM CELLS TO TREAT STRESS URINARY INCONTINENCE AFTER RADICAL PROSTATECTOMY: A PILOT STUDY

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HYPOTHESIS / AIMS OF STUDY
Stress urinary incontinence (SUI) post radical prostatectomy (RP) is reported in up to one-third of patients. Depending on the degree of leakage and associated bother, many patients will seek definitive surgical management. Options for surgical management generally include a male sling (MS) or artificial urinary sphincter(AUS)[1]. In a systemic review including analysis of data of 4022 patients, the efficacy (0-1 safety pads) was on average 65.7% for AUS and 48.2% for MS. The overall complication rate of the 2 techniques was more than 10% [2]. Stem cell therapy is a promising treatment for many urological conditions. Intrasphincteric injections of Adipose-derived stem cells (ADSCs) may have a role in treating SUI post RP. The objective of this study was to assess the safety and efficacy of intrasphincteric ADSC injections to treat SUI post RP

STUDY DESIGN, MATERIALS AND METHODS
Between January 2019 and December 2021, we performed a prospective trial that enrolled male patients with SUI post RP. A total of 10 patients were randomized into 1 of 2 groups: treatment group (received a single injection into the urethral rhabdosphincter 10ml of ADSC solution), or placebo group (single injection into the urethral rhabdosphincter of 10ml of normal saline). ADSCs were injected using a template showing 8 injections (1.25 ml/ injection) throughout the rhabdosphincter, at 12,6,3,9,2,10,5, and 7 o'clock positions. Injections were delivered at a depth of 5 mm with a rigid scope under general anesthesia using a bladder injection needle 22Gauge (tip length 4mm, working length 35cm). ADSCs solution was reconstituted in 5 ml of sterile saline. Liposuction was performed from the treatment group to isolate ADSCs. Briefly, the lipoaspirate was digested with collagenase, at 37 ˚C. Then it was washed 3 times with cold phosphate-buffered saline (PBS). The Stromal vascular fraction was plated into a culture flask. The medium was replaced every 3 days and cultured in expansion. The cells are used after confluence in the first passage.

Inclusion criteria were: patients with an SUI for > 18 months after surgery, localized low to intermediate-risk prostate cancer before surgery, have no biochemical recurrence at study enrollment, the patient had no adjuvant chemotherapy or radiotherapy, all patients had pelvic floor training for > 6 months. All patients had office cystoscopy before entering the study to exclude bladder neck contracture or urethral stenosis.

Exclusion criteria were: patients taking anticholinergic medications for overactive bladder symptoms or taking a diuretic for heart failure, patients with urinary tract infection, patients with any neurologic disease that may affect bladder function.

Eligible participants were randomly assigned to one of the 2 groups by a computer-generated lottery. Both the urologists and the patients were blinded to the treatment assignments.

The amount of incontinence was evaluated with a 24-h pad weight test. This test was noted in each evaluation period (baseline, 1, 3, 6, 12, and 18 months). Patients were allowed to use as many pads as they deemed necessary and were provided sealable bags labeled day 1, 2, and 3. They were asked to store their pads in the provided sealed bag in the refrigerator to minimize evaporation. The patient brings all pads to each clinical visit. Each soiled pad was weighed using a calibrated scale. The mean of 24-hour pad weight noted during the 3 days in each patient was calculated at baseline and during each clinical visit. Quality-of-life survey (International Consultation on Incontinence Questionnaire- Short Form (ICIQ-UI SF) was collected before therapy and during the follow-up visit.

Incontinence has been categorized into three categories based on the gram (g) weight of urinary loss–mild SUI, or <100g/24 hours, moderate SUI, or 100–400g/24 hours, and high-grade, or >400g/24 hours to help classify the degree of incontinence [3].

The primary outcomes of our study were the change from baseline in the mean of the 24-h pad weight test. The secondary outcomes were the change from baseline in the mean of ICIQ-UI SF score. Safety assessments included any reported adverse events.

The study was approved by our Institutional Review Board (N.05/2019). This trial was registered in the UMIN clinical trial registry (UMIN000047336). Written informed consent was taken by all the patients to participate in the study.

RESULTS
The mean follow-up period was 22 months in the treatment group and 23 months in the placebo group. A total of 10 patients were included in the study. Most of the patients in both groups had ages between 60 and 70 years, had SUI 20 to 24 months post-surgery (Table 1).

A significant reduction of the mean 24-h pad weight test in g was noted in the treatment group. In this group, the mean 24-h pad weight decreased from 320 g (moderate SUI) at baseline to 70 g (mild SUI). In the placebo group, the mean 24-h pad weight test in g was not significantly changed (remain in the moderate SUI category). Significant improvements from baseline were noted for the mean ICIQ-UI SF score in the treatment group. In this group, the mean ICIQ-UI SF score decreases significantly from 19 at baseline to 8 at the end of therapy. In the placebo group, the mean ICIQ-UI SF score remains the same till the end of the study. The outcomes of the study are summarized in table 2.

There were no serious adverse events reported in the treatment or placebo group

INTERPRETATION OF RESULTS
Our study report that intrasphincteric ADSCs could improve SUI progressively during the 18 months follow-up period, as determined by a decrease in 24-h pad weight test, and improved quality of life evaluated by a validated quality of life questionnaire.

We used the ICIQ-SF for the quality-of-life analysis and were able to prove quality-of-life improvement during the follow-up period in the treatment group

The main limitation of our study is the small sample size and relatively short-term follow-up

CONCLUDING MESSAGE
Findings from this study provide preliminary evidence in support of the safety and potential clinical utility of intrasphincteric ADSCs injections for the treatment of SUI post RP

FIGURE 1

Table 1. Patient demographic and other baseline characteristics.

	Treatment	Placebo
Age group, n		
[40-50[years	1	0
[50-60[years	1	1
[60-70] years	3	4
Duration of SUI post-surgery, n		
18-20 months	1	0
20-24 months	3	4
> 24 months	1	1
Duration of pelvic floor training offered, n		
6-9 months	1	1
9-12 months	3	3
>12 months	1	1
Mean duration of follow up (months)	22	23

SUI: stress urinary incontinence

Table 1. Patient demographic and other baseline characteristics

FIGURE 2

Table2. The difference from Baseline in treatment and Placebo groups for results of mean of 24-h pad weight test and ICIQ-UI SF score

	Treatment Group						Placebo Group					
	Baseline	1 m	3 m	6 m	12 m	18 m	Baseline	1 m	3 m	6 m	12 m	18 m
Mean of the 24-h pad weight test in grams	320	325	295	217	125	70	350	366	375	389	395	373
ICIQ-SF score	19	19	19	14	11	8	20	19	18	19	20	18

ICIQ-UI SF: International Consultation on Incontinence Questionnaire- Short Form; m: months

Table 2. The difference from Baseline in treatment and Placebo groups for results of mean of 24-h pad weight test and ICIQ-UI SF score

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Funding None **Clinical Trial** Yes **Registration Number** UMIN **Clinical Trial**s Registry (UMIN-CTR); (UMIN000047336) **RCT** Yes **Subjects** Human **Ethics Committee** Ethical committee of Al Zahraa Hospital, Beirut, Lebanon **Helsinki** Yes **Informed Consent** Yes

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BEST IN CATEGORY PRIZE: URODYNAMICS

THE EFFECT OF SINGLE-DOSE TADALAFIL ON URETHRAL PRESSURE AND VOIDING PARAMETERS: A DOUBLE-BLIND, RANDOMIZED, PLACEBO-CONTROLLED, CROSSOVER STUDY IN HEALTHY WOMEN

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HYPOTHESIS / AIMS OF STUDY

Available data suggest that the extensive vascular plexus surrounding the female urethra has an important impact on urethral pressure and thereby on urethral continence mechanism. A potential treatment strategy for urinary incontinence associated with decreased urethral pressure could, therefore, be a pharmacologically induced expansion of this vascular plexus caused by local increase in arterial blood flow. Theoretically, vasodilation mediated by phosphodiesterase-type 5 (PDE5) inhibitor action could facilitate such expansion of the urethral vasculature. PDE5 expression has been reported in human female reproductive tissues, as well as in male genital and bladder tissue [1], and findings from a preclinical study in female rats indicate that PDE inhibition may increase baseline urethral pressure [2]. However, PDE5 inhibitors may also induce relaxation of urethral smooth muscle and the external urethral sphincter (EUS) thereby facilitating micturition. Accordingly, Datta et al. evaluated the PDE5 inhibitor sildenafil (50 mg twice daily for four weeks) in women with bladder outflow obstruction, but did not find statistically significant differences in voiding parameters compared to placebo [3]. Thus, the effect of PDE5 inhibition on the female urinary tract remains unclear. This study aimed at evaluating the effect of the long-acting PDE5 inhibitor tadalafil on opening urethral pressure (OUP) and voiding parameters in healthy women.

STUDY DESIGN, MATERIALS AND METHODS

Healthy women were recruited for this double-blind, randomized, placebo-controlled, crossover study Participants were randomized to receive either single dose tadalafil (40 mg) or placebo at the first visit and then crossed over to the opposite treatment at the second visit. The visits were separated by a washout period of at least six days to avoid carry-over effects. Two hours after administration of study medication (at the reported time of peak plasma drug concentration), urethral opening pressure during resting and squeezing condition of the pelvic floor was measured using urethral pressure reflectometry. Immediately after urethral pressure measurements, uroflowmetry was performed with a prefilled bladder volume of 300 ml natrium chloride. We followed up on adverse events at the end of each clinic visit and by phone six days after the last visit. Based on an expected within-subject standard deviation of 5.4 cmH2O, we needed 24 women to complete the study to have a power of 99% to detect a 10 cmH2O difference in OUP between tadalafil and placebo with a significance level of 5%. We performed multiple regression analyses with subject, period, and treatment as covariates using SAS statistical software (v.9.4.6).

RESULTS

Twenty-four women were included in the study, and there were no drop-outs. Median age was 24.5 (range 20–43) years, and median body mass index 22.7 (range 19–26.9) kg/m2. Compared to placebo values, single dose 40 mg tadalafil caused a significant fall in resting OUP of 6.8 cmH20 (95% confidence interval [CI] 1.9–11.8, p = 0.009) and of 8.8 cmH20 during squeeze (95% CI 3.1–14.6, p = 0.005) (figure 1). Tadalafil did not cause any statistically significant change in voiding parameters compared to placebo (average flow rate: −0.8 ml/s [95% CI −2.0–0.4, p = 0.2]; maximum flow rate −1.7 ml/s [95% CI −4.8–1.5, p = 0.3]; voided volume −11.4 ml [−40.7–18.0, p = 0.4]) (figure 2). We observed a statistically significant period effect for average flow rate (p = 0.02) and maximum flow rate (p = 0.02) with increased flow rates at the second visit compared to the first. Of a total of 41 adverse events, 36 adverse events were related to tadalafil treatment and five adverse events were related to placebo treatment. Headache was the most common adverse event (tadalafil: 15; placebo: 3). Most adverse events were mild in severity, and no serious adverse events occurred.

INTERPRETATION OF RESULTS

To our knowledge this is the first randomized, placebo-controlled study to assess the effect of the PDE5 inhibitor tadalafil on urodynamic and urethral pressure parameters in healthy women. Single dose tadalafil decreased OUP during both resting and squeezing conditions. These findings suggest that tadalafil induce relaxation of urethral smooth muscle and the EUS (by means of the nitric oxide pathway). Furthermore, our data indicate that there is little or negligible PDE5 activity in the urethral vascular plexus, or that the net result of the simultaneous processes (in vascular smooth muscle and urethral smooth muscle and the EUS) is a mean decrease in urethral pressure, both during rest and voluntary contraction. In contrast, we found no statistically significant effect of tadalafil on voiding parameters. This might be explained by the fact that healthy women already have free flow. The observed period effect with increased flow rates at second visit is probably due to participants being more relaxed at the second uroflow measurement.

CONCLUDING MESSAGE

Compared to placebo, single-dose tadalafil decreased OUP during both resting and squeezing conditions in healthy women. No significant difference in voiding parameters were demonstrated. The observed fall in urethral pressure suggests a relaxing effect of PDE5 inhibition on EUS and urethral smooth muscle.

FIGURE 1

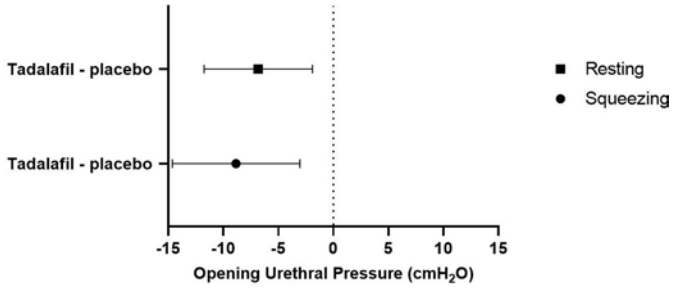

Figure 1. Mean opening urethral pressure at tmax corrected for the placebo value (mean OUP, cmH2O [95%CI]).

FIGURE 2

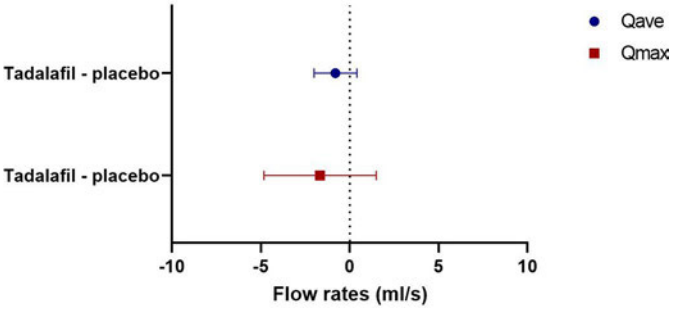

Figure 2. Mean flow rates (average flow rate [Qave] and maximum flow rate [Qmax]) corrected for the placebo value (ml/s [95%CI]).

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Subjects Human **Ethics Committee** Regional **Ethics Committee** of The Capital Region of Denmark **Helsinki** Yes **Informed Consent** Yes

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PREVALENCE OF SHORT-TERM FALSE POSITIVES AFTER SACRAL NEUROMODULATION THERAPY AND THE POTENTIAL ROLE OF A PLACEBO EFFECT: A PROSPECTIVE DESCRIPTIVE SINGLE CENTRE STUDY.

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HYPOTHESIS / AIMS OF STUDY
The aim of this study was three-fold: I. To describe the implantation ratio, the true success ratio, the false positive ratio and the subjective success ratio at 12 months follow-up in patients who received sacral neuromodulation (SNM) therapy. II. To explore differences in outcomes between true (TP) and false positive cases (FP). III. To examine the effect of SNM on the 24 hours diuresis and explore the potential role of diuresis as a surrogate variable to detect a potential placebo effect.

STUDY DESIGN, MATERIALS AND METHODS
Between March 2018 and December 2021 a multidisciplinary single centre prospective study was held. Patients from the Urology and Colorectal surgery department with therapy resistant pelvic floor disorders who were planned for a SNM 2-staged tined lead procedure with the Interstim II ® were enrolled. According to the current practice, the decision to proceed from Stage I (the first stage tined lead procedure) to Stage II (the definitive implantation), i.e. positive advice, was made at the control visit during the test period by the treating physician. The duration of the testphase varied from 2 to 4 weeks depending on the indication of therapy.

The evaluation was accomplished based on a quick, rather intuitive screening for changes in bladder and bowel diary parameters and on the anamnesis of patient satisfaction. As a quality control on the physician's advice for implant, a mathematical re-analysis of bladder and bowel diaries was performed after the control visit by the researcher.

Both bladder and bowel diaries were collected at baseline at during the testphase. Also symptom specific patient reported outcome measures (PROMS) (i.e. the Urological symptom (US) satisfaction score and the Bowel Symptom (BS) satisfaction score, both rated from 0 to 100% satisfaction) were completed. Objective success was defined as ≥ 50% improvement in for urological patients and as ≥ 50% improvement in one or more of the bothersome bowel symptoms for the colorectal surgery patients. Subjective success was assessed by the Patient Global Impression of Change score (PGIC) during the testphase and at 1, 6 and 12 months follow-up after stage II. A PGIC score of ≥ 5/7 (from 5 'moderately better and a slight but noticeable change' to 7 'A great deal better, and a considerable improvement that has made all the difference') was considered as having subjective success.

Independently from the advice of the physician, the true success ratio, i.e. having both objective success and subjective success during the testphase, was determined by the researcher. False positives were defined as the patients who did not show sustained therapeutic subjective success, i.e. a PGIC score < 5, despite having shown true success during the test phase. True positives were defined as patients who had true success during the testphase and did show sustained subjective success (PGIC ≥ 5) 1 month after stage II. Outcomes were compared between FP and TP. Descriptive statistics using SPSS version 25.0 were performed.

RESULTS
I. The implantation, true success and FP ratios were 76/93 (82%), 71/93 (76%) and 16% (11/67) %, respectively. Implantation ratios for the Urology department (53/65) and the Colorectal surgery department (23/28) were both 82%. After re-assessment 68 patients were correctly implanted, 14 cases were correctly refused, 8 cases were incorrectly implanted, and 3 cases were incorrectly refused. Four of the 8 incorrectly implanted cases did not show objective success on urological symptoms, but they did show objective success on bowel symptoms. The subjective success ratio for the total group at twelve months follow-up was 35/40 (87,5%).

II. In the TP group both urological symptoms and bowel symptoms improved significantly during the testphase ($p < 0{,}001$), whereas in the FP group only the number of voids and the number of urgency urinary incontinence symptoms significantly improved. Satisfaction scores for US and BS significantly improved in the TP group ($p < 0{,}001$), whereas only the BS satisfactions score improved in the FP group. TP and FP did not differ significantly in baseline outcomes, neither on diary variables nor on satisfaction scores.

III. The 24hour fluid intake, 24h diuresis and the adjusted diuresis for fluid intake did not change significantly during the testphase, neither in the TP, nor in the FP group.

INTERPRETATION OF RESULTS
The implantation ratios in this trial are similar to previously reported results. (1,2)

If a more strict definition (only implantation of patients with true success) would have been applied, only 76% would have been implanted. However, this would have implied that a group of patients, a part of the 'incorrectly implanted cases' would not have received an implant although showing subjective success and symptom improvement on the other pelvic floor domain than their main problem. This observation advocates for a more holistic approach to the assessment of symptom improvement and to the definition of objective success.

Using strict criteria for implantation cannot avoid the incidence of false positive cases after SNM on the short term. Therefore it was hypothesized that the immediate decline in subjective success after definitive implantation might be attributable to a certain placebo effect. Since baseline diary values or PROM scores do not differ between FP and TP false positives, a possible false positive case cannot be predicted unless a surrogate variable for the placebo effect exists. Derived from the finding that placebo is amongst others dopamine driven and that dopamine can increase natriuresis (3), an increased diuresis during the testphase in false positive cases can be expected, presuming that FP are attributable to a placebo effect. This hypothesis however, could not be confirmed from our findings.

CONCLUDING MESSAGE
SNM has a positive therapeutic effect on both urological symptoms and bowel symptoms in patients with sustained therapeutic subjective success. In the future a more holistic approach should be applied in the baseline history taking and during therapy assessment to optimize care. The number of FP one month after full implant is low but should not be neglected. The hypothesis that diuresis could be used as a predictor for false positives, in the light of a potential placebo effect, was not supported. More research for predictive factors notifying the decision-making physician for a potential placebo effect is needed.

FIGURE 1

Table 1. Positive advice for implant according to true success and the evolution of subjective success over time.

True success # Objective and subjective success during the test phase		Positive advice for implant according to the physician: No	Yes	Total	Subjective success at 6 months: No	Yes	Missing	Total	Subjective success at 12 months: No	Yes	Missing	Total
No	Subjective success at one month	14	8	22								
	No	NA	2 (25%) *		1		1		1		1	
	Yes	NA	6 (75%) **		1	3	2			4	2	
Yes	Subjective success at one month	3 ***	68	71	2	3	3		1	4	3	
	No	NA	11 (16%) (FP)		4	4	3		1	5	5	
	Yes	NA	57 (84%) (TP)		4	25	28		4	26	27	
Total		17 (18%)	76 (82%)	93	10	32 (76%)	34	42	6	35 (87,5%)	36	40

FP: False positives, TP: True positives , NA: Not applicable
* 2 patients (1 urological and 1 bowel patient) showed objective success, but no subjective success during the testphase.
** 4/6 patients (2 urological, 2 bowel patients) did not show objective success on urological symptoms but showing > 50% improvement in bowel symptoms and vice versa. 2/6 (both urological patients) showed objective success on urological symptoms, but did not have subjective success during the testphase.
*** 3 patient showing true success, but refused out of practical reasons.

Table 1. Positive advice for implant according to true success and the evolution of subjective success over time.

FIGURE 2

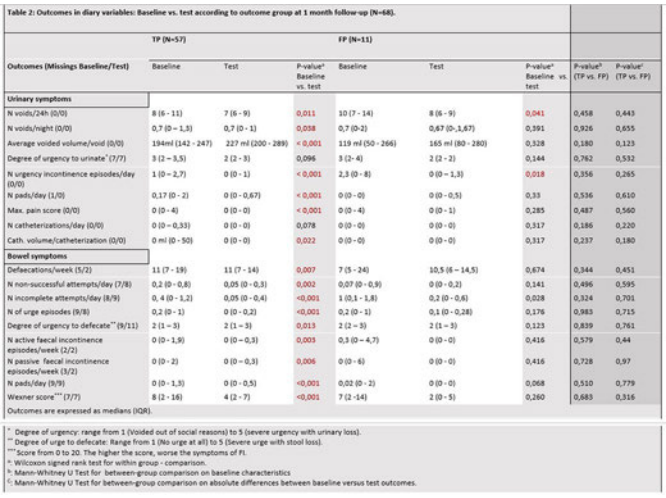

Table 2: Outcomes in diary variables: Baseline vs. test according to outcome group at 1 month follow-up (N=68).

	TP (N=57)			FP (N=11)				
Outcomes (Missings Baseline/Test)	Baseline	Test	P-value[a] Baseline vs. test	Baseline	Test	P-value[a] Baseline vs. test	P-value[b] (TP vs. FP)	P-value[c] (TP vs. FP)
Urinary symptoms								
N voids/24h (0/0)	8 (6 - 11)	7 (6 - 9)	0,011	10 (7 - 14)	8 (6 - 9)	0,041	0,458	0,443
N voids/night (0/0)	0,7 (0 – 1,3)	0,7 (0 - 1)	0,038	0,7 (0-2)	0,67 (0-1,67)	0,391	0,926	0,655
Average voided volume/void (0/0)	194ml (142 - 247)	227 ml (200 - 289)	< 0,001	119 ml (50 - 266)	165 ml (80 - 280)	0,328	0,180	0,123
Degree of urgency to urinate[*] (7/7)	3 (2 – 3,5)	2 (2 - 3)	0,096	3 (2- 4)	2 (2 - 2)	0,144	0,762	0,532
N urgency incontinence episodes/day (0/0)	1 (0 – 2,7)	0 (0 - 1)	< 0,001	2,3 (0 - 8)	0 (0 – 1,3)	0,018	0,356	0,265
N pads/day (1/0)	0,17 (0 - 2)	0 (0 - 0,67)	< 0,001	0 (0 - 0)	0 (0 - 0,5)	0,33	0,536	0,610
Max. pain score (0/0)	0 (0 - 4)	0 (0 - 0)	< 0,001	0 (0 - 4)	0 (0 - 1)	0,285	0,487	0,560
N catheterizations/day (0/0)	0 (0 – 0,33)	0 (0 - 0)	0,078	0 (0 - 0)	0 (0 - 0)	0,317	0,186	0,220
Cath. volume/catheterization (0/0)	0 ml (0 - 50)	0 (0 - 0)	0,022	0 (0 - 0)	0 (0 - 0)	0,317	0,237	0,180
Bowel symptoms								
Defaecations/week (5/2)	11 (7 - 19)	11 (7 - 14)	0,007	7 (5 - 24)	10,5 (6 – 14,5)	0,674	0,344	0,451
N non-successful attempts/day (7/8)	0,2 (0 - 0,8)	0,05 (0 - 0,3)	0,002	0,07 (0 - 0,9)	0 (0 - 0,2)	0,141	0,496	0,595
N incomplete attempts/day (8/9)	0, 4 (0 - 1,2)	0,05 (0 - 0,4)	<0,001	1 (0,1 - 1,8)	0,2 (0 - 0,6)	0,028	0,324	0,701
N of urge episodes (9/8)	0,2 (0 - 1)	0 (0 - 0,2)	<0,001	0,2 (0 - 1)	0,1 (0 - 0,28)	0,176	0,983	0,715
Degree of urgency to defecate[**] (9/11)	2 (1 – 3)	2 (1 – 3)	0,013	2 (2 – 3)	2 (1 – 3)	0,123	0,839	0,761
N active faecal incontinence episodes/week (2/2)	0 (0 - 1,9)	0 (0 – 0,3)	0,003	0,3 (0 – 4,7)	0 (0 - 0)	0,416	0,579	0,44
N passive faecal incontinence episodes/week (3/2)	0 (0 - 2)	0 (0 – 0,3)	0,006	0 (0 - 6)	0 (0 - 0)	0,416	0,728	0,97
N pads/day (9/9)	0 (0 - 1,3)	0 (0 - 0,5)	<0,001	0,02 (0 - 2)	0 (0 - 0)	0,068	0,510	0,779
Wexner score[***] (7/7)	8 (2 - 16)	4 (2 - 7)	<0,001	7 (2 -14)	2 (0 - 5)	0,260	0,683	0,316

Outcomes are expressed as medians (IQR).

[*] Degree of urgency: range from 1 (Voided out of social reasons) to 5 (severe urgency with urinary loss).
[**] Degree of urge to defecate: Range from 1 (No urge at all) to 5 (Severe urge with stool loss).
[***] Score from 0 to 20. The higher the score, worse the symptoms of FI.
[a]: Wilcoxon signed rank test for within group - comparison.
[b]: Mann-Whitney U Test for between-group comparison on baseline characteristics
[c]: Mann-Whitney U Test for between-group comparison on absolute differences between baseline versus test outcomes.

Table 2: Outcomes in diary variables: Baseline vs. test according to outcome group at 1 month follow-up (N = 68).

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Funding Medtronic **Clinical Trial** Yes **Registration Number** Clinical trial. gov: EC2018/0244 **RCT** No **Subjects** Human **Ethics Committee Ethics Committee** of the Ghent University hospital **Helsinki** Yes **Informed Consent** Yes

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BEST IN CATEGORY PRIZE: URETHRA MALE / FEMALE

FIRST REPORT ON PERFUSION FLOW ON UROGENITAL EPITHELIAL CELLS FOR URETHRAL TISSUE ENGINEERING PURPOSES

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HYPOTHESIS / AIMS OF STUDY

For urethral reconstruction in urethral stricture or hypospadias, over 300 surgical techniques are known. A wide variety of grafts, including autologous skin and oral mucosa, have been used. However, these substitutes are inferior to native urethral tissue and can lead to (recurrent) stricture and/or graft failure.

Tissue engineering may be a solution for restoration of the urethra in complex stricture or hypospadias cases. This project will focus on the luminal epithelial cells. Previous research has revealed that urethra epithelium is different from bladder epithelium [1]. However, as urethral biopsies to extract urethral cells may lead to stricture formation, bladder cells may be an alternative in urethral tissue engineering.

Epithelium in the urethra is exposed to fluid flow, unlike bladder epithelium, were fluid is more constantly present. Biomechanical cues influence the behavior and differentiation of cells, and our hypothesis is that fluidic flow induced shear stress may stir cells towards different organization. To investigate whether bladder epithelial cells may be used as a substitute for more difficult to obtain urethra epithelial cells for tissue engineering purposes, we compared the cell response to fluidic flow induced shear stress, comparing urethral epithelial cells with bladder epithelial cells.

STUDY DESIGN, MATERIALS AND METHODS

Primary cells from both bladder and urethra were isolated from male pigs [2]. Microfluidic devices were used to study effects of shear stress. Pump driven systems (ibidi GmbH, Gräfelfing, Germany) were compared with the F300R microfluidic device (Finnadvance, Oulo, Finland) on the rocking system (WAVE) (FinnAdvance, Oulo, Finland). The bladder and urethra derived epithelial cells were exposed for 72 hours to flow, causing fluidic shear stress (FSS) of $\tau max =$ 10.0 dyn/cm2 and $\tau max =$ 20.0 dyn/cm2 in a ibidi flow system.

The F300R microfluidic device was placed on the platform of the rocking machine with the following settings: set timer: 0,00 min; set hold time: 0,29 min; set speed: 30 rpm; and set angle: -18,43º / 18,43º. These settings together with a volume of 240 µL for each channel, results in a FSS of 0,049 dyne/cm2, which is the maximum FSS that the set-up consisting of the F300R microfluidic device and the rocker can generate.

For both systems, cell elongation, cell alignment and actin fiber alignment were analyzed.

RESULTS

In an ibidi flow system, both urethral cells as well as bladder cells aligned to FSS. No significant difference was observed between urethral and bladder cells in cell elongation and orientation.

In a FinnAdvance microfluidic system, we could not achieve similar high FSS as in the ibidi systems. Nevertheless we saw that even low FSS improved the formation of a tight monolayer. However no cell alignment in the direction of the flow was observed.

INTERPRETATION OF RESULTS

Both bladder and urethral epithelial cells similarly adapted to FSS: they both elongate and align in the direction of the flow. So in this respect, both cell types could potentially be used in tissue engineering for urethral reconstruction. This is important information, because the harvesting of bladder epithelium is much easier than of urethra epithelium: bladder epithelial cells can be isolated from urine or bladder washout or may be obtained by biopsy, in contrast to urethral epithelial cells. Next steps in our approach would be creating intermitted flow to mimic natural voiding in patients as well as comparing other sources of cells (like oral keratinocytes) to these urogenital epithelial cells.

CONCLUDING MESSAGE

Although from different origin, epithelial cells derived from the urethra and bladder behave similarly in vitro under fluid induced shear stress, mimicking urethral fluid flow. Bladder cells, which are more easy to obtain than urethral epithelial cells, may be used as a cell source in tissue engineering for urethral reconstruction.

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Funding None **Clinical Trial** No **Subjects** None

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BEST IN CATEGORY PRIZE: OVERACTIVE BLADDER

EFFICACY AND SAFETY OF A NOVEL GENE THERAPY (URO-902; PVAX/HSLO) IN FEMALE PATIENTS WITH OVERACTIVE BLADDER SYNDROME AND URGENCY URINARY INCONTINENCE: RESULTS FROM A PHASE 2A TRIAL

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1. Oakland University William Beaumont School of Medicine; Beaumont Health System, 2. Stanford University School of Medicine, 3. Urologic Associates of Southern Arizona, 4. Chesapeake Urology, 5. Urovant Sciences

HYPOTHESIS / AIMS OF STUDY

There is a need for new agents that can effectively and safely treat overactive bladder (OAB) syndrome when oral pharmacologic therapy is insufficient. URO-902 is an investigational gene therapy for OAB and consists of a plasmid vector that expresses the α subunit of the large-conductance Ca2+-activated K+ channel in the detrusor to reduce bladder hypercontractility. A previous phase 1b trial in patients with OAB showed promising safety and efficacy results for URO-902 [1]. We report interim results from a phase 2a trial assessing the safety and efficacy of URO 902 in OAB.

STUDY DESIGN, MATERIALS AND METHODS

This was a prespecified, 12-week interim analysis of a 48-week multicenter, randomized, double-blind, placebo-controlled, dose-escalation study (NCT04211831). The study protocol was approved by institutional review boards at each study center, and all participants provided written informed consent. Women aged 40–79 years with OAB and urgency urinary incontinence (UUI) who were not adequately managed with oral OAB medications were randomly assigned to receive single-dose URO-902 24 mg, URO-902 48 mg, or placebo administered by intradetrusor injection via cystoscopy under local anesthesia. Safety was assessed by adverse events (AEs) and postvoid residual (PVR) urine. Exploratory endpoints included change from baseline to week 12 in mean daily micturitions, urgency episodes, UUI episodes, and quality of life (QoL) measures. This trial had no formal statistical primary endpoint hypothesis and was not powered to detect statistically significant differences between groups in efficacy measures; 23 evaluable patients in each treatment would provide approximately 55% power to detect a between-group difference of 1.8 episodes in the mean change from baseline to week 12 in the number of UUI episodes per day between the URO-902 and placebo treatment groups.

RESULTS

Of the 80 patients randomized, 68 completed week 12, and 74 were included in the intent-to-treat exposed (ITT-E) population. Mean (SD) age was 64.7 (7.1) years, and 13.5% had prior treatment with onabotulinumtoxinA. At week 12, URO-902 24 and 48 mg were associated with clinically relevant improvement vs placebo in mean daily micturitions (LS mean change from baseline, –2.5 and –3.0 vs –1.0, respectively), urgency episodes (–2.4 and –3.4 vs –1.2), UUI episodes (–2.4 and –2.6 vs –2.3), OAB questionnaire symptom bother score (–24.1 and –25.3 vs –11.2), and proportion of patient global impression of change responders (40.9% and 57.7% vs 30.8%) (Table). Treatment-emergent AEs occurred in 45.5% of patients receiving URO-902 24 mg, 46.2% receiving 48 mg, and 50.0% receiving placebo. The most commonly occurring AE (24 mg/48 mg/placebo) was urinary tract infection (0%/15.4%/3.8%). One patient (48-mg arm) had asymptomatic elevated PVR urine volume at week 2 (resolved spontaneously, did not require catheterization).

INTERPRETATION OF RESULTS

In this phase 2a trial of women with OAB and UUI, a single dose of URO-902 24 or 48 mg was associated with clinically relevant improvement in efficacy and QoL endpoints and was safe and well tolerated.

CONCLUDING MESSAGE

The safety and efficacy demonstrated in this interim analysis of a phase 2a trial suggest that expressing the α subunit of the large-conductance Ca2+-activated K+ channel in the detrusor is a promising potential therapy for OAB and warrants further investigation.

FIGURE 1

Table. Change from Baseline at Week 12 in Efficacy and Quality of Life Endpoints (ITT-E Population*)

Outcome	URO-902 24 mg (N=22)	URO-902 48 mg (N=26)	Placebo (N=26)
Micturitions			
Mean (SD) baseline	9.8 (1.6)	10.8 (2.7)	11.5 (2.7)
LS mean (95% CI) change from baseline	−2.5 (−3.5 to −1.4)	−3.0 (−4.0 to −1.9)	−1.0 (−2.0 to 0.1)
LS mean difference (95% CI) vs placebo	−1.5 (−2.9 to −0.2)	−2.0 (−3.3 to −0.6)	–
Nominal *P* value vs placebo	0.0297	0.0044	–
Urgency episodes			
Mean (SD) baseline	7.4 (2.8)	8.4 (3.1)	9.3 (3.4)
LS mean (95% CI) change from baseline	−2.4 (−3.9 to −0.8)	−3.4 (−4.9 to −1.9)	−1.2 (−2.7 to 0.3)
LS mean difference (95% CI) vs placebo	−1.2 (−3.1 to 0.7)	−2.2 (−4.0 to −0.4)	–
Nominal *P* value vs placebo	0.2060	0.0176	–
UUI episodes			
Mean (SD) baseline	5.3 (3.3)	4.3 (2.4)	5.9 (3.9)
LS mean (95% CI) change from baseline	−2.4 (−3.4 to −1.4)	− 2.6 (−3.6 to −1.6)	−2.3 (−3.3 to −1.2)
LS mean difference (95% CI) vs placebo	−0.1 (−1.4 to 1.2)	−0.4 (−1.7 to 0.9)	–
Nominal *P* value vs placebo	0.8564	0.5690	–
OAB-q symptom bother score			
Mean (SD) baseline	67.6 (20.9)	72.4 (16.6)	67.5 (22.9)
LS mean (95% CI) change from baseline	−24.1 (−34.5 to −13.7)	−25.3 (−35.3 to −15.2)	−11.2 (−21.6 to −0.8)
LS mean difference (95% CI) vs placebo	−12.9 (−25.4 to −0.4)	−14.1 (−26.3 to −1.9)	–
Nominal *P* value vs placebo	0.0431	0.0246	–
PGI change responders†			
Week 12 responders, n (%)	9 (40.9)	15 (57.7)	8 (30.8)
CMH difference (95% CI) vs placebo	11.2 (−15.4 to 37.9)	28.1 (3.4 to 52.8)	–
Nominal *P* value vs placebo	0.4093	0.0256	–

CMH, Cochran-Mantel-Haenszel; ITT-E, intent-to-treat exposed; LS, least squares; OAB-q, overactive bladder questionnaire; PGI, patient global impression of change; UUI, urgency urinary incontinence.

*Defined as all patients who were randomized and treated.

†Defined as a patient who answered "much better" or "moderately better" on the PGI change. A patient with a missing PGI change response was considered as nonresponder.

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Funding Urovant Sciences **Clinical Trial** Yes **Registration Number** ClinicalTrials.gov, NCT04211831 **RCT** Yes **Subjects** Human **Ethics Committee** Central IRB: Advarra IRB **Helsinki** Yes **Informed Consent** Yes

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SESSION 2 - PRODUCTS, DEVICES AND INNOVATIVE THERAPIES

Abstracts 7-18
09:05 - 10:35, Hall K
Chairs: Mrs Frankie Bates (Canada), Ms Karin Müller (Austria)

7 | www.ics.org/2022/abstract/7

COMPLIANCE WITH URESTA (CURE) STUDY; A 12 MONTH FOLLOW-UP OF 40 WOMEN.

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HYPOTHESIS / AIMS OF STUDY

Stress urinary incontinence (SUI) has been shown to affect almost half of women who attend gyms or exercise classes [1,2]. Women who continue to exercise or take part in sporting activities may describe discomfort, reduced levels of enjoyment, embarrassment and loss of confidence. Vaginal devices are an appropriate management option for this cohort of women, especially those who wish to avoid surgery for incontinence [3]. Research on incontinence devices is limited and has typically focussed on clinical parameters such as pad tests, rather than long-term compliance and patient reported outcomes.The Uresta bladder support is an effective management option for women with stress urinary incontinence (SUI), however, there is a lack of data assessing long-term compliance. The aim of this study was to assess compliance at 12 month follow-up in women using the Uresta bladder support for exercise related SUI.

STUDY DESIGN, MATERIALS AND METHODS

This was a prospective study of the Uresta bladder support in women who reported SUI during exercise in the United Kingdom. The study was advertised on social media, running clubs and gyms. Participants were fitted with a Uresta bladder support and followed up over a 12 month period. Power calculation recommended a sample size of 43. Ethical approval was obtained. Outcomes were assessed using the PUQ, ICIQ-FLUTS, UDI-6, IIQ-7, QUID and PGI-I questionnaires.

RESULTS

Forty-six women were recruited with an average age, BMI and parity of 42, 24 and 2.3 respectively. The most common activities were running (48%) and CrossFit (22%). Six participants withdrew after 2 weeks. Compliance was 90% at 12 months (n = 40). Uresta insertion was 'okay', 'easy' or 'very easy' for 86% of participants and removal was 'okay', 'easy' or 'very easy' for 75% of participants, Leakage was improved (n = 13), greatly improved (n = 12) or stopped (n = 5) for 83% of participants, 75% were ‘much better’ or ‘very much better’ on the PGI-I scale, and 94% would recommend Uresta to a friend. There were no adverse events.

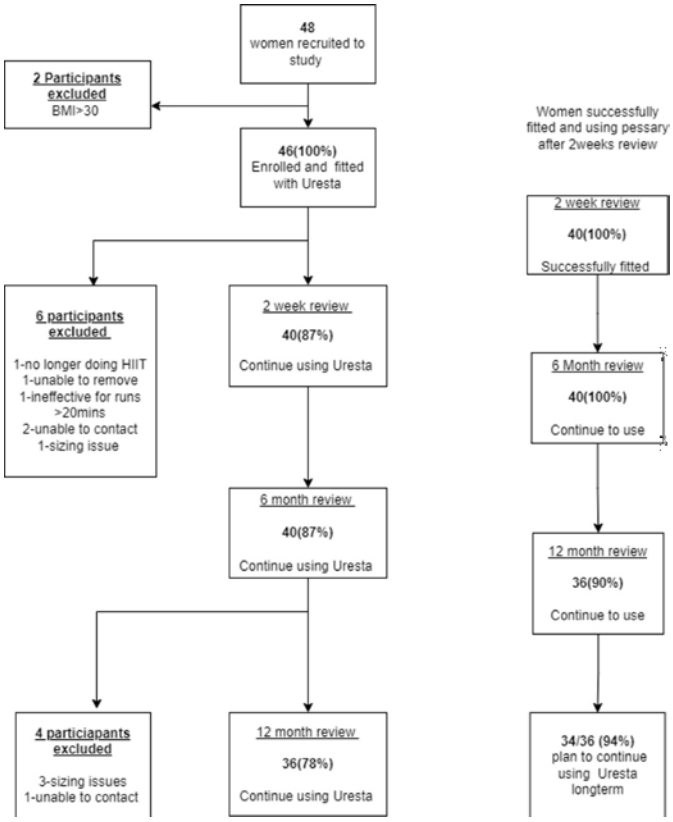
INTERPRETATION OF RESULTS

The Uresta bladder support is a safe, effective, user-friendly management option for women who experience SUI during exercise with excellent long-term compliance. Future studies should identify predictors of successful fitting with incontinence devices and compare the efficacy, ease of use, compliance and cost-effectiveness between different devices currently available. Furthermore, development of a specific, validated questionnaire assessing impact of SUI with exercise and impact of incontinence devices would be a valuable resource for future research in this area.

CONCLUDING MESSAGE

The Uresta bladder support is a safe, effective, user-friendly management option for women with exercise related SUI with 90% compliance at 12-month follow up.

FIGURE 1



Study flow chart

FIGURE 2

Uresta bladder support

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Funding The study design was not influenced by the supplier or inventor of Uresta and the research team did not receive any financial reward for conducting the study. The study was conducted in a private clinic. **Funding** for room hire and nurse chaperone, as well as a supply of Uresta bladder supports, was provided by the UK supplier of Uresta. **Clinical Trial** No **Subjects** Human **Ethics Committee** Northern Ireland Research **Ethics Committee Helsinki** Yes **Informed Consent** Yes

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POWER: AN OPEN, SINGLE-ARM, POST-MARKET CLINICAL TRIAL USING THE TENA SMARTCARE CHANGE INDICATOR™ IN A HOME ENVIRONMENT.

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HYPOTHESIS / AIMS OF STUDY
The TENA SmartCare Change Indicator is a medical device accessory intended to aid caregivers in deciding when to change an absorbing incontinence product. The aim of this interventional, post-market clinical trial was to demonstrate the performance and safety of this device in a home environment with a family caregiver. The primary objective of the trial was to demonstrate that use of the device can reduce the number of manual checks needed in incontinence care.

STUDY DESIGN, MATERIALS AND METHODS
Typically, an absorbing incontinence product is changed several times per day. Changing too early leads to unutilized products being discarded and changing too late implies a risk of urine leakages as well as risk of moisture-associated skin damage. To provide quality care and reassure that the incontinent individual is comfortable, a family caregiver checks the saturation status of each pad on average 2-3 times between changes, a manual process involving touch-feel, looking, and/or asking that not only implies worry for the caregiver and hygienic consequences but also is an invasion of the privacy of the incontinent individual being cared for. The device is a system that consists of a reusable electronic sensor and a smart phone app. The device estimates the saturation level of the absorbing incontinence product and informs the caregiver about the urine saturation level via the app. This information support decisions in incontinence care, complementing a manual check routine.

The POWER clinical trial was conducted in Poland and designed to be open, prospective, interventional and single arm. The trial population consisted of 35 subjects suffering from urinary incontinence, cared for in a home environment with most of the care provided by a main caregiver, and confirmed eligible for participation according to the inclusion and exclusion criteria. The trial duration was three weeks. A diary was used during the trial for the caregiver to enter information about manual checks, product changes and leakages. During the first week (baseline week), TENA incontinence products was to be used without the addition of the device. During the second week (learning week), the device was introduced, and the caregiver learned how to set up and use it as intended by the manufacturer. During the third week (investigational week), the caregiver was to use the device as intended. In the trial there were five mandatory, and three optional visits were planned for each subject. At the final visit a questionnaire was supplied to the caregiver to assess usability of the device.

The primary endpoint was the change in the number of manual checks in-between the daily changes of the absorbing incontinence product at the investigational week compared to the baseline week. There were also multiple secondary endpoints regarding safety, number of product leakages, fecal incidents, skin irritation and device usability. In the trial the subjects act as their own control and data from the investigational week is compared to that from the baseline week.

Descriptive statistics was given for each variable in the trial. The level of significance was set to 0.05 for all variables. Paired t-test or Wilcoxon signed-rank test was used for analyzing the variables. The primary variable was the percentage change of the mean number of checks/day between week 1 (baseline) and week 3 (investigational) of the trial. Secondary variables were analyzed in a similar fashion except the safety, skin and usability variables which were covered by descriptive and summary statistics. Furthermore, the skin redness/irritation variable was evaluated using the Ghent Global IAD Categorization Tool (GLOBIAD) 15. The analysis was to determine if there is a significant difference in scoring between the time points.

RESULTS
35 subjects completed the trial. The subjects consisted of 28 females and 7 males with a mean age of 74 years. The family caregivers consisted of 30 females and 5 males with a mean age of 54 years. All subjects suffered from urinary incontinence and were current users of TENA absorbing incontinence products.

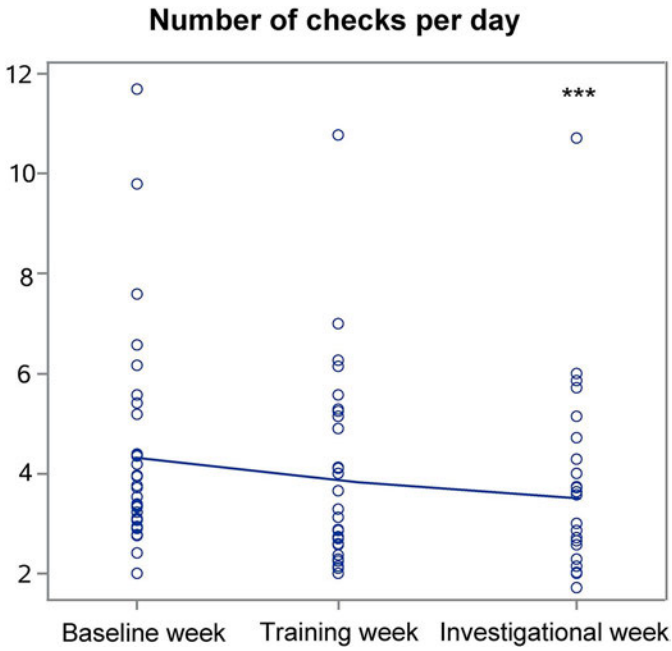
For the primary endpoint, the change in the number of manual checks performed by the caregiver saw an average reduction of 0.8 ± 1.7 checks/day from baseline week to investigational week (Figure 1). This reduction was statistically significant ($p = 0.0006$). This corresponds to a reduction in daily checks by 16%.

For the secondary endpoints, the number of daily leakages saw a reduction of 0.13 ± 0.29 leakages/day from baseline week to investigational week (figure 2), or a 40% reduction in the number of daily leaks. This reduction was statistically significant ($p = 0.0051$). No statistically significant reduction in the number of fecal incidences was shown in the investigation. Only two subjects showed signs of skin redness and irritation at the end of baseline week and after the investigational week, no subjects suffered from skin redness. The questionnaires filled out by the caregiver regarding the use of the device generally showed very positive results for the device. After 2 weeks of use, more than 80% of caregivers rated the ease of use as “very easy to use”. More than 70% of the caregivers assessed that the use of the device facilitated their decision on product changes and reduced their worries about subject comfort. 60% of caregivers also perceived that the wellbeing of the subject was improved by using the system. 89% of the caregivers rated the overall usefulness of the system as “good” or “very good” and a majority would continue to use the system. For the safety endpoint, a total of 5 adverse events were reported in the clinical investigation. None of them were considered related to the investigational device or procedure and none of them were serious. No subjects withdrew from the trial.

INTERPRETATION OF RESULTS
The results indicate that the use of the device reduces the number of manual checks needed in-between changes of absorbing incontinence products. Furthermore, the number of daily leakages is reduced. Using the device could therefore reduce the amount of work and worry associated with incontinence care in the home without affecting the skin negativity. Additionally, the device raises few safety concerns and appear well tolerated.

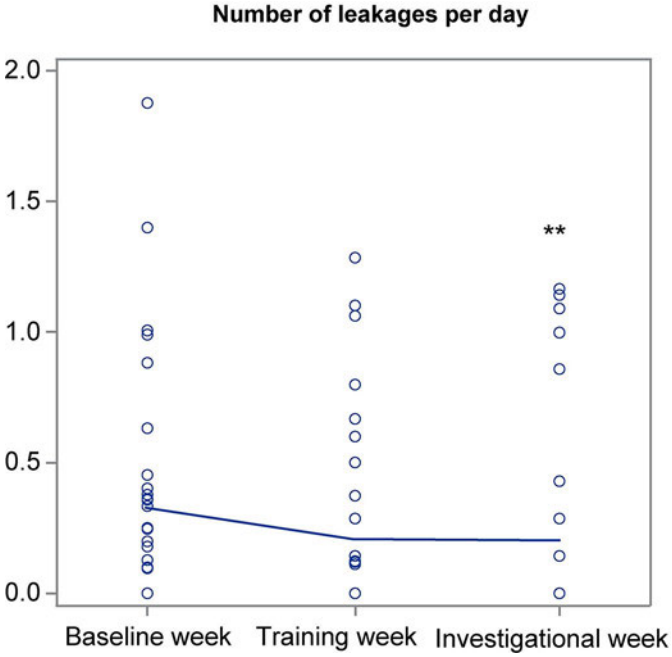
CONCLUDING MESSAGE
The trial results suggest that the device helps caregivers decide when incontinence products need to be changed, as demonstrated by a reduction both in the number of manual checks needed between changes and in the number of leakages. Additionally, the device appears to be safe to use in its intended setting and in a home environment. Overall usability aspects of TENA SmartCare Change Indicator handling were reported to be satisfactory, and caregivers believe the device is easy to use and give benefit to them and also to the comfort of the subjects.

FIGURE 1



Number of daily checks for the three study weeks. Line shows the average. The average number of daily checks was significantly (*, $p < 0.001$) reduced by 0.8 ± 1.7 between baseline and investigational week.**

FIGURE 2



Number of leakages for the three study weeks. Line shows the average. The average number of daily leakages was significantly (, $p < 0.01$) reduced by 0.13 ± 0.29 between baseline week to investigational week.**

Funding Essity Hygiene and Health AB funded this clinical trial. **Clinical Trial** Yes **Registration Number** NCT04846270 **RCT** No **Subjects** Human **Ethics Committee** the Regional Medical Chamber in Warsaw, Poland. **Helsinki** Yes **Informed Consent** Yes

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A SHORT STORY IN PROPRIOCEPTIVE FACILITATION TO THE PELVIC FLOOR – A PROOF OF CONCEPT STUDY USING INNOVO

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HYPOTHESIS / AIMS OF STUDY
An estimated 30 - 50% of women cannot volitionally recruit their pelvic floor muscles (PFM). Proprioception is fundamental to motor learning, and sensorimotor afferents may facilitate changes in motor control. Neuromuscular electrical stimulation (NMES) is used clinically as an adjuvant intervention to facilitate pelvic floor muscle (PFM) contractions. Neural imaging shows that NMES contractions activate similar cortical and subcortical structures to volitional ones. Consequently, these NMES elicited contractions may enhance proprioception and PFM function. This study aimed to determine if NMES delivered in a pair of shorts (INNOVO) provided a proprioceptive stimulus to enhance PFM function in healthy women.

STUDY DESIGN, MATERIALS AND METHODS
Ten healthy continent women aged 23 – 57 years gave written informed consent and participated in this study. Inclusion criteria included women 18 years or older and the ability to perform a PFM contraction. Exclusion criteria included confirmed pregnancy, neurological disease, pelvic organ prolapse, lumbopelvic surgery, recurrent urinary tract infections, and cardiac pacemaker. A bladder-filling protocol facilitated the delineation of structures during transabdominal ultrasound imaging (TAUS). The magnitude of bladder base displacement (BBD) was measured in centimeters (cm) under three conditions in standing: pre-NMES volitional contractions, INNOVO NMES contractions, and post-NMES volitional contractions with at least a 5-minute washout period between conditions. INNOVO shorts consist of eight embedded electrodes, with a cumulative stimulating surface area of 1200cm2 with a maximum current density of 0.189 mA/cm2. The electrodes are positioned bilaterally around the pelvis, anterior and posterior thighs. INNOVO uses patented multipath stimulation delivered via a pulsed, symmetrical, rectangular biphasic waveform at 50Hz. A pulse duration of 620μs was delivered for 5 minutes (on:off time of 5sec:5sec), resulting in 30 elicited PFM contractions. Participants were blinded to ultrasound imaging and verbally cued to perform volitional PFM contractions pre and post-INNOVO NMES. No verbal cues were given during INNOVO NMES, which was delivered at each participant's maximum tolerable amplitude (mA) to elicit a PFM contraction confirmed by a cranial displacement of the BBD observed with TAUS.

RESULTS
A one way repeated measures analysis of variance (ANOVA) revealed a significant difference over time and large effect $F(1,9 = 29.57)$, $p < .001$, partial $\eta 2 = .77$. Post-hoc analysis with a Bonferroni adjustment revealed INNOVO NMES contraction with BBD = 1.31cm statistically significantly increased from baseline contraction with BBD = 0.42cm (95% CI, 0.47-1.30), $p < .001$ and post-NMES volitional contraction with BBD = 1.1cm (95% CI, 0.07-0.53), $p = .011$, while post-NMES volitional contraction with BBD = 1.1cm statistically significantly increased (95% CI, 0.27-0.90), $p = .001$ from baseline volitional contraction with BBD = 0.42cm.

INTERPRETATION OF RESULTS
The findings of this proof of concept study suggest that a 5-minute bout using INNOVO NMES provided a proprioceptive sensorimotor stimulus that significantly enhanced pelvic floor function. All PFM contractions post-NMES showed a greater magnitude of BBD when compared to baseline. Studies report that NMES elicited muscle contraction plays a role in proprioception by stimulating muscle spindles and Golgi tendon organs that send afferent information to the somatosensory cortex. High NMES amplitudes, which elicit a motor response, induce a cortical facilitation effect. In contrast, low amplitudes are associated with a cortical inhibitory effect, thus showing an amplitude-based dose effect. Consequently, the presence or lack of a contraction directly impacts the somatosensory cortex and, ultimately, cortical excitability as determined by motor evoked potentials (MEP).

CONCLUDING MESSAGE
A 5-minute bout of brisk INNOVO elicited contractions significantly improved PFM function compared to pre-INNOVO function in healthy continent women. Since this improvement cannot be explained by increased strength, it is plausible that INNOVO stimulated a large number of proprioceptive receptors and sensory afferents, which led to the immediate change in motor response. This finding should not be a surprise since numerous studies have shown that NMES can induce neural plasticity. Future studies should look at the longevity of these effects and their impact on pelvic floor function in those who cannot volitionally recruit their PFM.

FIGURE 1

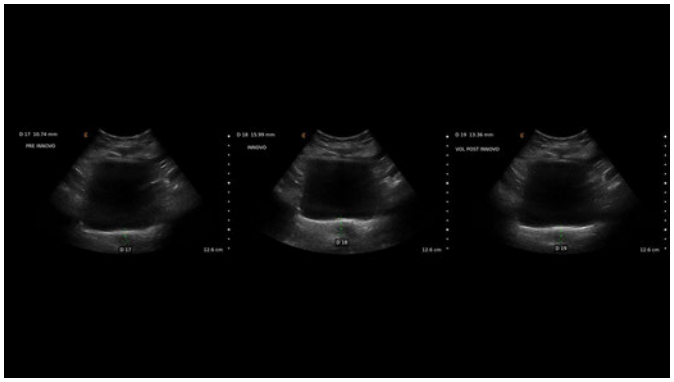

Figure 1. Bladder Base displacement across all testing conditions

FIGURE 2

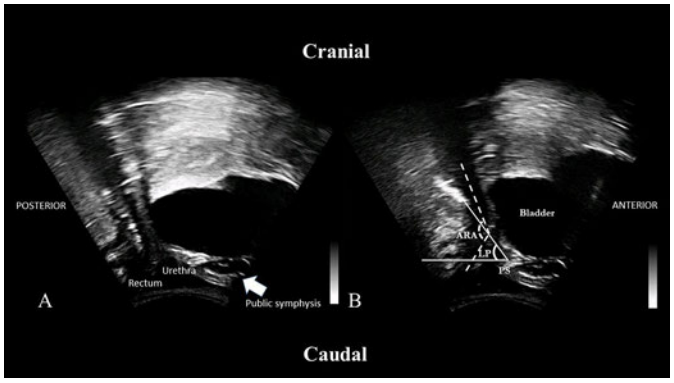

Figure 2. Transperineal US image of PFM at Rest (A) and during INNOVO NMES (B)

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BEST IN CATEGORY PRIZE: CONTINENCE CARE PRODUCTS / DEVICES / TECHNOLOGIES

A PRESSURE SENSOR ARRAY CAN BE USED TO SHOW MAXIMAL PELVIC FLOOR MUSCLE CONTRACTION IN DIFFERENT POSTURES.

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HYPOTHESIS / AIMS OF STUDY

Pressure changes within the vagina have historically been used to assess the effectiveness of a voluntary pelvic floor muscle (PFM) contraction. The perineometer, a balloon type device has been used extensively to determine 'strength' and 'function' of the pelvic floor. However, due the design of these devices, the pressure changes reflect global pressure change within the vagina, making it impossible to discriminate between an increase in abdominal pressure and that induced by PFM.

It is well recognised that a pressure profile exists along the vagina, and the mid (high) pressure zone corresponds to the anatomical location of the PFM (1). Measurement and display of this profile provides a more comprehensive and effective means of biofeedback to inform women whether they are performing effective voluntary PFM contractions. This information should thus be provided when using a biofeedback device for PFM training (PFMT).

femfit® (Figure 1) is an intravaginal biofeedback device, consisting of eight pressure sensors (positioned at 10 mm intervals), that measures the vaginal pressure profile (2). Simultaneous detection of different vaginal pressure zones enables the user to discriminate between abdominal and PFM pressures, and provide comprehensive biofeedback on PFMT technique.

The aim of this study was to investigate if a pressure sensor array is more effective at determining PFM contractions, and to understand which of the distal sensors measured peak PFM pressure when contracting in supine and upright positions.

STUDY DESIGN, MATERIALS AND METHODS

This is a secondary analysis from a prospective interventional randomised pilot study of women with predominately stress urinary incontinence (leakage at least 3 times per week, over the last 3 months).

In the parent study, sixty participants were randomised into two groups. The biofeedback group used the femfit® system (device and mobile application) to complete PFMT (intervention) for twelve weeks. Non-biofeedback used the same mobile application and followed the same PFMT protocol as the biofeedback group, but did not but did not use a femfit® device (control).

A PFM physiotherapist completed blinded assessments of each participant. The femfit® was used to measure pressure generated by the pelvic floor during a voluntary maximal PFM contraction while supine, which was then repeated while upright (3 × 5 second contractions in each position). The physiotherapist inserted the femfit® to ensure it was positioned correctly for each participant. To minimise study bias, the physiotherapist did not provide guidance or encouragement to the participant on how to perform a contraction. These PFM contractions (as measured by the femfit®) captured PFM function characteristics.

This secondary analysis used descriptive statistics to investigate the sensor that detected peak PFM pressure (during maximal voluntary PFM contraction). Pressure data from distal sensors 1 to 6 (Figure 1) was used to identified peak PFM pressure for each PFM contraction in both supine and upright positions. When participants had the same sensor detect peak PFM pressure for at least two of their three PFM contractions (for that posture position), this was defined as the dominant sensor.

RESULTS

A total of 99 voluntary maximal PFM contractions in supine, and 99 in the upright position were analysed from 33 study participants.

In the supine position, 28 women (85 %) had the same sensor detect peak PFM pressure for each of their three PFM contractions, indicating internal consistency. The remaining five women (15 %) had the same sensor detect peak PFM pressure for 2/3 of their contractions. Between participants, the most frequent dominant sensor was sensor 3 (33 %), followed by sensor 1 (18 %). Only one participant (3 %) had sensor 6 as their dominant sensor.

In the upright position, 22 women (67 %) had the same sensor detect peak PFM pressure for all three PFM contractions. Four participants (12 %) had the same sensor for 2/3 contractions, and two participants (6 %) had a different sensor for each of the three contractions. For the 31 participants with a dominant sensor, the most frequent sensor was sensor 6 (35 %), followed by sensor 1, 2 and 5 with five participants (16 %) each.

A summary of the dominant sensor spread between patients is given in Figure 2. Overall, the mean dominant sensor was sensor 3 in supine (SD: ±1.4) and sensor 4 in upright (SD: ±2.0). In supine, the median dominant sensor was sensor 3, while in upright the median was sensor 5.

When changing posture from supine to upright, seven participants (21 %) had the same sensor detect peak PFM pressure for all three contractions in both positions. For 11/31 participants (35 %), their dominant sensor while upright was adjacent to their dominant sensor in supine (e.g. sensor 1 in supine and sensor 2 in upright).

INTERPRETATION OF RESULTS

Overall, multiple distal sensors detected a peak PFM pressure during maximal voluntary PFM contraction. The vaginal pressure profile is likely to change dependent on posture, device placement, anatomical adjustment to an internal device and natural anatomical movement. The array of eight pressure sensors used in this study can accommodate this variation. This analysis highlights that a global pressure change (measured by a perineometer) would not capture the magnitude of PFM pressure generated during a voluntary PFM contraction, whereas a pressure sensor array can.

It is promising to see that, for the majority of women when performing repeated PFM contractions in the same position, femfit® detects peak PFM pressure in the same anatomical location, demonstrating the repeatability and reliability of the device.

CONCLUDING MESSAGE

This study shows there is intra-participant sensor variation when detecting peak PFM pressure across a posture change, and inter-participant variability when comparing PFM contractions in similar and different postures. Overall, a pressure sensor array enables users to identify peak PFM pressures and this information can help to determine effective PFM contraction. Women (and clinicians) need to be aware of the shortcomings of single sensor, and perinemoter-like devices for PFM contraction assessment.

FIGURE 1

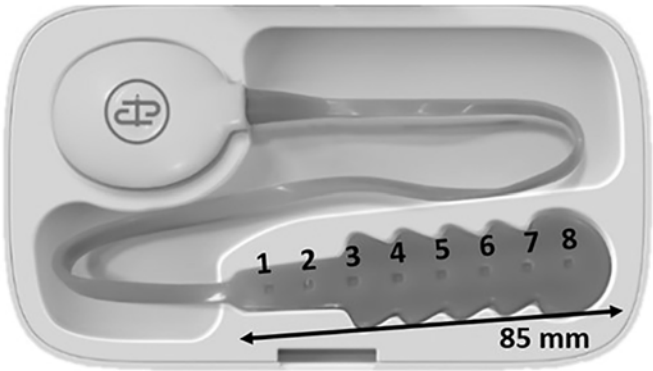

Figure 1. femfit® device , with pressure sensors number 1 through 8.

FIGURE 2

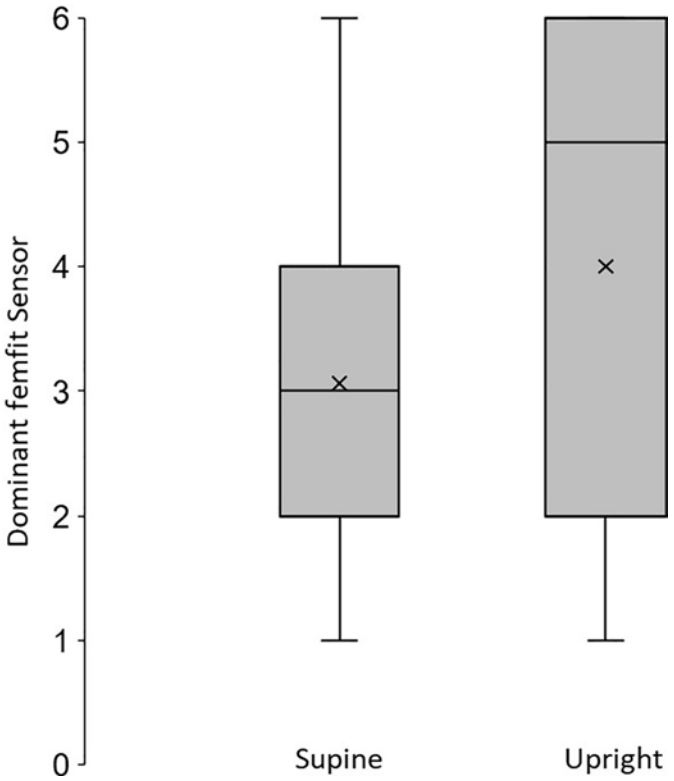

Figure 2. The spread of the dominant femfit® sensor that detected peak PFM pressure during maximal voluntary contraction.

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Funding Ministry of Business, Innovation & Employment - Smart Sensors for the Medical Industry **Clinical Trial** No **Subjects** Human **Ethics Committee** Health and Disability **Ethics Committee**, New Zealand **Helsinki** Yes **Informed Consent** Yes

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UCON; A NONINVASIVE NEUROSTIMULATION SYSTEM SPECIFICALLY DESIGNED FOR GENITAL NERVE STIMULATION

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HYPOTHESIS / AIMS OF STUDY
Neuromodulation is used to treat overactive bladder symptoms like urgency, frequency, and incontinence. In addition, nonobstructive urinary retention and fecal incontinence can also be addressed with neuromodulation. Clinically available neuromodulation therapies in urology and gastroenterology use either the sacral nerve roots or the posterial tibial nerve as target for stimulation. Another promising stimulation target is the dorsal penile/clitoral nerve (also called dorsal genital nerve (DGN)). Studies have shown that DGN stimulation can suppress detrusor contraction [1] and could thus be used to prevent incontinence when stimulation is started soon after the onset of a detrusor contraction (on-demand stimulation).

Studies on DGN stimulation have mostly used off-the-shelf components. These components are fine for short-term studies but have several drawbacks when doing long-term studies or when considering offering DGN stimulation as treatment. The main drawback is a relative bulky stimulator with too many buttons and programs. In addition, the stimulator usually lacks a way to quickly start stimulation, which is essential for on-demand stimulation. Furthermore, there is the problem of the stimulation electrode. A stable long-term electrode-nerve interface is required but is difficult to obtain with off-the-shelf surface patches, especially in female patients.

In this project, we designed and build a neurostimulation system (both stimulator and electrode) for DGN stimulation.

STUDY DESIGN, MATERIALS AND METHODS
A literature study was conducted to draw up a list of stimulation parameters that are typically used in DGN stimulation. This resulted, in combination with our own experiences in DGN stimulation, in design specifications for the electrical capabilities of the stimulator. In addition, the stimulator had to be designed for patient-operated treatment offering convenient access to different stimulation modes, including quick access to on-demand stimulation.

A surface electrode for DGN stimulation had to be designed based on the local anatomy where also the large inter-person anatomical variation had to be taken into account. Human genitals vary largely in both shape and size. Beside gender differences there are large differences within the same gender, In addition, even dimensions can vary in the same person over the course of one day.

Several design criteria were taken into consideration including adhesive-, electrical-, and biocompatibility capabilities, mechanical integrity, comfort, and convenient to use for the patient. Especially, good adhesion to the moist mucosa and mechanical adaptation to the irregular surfaces of the genitals were important design criteria.

RESULTS
A small (69x53 mm, weight: 32 g), water tight, body worn, electrical stimulator for patient-operated treatment was designed and build (Fig. 1). It has a rechargeable battery with a capacity to last for a few days with normal use. There are only three buttons. One for ON/OFF, one for stimulation amplitude UP/DOWN and one for START/STOP On-demand stimulation. The following stimulation parameters are available: stimulation frequency: 20 Hz, pulse duration: 200 μs, pulse amplitude: 0-25 mA, maximum output voltage: 120 V. The stimulation pulses are rectangular, charge balanced and current controlled. The stimulator logs all stimulation sessions. Logs can be read by connecting the stimulator to a computer during follow-up at the hospital.

There are two operation modes: (1) Time-limited stimulation and (2) On-demand stimulation. Time-limited stimulation provides continuous stimulation for a set duration (15 min – continuous). On-demand stimulation provides 60 s of stimulation, which is initiated on-demand by pressing a button on the stimulator or on the remote control.

The remote control (27 mm diameter, weight: 5 g) (Fig. 1) has only one button and is powered by a button cell battery. It connects wirelessly to the stimulator using Bluetooth.

Dedicated DGN electrodes (19x21 mm, weight: 0.5 g) (Fig. 2) have been developed in collaboration with Axelgaard Manufacturing Co (California, USA). They are heart shaped and are suitable for use in both males and females. The electrodes consist of a silicone shell, a metal connector for the lead and, a customized hydrogel. The hydrogel (developed by Axelgaard Manufacturing Co) ensures optimal tissue friendliness and electrical properties along with biological safety. It has a thickness of 3 mm, and absorbs irregularities of the surface under the electrode. In this way both gender variances and variances within same gender or person can be handled by the same electrode. The triangular shape of electrode is specifically adapted for the female outer genital anatomy, which is most challenging. The pointy tip of the electrode is placed in the apex of prepuce/hood, with the two wings of the electrode extending down on the surface of the clitoral hood/clitoris and inner labia, depending on the dimensions of the individual anatomy.

UCon has been fully verified in all aspects relating to biocompatibility, electrical and mechanical safety, and usability and complies with relevant standards and regulations.

INTERPRETATION OF RESULTS
A complete neurostimulation device (UCon) has been designed and build for DGN stimulation. The main components are a stimulator, a remote control, electrodes, and leads. Bench tests and other required non-clinical tests have been conducted successfully so the device is ready to be tested in a clinical trial. It is expected that the availability of UCon would boost clinical research into DGN stimulation. In addition, UCon would allow DGN stimulation to become a medical treatment because the device has been developed according to requirements for regulatory clearance.

CONCLUDING MESSAGE
A non-invasive neuromodulation device for DGN stimulation has been build. All required verification tests were successfully completed. Approval for the first clinical study using UCon has been obtained from both the local medical device agency and the local medical-ethical committee. This study will enroll a total of 40 patients in 3 different hospitals and was initiated in March 2022.

Next steps involve development of a percutaneous electrode for DGN stimulation. This will be especially attractive for patients using on-demand stimulation because it would allow for a permanent electrode-nerve interface.

FIGURE 1

UCon stimulator and remote control

FIGURE 2

UCon surface electrode

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EXPLORATORY SAFETY STUDY OF AN UMBILICAL CORD DERIVED URETHRAL SLING IN BILATERAL PUDENDAL NERVES INJURY-INDUCED URINARY INCONTINENCE IN FEMALE RATS

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HYPOTHESIS / AIMS OF STUDY
Urinary incontinence is a common disease affecting about 8% of worldwide population. Stress urinary incontinence (SUI), caused by intrinsic sphincter deficiency or hypermobility of the urethra, represents approximately 50% of the cases. Urinary incontinence, and especially SUI, have detrimental effects on women quality of life but also on sexual functions.

Mid-urethral slings (MUS) is the standard treatment for women with SUI refractory to intensive pelvic floor muscle training. A majority of MUS are synthetic surgical mesh materials composed of polypropylene. Although clinical efficacy of MUS has long been demonstrated, recent warnings from scientific societies and regulatory agencies in various countries led to recall some mesh products used in pelvic organ prolapsus surgery. Infection, chronic pain and erosions are the main complications reported for MUS and are likely to be associated with the synthetic material used.

In light of these findings, biological mesh materials have been proposed for SUI and pelvic prolapsus management in order to reduce these adverse events. Biological materials, such as autologous fascial slings, have been proven efficient and safe in the management of SUI. However, heterologous materials still lack high level clinical evidence especially for SUI surgical management. Moreover, the biomechanical properties of these materials have to be well understood in order to propose our patients the best care.

The human umbilical vein has shown advantage of the longitudinal mechanical properties to use it as a scaffold material. Umbilical vessel slings (UVS), extracted from umbilical cord lining, could be promising biological meshes for the management of SUI related to urethral hypermobility.

In this study, we evaluate the efficiency and the safety of UVS placement in the management of induced SUI in female rats.

STUDY DESIGN, MATERIALS AND METHODS
Twenty-four females were randomly divided into three groups, including a naive group (group 1, n = 4), a group who underwent bilateral pelvic nerves injury (PNI) (group 2, n = 10) and a group who underwent both PNI and UVS placement (group 3, n = 10). UVS were extracted from human umbilical cord lining. After written consent, umbilical cord was obtained from women seronegative for hepatitis B virus, hepatitis C virus, syphilis, human T-lymphotropic virus and human immunodeficiency virus. The umbilical vessels were chemically viro-inactivated and flattened during the freeze-drying step.

Micturition calendar was frequently recorded and leak pressure point (LPP) test was performed at day 28. After LPP test, rats were euthanized, and bladder/urethra were collected for histopathological analysis.

All experiments were performed according to the European Community Council Directive 2010/63/UE and the French Ministry for Agriculture, Agrifood and Forestry (Decree 2013-118). Experimental protocols were reviewed by CEEA-122 Ethical Committee for Protection of Animals used for Scientific Purposes and approved by French Ministry for National Education, Higher Education and Research under the number APAFIS # 26650-2020072010588593 v3. All studies were performed according to local hygiene and risk prevention regulations.

RESULTS
Overall, 24 rats were included whom 10 had both PNI and UVS placement. Compared with group 2, group 3 had increased maximal LPP (respectively 21.8 ± 2.1mmHg versus 28.4 ± 4.1mmHg, p = 0.2). Micturition frequencies were similar between the groups. Total voided volume was higher in the group 3 at the end of the study compared with group 2 (12.5 ± 1.1mL versus 9.4 ± 0.6mL respectively, $p < 0.05$). Histopathological findings evidenced a good local tolerance and a moderate to high tissue integration of the UVS.

INTERPRETATION OF RESULTS
Biological sling derived from human umbilical vessel could be safely placed with a slight improvement of LPP in a population of rats who had bilateral PNI without major modification of micturition calendar. Moreover, there was no evidence of implant-induced inflammation or tissue damage in or around the urethra or the bladder. Only rare inflammatory cells were observed in a few sites and no fibrosis could be seen. Comparison of groups PNI and PNI/UVS suggested that the presence of the sling had no negative impact on the integrity of the urethra or urinary bladder regardless of the site.

CONCLUDING MESSAGE
UVS could be a promising biomaterial in the management of SUI in women. Clinical studies are needed.

FIGURE 1

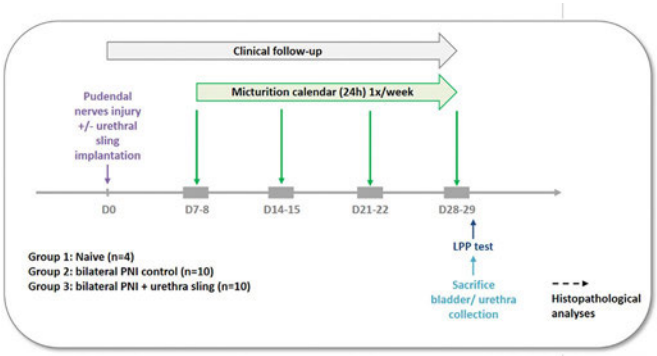

Figure 1 - Study protocol

Funding Tissue bank of France (TBF) **Clinical Trial** No **Subjects** Animal **Species** Rat **Ethics Committee** CEEA-122 Ethical Committee for Protection of Animals used for Scientific Purposes and approved by French Ministry for National Education, Higher Education and Research under the number APAFIS # 26650-2020072010588593 v3.

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BEST IN CATEGORY PRIZE: CONSERVATIVE MANAGEMENT

LED LIGHT IN THE TREATMENT OF GENITOURINARY SYNDROME OF MENOPAUSE IN BREAST CANCER SURVIVORS: PRELIMINARY RESULTS OF A RANDOMIZED CLINICAL TRIAL

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HYPOTHESIS / AIMS OF STUDY

Genitourinary Syndrome of Menopause (GSM) is characterized by a set of physical signs and symptoms associated with estrogen deficiency, such as vulvovaginal dryness, burning, dyspareunia, and urinary symptoms. These symptoms associated with side effects of oncological treatment, that induce functional changes in the vagina, decrease quality of life and sexual function [1]. The Light Emitting Diode (LED) is a phototherapy instrument non-invasive, athermic, and safe, potentially capable of stimulating the epithelium, as it can provide fibroblast stimulation and increase microcirculation, restoring the quality of vaginal tissue [2]. We hypothesize that the use of LED has the potential to promote an increase in the vaginal mucosa, leading to improvement of symptoms of Genitourinary Syndrome of Menopause (GSM). The aim of this study is to evaluate the impact of blued light LED in reducing atrophy of the vaginal mucosa, evolution of symptoms, quality of life and safety in breast cancer survivors with Genitourinary Syndrome of Menopause.

STUDY DESIGN, MATERIALS AND METHODS

This is a double-blind, randomized clinical trial that evaluated women with a history of breast cancer stage 0-III with at least one sign and symptom of GSM. Inclusion in the study was performed after completion of the cancer treatment (surgery, chemotherapy and radiotherapy) and also in those undergoing adjuvant hormone therapy regardless the class of medication used. Exclusion criteria were having taken topical or systemic hormone replacement therapy with estrogen or testosterone during the last 6 months, pregnancy, inability of understanding the proposed evaluation instruments, progression to metastasis disease during the protocol, the presence of vaginal infection or chronic neurological degenerative diseases that preclude to be on gynecological position. The presence of GSM was established by the identification of at least one symptom and a sign characterized on inspection of pelvic structures by an experienced physiotherapist. Vaginal pH measurement was performed with MColorpHast™ tape, Merck, Darnstadt-Germany, with possibility of immediate inclusion in the study if pH > 5.0. For participants with pH measurement <5.0 was awaited the cytological study to confirm the condition of hypotrophy or atrophy of the vaginal mucosa. The patients were evaluated by Vaginal Maturation Index (VMI) and Vaginal Health Index (VHI) and answered three questionnaires: International Consultation on Incontinece Questionnaire-Short Form (ICIQ-SF), Functional Assessment of Cancer Therapy-Breast Cancer (FACT-B + 4), and Likert scale before and after 3 weeks, 2 and 3 months of treatment. The participant was randomly divided into two groups, 1:1, to either the sham session procedure or Intracavitary active LED with the Model Energy equipment of the DGM® brand (patent number: BR BR 10 2017 026980 9). The protocol consisted of 5 weekly sessions of 8 minutes of 405nm LED, 1.66W/m2, or sham, both associated with pelvic floor muscle training, in the same day. The study was carried out in a physiotherapy clinic with a specialized urogynecology service. The sample size was established using a Winpepi calculator (version 11.65): 74 patients, 37 in each group, would be enough to detect a difference of 10 points in the VMI (considering a standard deviation of 15 and 8 in each group) [3]. The patients signed the informed consent form and the study was approved by the Ethical Committee.

RESULTS

At the moment, the sample consists of 71 randomized women and 57 completed treatment, 30 in the LED group and 27 in the sham. The mean ages were 53.1(±7.9) and 50.5(±8.3) years in the LED and sham groups, respectively ($p = 0.36$). There was no difference in sociodemographic or clinical characteristics. The VHI from LED group was 15.7 and sham group 14.6 ($p = 0.25$); the median baseline VMI from LED group was 44 and from sham group was 21.5 ($p = 0,54$). There was an increase in the domains of physical and social health and total score in the LED group in the first reassessment, however, with no difference in the inter group tests and at the end of the 3 evaluations. Similarly, there was an improvement in the ICIQ-SF scores and in the VHI in the first evaluation of the LED group, with no difference in the final analysis. In both groups there was a predominance of satisfied or very satisfied patients in the end of the treatment.

INTERPRETATION OF RESULTS

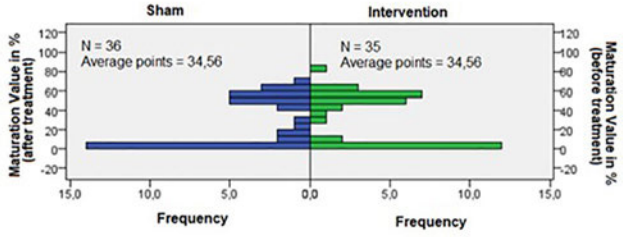
Our findings can be explained by the fact that most patients are classified as having severe atrophy and, consequently, it is not possible to verify a change in VMI. In the other rand, the pelvic floor exercises performed by both groups may have been the factor causing satisfaction in both groups, since it leads to an increase in the vaginal health index, causing an increase in vaginal lubrication, a decrease in dryness and friability, resulting from increased tissue perfusion. Finally, with the preliminary sample, the large sample loss, and the high standard deviation may have been the main factor associated with the non-identification of differences between the groups.

CONCLUDING MESSAGE

Blue light-emitting diode was shown to be safe and well tolerated without adverse events, however, in this study it was not possible to demonstrate the presence of a lasting effect of the exposure of this intervention in GSM.

FIGURE 1

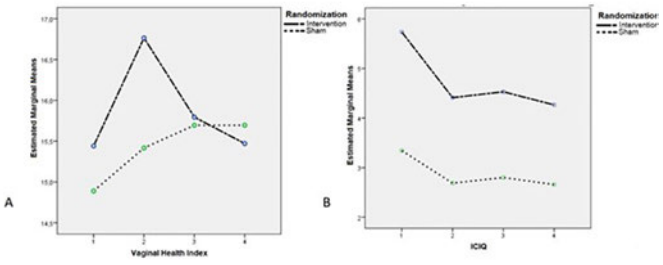
Graph 1. Distribution of Vaginal Maturation Index values in pre-treatment.



Caption: Mann Whitney U test.

FIGURE 2

Graph 2. A- Evolution of the Vaginal Health Index. B- Evolution of ICIQ-SF responses



Caption: ANOVA test of repeated measures of serial comparisons

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Funding None **Clinical Trial** Yes **Registration Number** NCT03833726 **RCT** Yes **Subjects** Human **Ethics Committee** Bahiana School of Medicine and Publica Health **Helsinki** Yes **Informed Consent** Yes

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BEST IN CATEGORY PRIZE: HEALTH SERVICES DELIVERY

TEACHING EFFECTIVE PELVIC FLOOR MUSCLE EXERCISES IN ANTENATAL CARE: DESIGN AND DEVELOPMENT OF A TRAINING PACKAGE FOR COMMUNITY MIDWIVES IN THE UNITED KINGDOM.

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HYPOTHESIS / AIMS OF STUDY

Urinary incontinence (UI) is common in women during childbearing years, onset of UI for many women occurs postpartum, but may also commence during pregnancy. Evidence suggests antenatal pelvic floor muscle exercise (PFME) is effective for preventing UI during and after pregnancy in women with no previous symptoms [1]. However, midwives lack access to adequate training to support implementation of PFME in antenatal care [2]. The study aim was to develop a comprehensive training package for midwives and resources for pregnant women to support teaching of PFME within the antenatal care pathway to be evaluated in a feasibility and pilot randomised controlled trial (RCT). This study is being reported for the first time, it is part of the six-year research programme leading up to the RCT.

STUDY DESIGN, MATERIALS AND METHODS

The study comprised four iterative phases of intervention development, including a stakeholder event and multiple patient and public involvement and engagement (PPIE) activities. The PPIE advisory group included mums with young children, with meetings held in the community.

Phase 1: focus groups with women and midwives

Women who were pregnant or had given birth within the previous 12 months, and midwives providing antenatal care were invited to take part in separate focus groups in three sites (small city, inner city and rural town) in England. Data were analysed using thematic analysis.

Phase 2: development of a training programme including intervention mapping

Data from phase 1 and from previous studies in this research programme were mapped to the Behaviour Change Wheel (BCW) informed by the Capability-Opportunity-Motivation and Behavioural Skill (COM-B) model, Theoretical Domains Framework and Behaviour Change Technique (BCT) taxonomy (v1) and used to develop the intervention. Extensive input from PPIE and stakeholder consultations included PPIE advisors trying out mobile phone Apps to support PFME and stakeholders considering training needs and service provision.

Phase 3: practice training event

A member of the research team delivered the draft training package in person to a cohort of midwives. Midwives rated their confidence before and after training regarding pelvic floor knowledge and teaching PFME using a 5-point Likert questionnaire (0= not at all confident, 4=completely confident) designed for the study. After training, participants were asked to provide feedback on intervention format, content and methods of delivery in one of two discussion sessions. Participants completed an anonymous evaluation questionnaire with options to rate the training and provide free text comments.

Phase 4: intervention refinement

Findings from Phase 3 and further PPIE helped refine format and content of the intervention package. Additional refinements, made in response to the COVID-19 pandemic, enabled online intervention training delivery as in person meetings were not permitted.

RESULTS

In Phase 1, 12 women (age range: 20-44 years; education range: secondary education to postgraduate degree; ethnicity: white (n=11), multiple ethnicity (n=1)) and 14 midwives (age range: 25-59 years; range of experience in midwifery: 3-32 years) took part in six focus groups. The practice training in Phase 3 was attended by 18 midwives (age range: 25-60 years; range of experience in midwifery: 2-20 years). Of the 32 midwives who took part in Phases 1 and 3 of the study, eight (25%) did not provide data regarding previous PFME training, 13 (41%) reported no previous PFME training (formal or informal), two (6%) had attended specific pelvic floor rehabilitation courses, and the remaining nine (28%) reported varying amounts of training from various sources.

Data from Phase 1 and previous research in this programme were mapped onto the BCW, and ideas for possible intervention content and BCTs were discussed by the research team. This resulted in the first iteration of the intervention. Intervention materials included a midwife training programme and resources for midwives to support PFME implementation, and a package of resources for women to be given out by midwives during the antenatal booking appointment.

The training programme for midwives included five steps for putting PFME into antenatal clinical practice: 1. Raise the topic of PFME early in pregnancy; 2. Screen for UI at each appointment; 3. Teach PFME at 16 weeks gestation; and throughout pregnancy 4. Prompt/remind women about how to perform PFME and 5. Refresh women's understanding about PFME and refer on to specialist services if required. Midwives were provided with a training handbook containing session slides, summary leaflets and additional resources about PFME and UI.

Resources for women, co-developed with PPIE advisors, included a bag provided at the antenatal booking appointment. The bag contained a leaflet with information about PFME and how to perform a correct pelvic floor muscle contraction, stickers to use as prompts/reminders for PFME, and an app decision card, with QR code, with details of three high-rated smart phone apps chosen by PPIE advisors to support PFME.

Evaluation scores indicated that midwives participating in the practice training event (n=18) found it useful, with positive ratings for content and delivery. Post-training qualitative feedback noted that midwives recognised the importance of taking the lead regarding PFME, but lack of time, confidence, and skills to raise the issue presented challenges for implementing PFME in practice. Following training, participants reported an increase in total confidence relating to PFME from 2.70 (range 1.18 to 3.50) before training to 3.68 (range 3.37 to 4.00) after training, indicating potential for the training programme to address some of these challenges.

Practice training event participants raised additional considerations for implementation of PFME, including:

- Time constraints of antenatal appointments
- Information overload for women in this phase of their maternity care
- Concerns regarding continuity of care
- Importance of establishing PFME champions within midwifery teams
- Need for buy-in from senior midwives / clinical managers to support implementation and delivery

Intervention materials and content were modified and refined by the research team and PPIE advisory group in response to feedback from the practice training event, for examples: including anatomy refresher and more detail on muscle training physiology; to package resources for women in a cloth bag big enough to hold a clean nappy. A trainer manual was developed to support fidelity of training delivery. Additional training and resources were developed to support a PFME champion role. Further modifications were made at the onset of the COVID-19 pandemic to enable training delivery via Zoom online virtual platform, and to support midwives to deliver intervention elements via telephone appointments.

INTERPRETATION OF RESULTS

Despite challenges identified by midwives regarding wider system pressures [3], past difficulty accessing training, and time constraints within clinic appointments, midwives and women believed that implementing PFME in the antenatal care pathway would be beneficial for large numbers of women. This study aimed to ensure that whatever was asked of women and midwives for implementing PFME was evidence based, with sound theoretical underpinnings and consensus acceptance from experts and lay members of the public. We benefitted from working closely with the PPIE advisors and drew upon known BCTs throughout the four developmental phases to develop a comprehensive understanding of the needs of midwives, women and stakeholders within the current organisational context. The BCW and COM-B helped us to identify how these could be brought together into a training package for midwives and resources for supporting women to address these needs.

CONCLUDING MESSAGE

After extensive iterative refinements of the training package and resources the success of this approach to development is now being tested in the feasibility and pilot RCT.

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PELVIC FLOOR MUSCLE TRAINING ADHERENCE: EVALUATING WOMEN'S ADHERENCE TO HOME EXERCISE PRESCRIPTION IN A MULTICENTRE RANDOMISED CONTROLLED TRIAL.

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HYPOTHESIS / AIMS OF STUDY

Urinary Incontinence (UI) is involuntary leakage of urine, with lifetime prevalence for women about 30%. The multicentre randomised controlled trial (RCT) assessed whether standard pelvic floor muscle training (PFMT) for women with stress or mixed (stress and urgency) UI could be enhanced by the addition of electromyography biofeedback (BF). The RCT results showed no additional benefit of BF in UI outcomes observed at two-year follow-up. [1] Process evaluation research showed both RCT groups (PFMT versus PFMT + BF) received a well delivered high quality standard PFMT programme. [2,3] In this study we add to existing knowledge reported from the RCT, specifically investigating diary entries completed by women in response to their exercise prescription: findings not previously reported. Aims were to: quantitively summarise how much home PFMT women reported doing, creating an adherence metric; explore associations between women's self-report of PFMT and their PFMT prescription; identify baseline variables predicting self-reported PFMT adherence; explore and summarise barriers to PFMT adherence reported by women.

STUDY DESIGN, MATERIALS AND METHODS

For RCT details (inclusion/exclusion criteria, randomisation techniques and treatment protocols) see [1]. At each appointment women were issued diaries to complete and return at the next appointment. These were designed as clinical tools for recording exercise prescription with space for women to report their adherence and make free text comments. Prescriptions were summarised [3] and for this study were based on sets of repetitions (number in a set/length of hold) and number of sets per day (days per week also recorded). The PFMT + BF group were given a BF machine; its home use was incorporated into their prescription. Due to the complex nature of data this study focuses on analyses from 1st diaries returned (at the 2nd appointment) meaning only a subset of women from the RCT provided data: those who attended first follow-up, returned their completed diary, and had available prescription data.

Quantitative diary data were subjected to complex data cleaning processes prior to a mean exercise score calculation. These scores were compared to prescribed sets and times per day to create a percentage adherence metric for each woman. An 'a priori' conservative cut-point for adherence versus non-adherence was set at 50%; subsequent review of data meant two additional cut-points (65% and 80%) were added as exploratory analyses. The adherence metric was used in multivariable logistic regression models to determine whether any baseline characteristics (age (dichotomised), incontinence severity, incontinence type, number of deliveries) and treatment group allocation predicted exercise adherence. Free text entries were analysed using Thematic Content Analysis, to summarise barriers to PFMT adherence.

RESULTS

A total of 600 women were randomised, and 409 women returned their 1st diary. Mean adherence percentage was higher in the PFMT + BF group (131%) than the PFMT group (94%). Median adherence across two groups combined was 97%, suggesting women were overall highly adherent. Of the 409 women, only 15 (4%) were less than 50% adherent; 10% were less than 65% adherent to their exercise programme, hence addition of post hoc cut-off adherence thresholds of 65% and 80% for analyses.

Due to missing data when calculating the adherence metric, 395 women were included in regression analyses, 199 from the PFMT group, and 196 from the PFMT + BF group. Baseline characteristics were similar between women in the overall RCT versus this subset, and between the two groups in this subset. We studied baseline characteristics as predictors for adherence. A large percentage of women exhibited adherence at each threshold, with minimal differences between groups (PFMT was the exposure group and PFMT + BF the reference group in the models). Logistic regression modelling results at the 50% adherence threshold revealed only treatment group potentially predicting adherence with weak evidence (odds ratio = 2.8, 95% CI = 0.88; 9.98, p = 0.08). Modelling results at the 65% adherence threshold showed no statistically significant variables predicting adherence. At the 80% adherence threshold, there was little evidence to indicate that baseline characteristics were associated with adherence but there was moderate evidence (odds ratio = 1.75, 95% CI = 1.04, 2.95, p = 0.029) that when compared to the PFMT + BF group, those in PFMT group were less likely to adhere. The odds of non-adherence in the PFMT group were 1.8 times more likely than in the PFMT + BF group.

Thematic Content Analysis identified 7 themes arising from 20 categories. Common reasons for non-adherence to PFMT for both groups related to 'Illness, health and general wellbeing' and 'social and personal commitments'. Issues such as menstruation, stomach pain, back pain, urine leakage and general feelings of ill health were barriers to exercise adherence. 'Social and personal commitments' such as childcare, work and holidays were mentioned equally across both groups. Comments regarding problems with BF equipment occurred 57 times in the PFMT + BF group, a large proportion of their total comments. Despite being intended to increase exercise motivation, comments about BF suggested it caused unnecessary burden: problems with equipment, battery life and difficulty finding both time and privacy to use it.

INTERPRETATION OF RESULTS

Results indicate that women who completed and returned their first diary were highly adherent to the early phase of their PFMT programme, as might be expected. Despite some reported barriers, initial BF use was a positive influence when applying the stricter 80% adherence threshold, even though BF did not show an effect later in the RCT outcomes [1]. This in-depth examination of PFMT exercise diaries, from a large subset of women from the RCT, may help understanding of what factors determine adherence, albeit from the perspective of women reporting high levels of adherence. Learning from such positive (adherent) examples highlights potential importance of not just encouraging women to do their exercises but also to attend appointments, fill out and return their diaries. Even so, these women still encountered barriers to adherence; ill health in general and menstrual symptoms in particular, may warrant therapists discussing with women how to modify or restart their exercises. Research limitations include the degree to which this sample is representative given they were already demonstrating adherent behaviour (this potentially impacts representativeness: they are a self-selected rather than a random, sample) and means results must be interpreted with caution. There was variation in what women recorded, with some women appearing to report number of repetitions instead of sets (diary instructions asked for sets), and this may account for some of the very high levels of adherence. Some women made similar comments on multiple occasions; therefore, number of comments is not indicative of number of women who experience this problem. Finally, percentage cut-off thresholds used to distinguish adherence were initially conservative or decided post hoc, due to lack of research to draw upon when determining levels of therapeutic adherence. Next steps will assess adherence over subsequent appointments in the RCT, examining associations between the adherence metric and the RCT self-efficacy and UI outcomes. Future research could involve women to help better design exercise diaries to avoid variation in reporting and data cleaning problems.

CONCLUDING MESSAGE

Women in this study reported high levels of exercise adherence, and they had completed and returned their diaries: behaviours that also act as markers of adherence. For these women BF use may impact positively upon adherence at the start of their PFMT programme. Future research to improve methods of adherence measurement, including better diary design as research data collection tools, will enhance ability to quantify therapeutic adherence and link these adherence levels with clinical outcomes.

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Funding The OPAL (Optimizing Pelvic floor exercise to Achieve Long-term benefits) trial was funded by the National Institute of Health Research (NIHR) Health Technology Assessment programme. The NIHR Applied Research Collaboration South West Peninsula also supported SD's position at Exeter during this work. The views expressed are those of the researchers and not necessarily those of the NHS, the NIHR or the Department of Health and Social Care. **Clinical Trial** Yes **Registration Number** Trial registration: IS**RCT**N57746448. **RCT** Yes **Subjects** Human **Ethics Committee** The West of Scotland Research **Ethics Committee** 4 (NRS13/UR13) **Helsinki** Yes **Informed Consent** Yes

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TRAINING FOR MIDWIVES TO SUPPORT WOMEN TO DO THEIR EXERCISES DURING PREGNANCY. A MIXED METHOD EVALUATION OF THE MIDWIFE TRAINING DURING A FEASIBILITY AND PILOT RANDOMISED CONTROLLED TRIAL.

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HYPOTHESIS / AIMS OF STUDY
Urinary Incontinence (UI) affects around 30% of women after childbirth and in many cases can be prevented.(1) One of the biggest risk factors for women developing UI is pregnancy and childbirth.(1) Pelvic Floor Muscle Exercises (PFME) can be used for both prevention antenatally and as a treatment antenatally and postnatally.(1) However, an ethnographic study found that women do not have basic knowledge about their pelvic floor (2) and midwives lack confidence teaching PFME antenatally.(2) The study also described how local and national guidelines surrounding PFME lack clarity and consistency.(2) Yet, midwives are perfectly placed within the healthcare system to provide this kind of support during pregnancy.(2) A feasibility and pilot randomised controlled trial currently being conducted aims to increase the number of women practising PFME antenatally with the objective of preventing postnatal UI. To achieve this, midwives in the intervention arm of the trial received a training package about PFME and how to teach and support women to do their exercises along with resources for both themselves and the women in their care. This study aims to evaluate the feasibility and acceptability of the training package delivered to midwives during this trial, reporting the training evaluation for the first time.

STUDY DESIGN, MATERIALS AND METHODS
A mixed methods approach was used to collect and analyse data: training observations, Likert-scale questionnaires (pre- and post-training) and post-training qualitative interviews. During the training session observations, researchers used a checklist to assess the facilitator's fidelity to deliver the training according to the protocol. Participating midwives completed two questionnaires before the training session. A questionnaire, created for this study, gathered demographic information (years qualified as a midwife and working in the community and any previous PFME experience). A Confidence questionnaire recorded self-reported confidence scores on eight items: 1) Raising the topic of PFME; 2) Raising the topic of UI; 3) Understanding pelvic floor anatomy; 4) Assessing whether a woman is correctly able to do a pelvic floor muscle contraction; 5)Teaching a pregnant woman to do PFME; 6) Giving further advice about how to do PFME; 7) Referring women who cannot do a pelvic floor muscle contraction for further help; 8) Advising women on how to manage UI. The Confidence questionnaire was completed immediately before and also after the training session, allowing for a direct comparison of confidence scores per question pre- and post-training. Descriptive and inferential statistics were used to determine any significant changes in confidence after the training session. Midwives also completed an evaluation questionnaire post-training to assess the acceptability of the training content and delivery. Responses to six Likert-scale questions (0-10 response range, 10 = highly positive) about usefulness, content, delivery method, resources for women, resources for midwives and whether to recommend this training to other midwives) were summarised quantitatively and free-text responses summarised in categories. A subset of midwives consented to be interviewed about their experiences of the training session, the audio-recorded data were transcribed and analysed using qualitative Thematic Analysis.

RESULTS
71 midwives consented to take part in the training evaluation, with 13 participating in an interview. The average number of years working as a midwife and in the community were 11.3 (SD 9.2) and 6.2 (SD 6.4) respectively. Previous PFME experience varied, with half of midwives (50%) having no previous PFME training. The mean for the training session fidelity was 86.4% (SD 9.2%), although observation of an early training session revealed lower fidelity to the training protocol (75.8%) compared to sessions observed later (92.4%). A positive change in confidence occurred following training; the median change was at least +1 for every question. Wilcoxon signed-rank test detected a significant change in confidence for every question ($p < 0.001$). Figure 1 demonstrates high scores for overall acceptability of training content and delivery; free text responses endorsed this positive experience, many stated the training was informative and engaging, enhanced by use of mixed media and would make a difference to women's lives. Some expressed concerned about impediments to implementation: lack of time and language barriers. One main suggested improvement was to embed a prompt (to implement the training) in their clinical record software system.

From the interviews six main themes were identified: 1) Past Training and Experience varied but most reported little or no former training in PFME; 2) Acceptability of Online Delivery (Pros and Cons) which revealed polarising views reflecting difficulties faced due to COVID and poor internet connectivity which impacted group discussions, yet for some remote attendance was more convenient. 3) Midwives' Engagement (what enhanced and detracted from the training session) included the 'two-way' atmosphere created by the facilitators 'rather than just being lectured at'. 4) How the training influenced their PFME knowledge included improved PFME teaching skills and ability to ask questions about UI 'which I haven't asked about before' and referral knowledge 'I wouldn't have known what to do'. 5) Midwives' Attitude toward the Training was an enthusiasm for the training with midwives believing that PFME is an important topic to be raised antenatally, several midwives suggesting it should be part of standard care with mandatory training. The midwives were interested and keen to teach PFME, but the service delivery system stood in their way with insufficient appointment time; furthermore, inadequate PFME education at university left midwives ill-equipped to teach PFME effectively. 6) Suggestions to improve training. Many of the suggestions made were about changing the local and national system to accommodate for the training rather than actual changes to the training package.

INTERPRETATION OF RESULTS
High average fidelity demonstrated good feasibility of facilitators delivering the training according to the protocol. The training session showed immediate benefits with significant improvement in midwives' confidence observed for the key training package elements. Evaluation questionnaires and qualitative interviews indicated good overall acceptability of the training content and delivery. In line with the NHS 10 Year Long Term Plan (3), the training package supports midwives to provide women with up-to-date and accurate information on PFME, and to support them to do PFME throughout pregnancy.

CONCLUDING MESSAGE
This training programme equipped midwives with knowledge, confidence, and resources to help pregnant women take preventative measures against UI. Demonstrating good feasibility, effectiveness and most importantly acceptability amongst the intervention midwives, this investigation also highlighted some areas for improvement. For midwives who find online delivery methods difficult, enabling access to improved WIFI could help, and hybrid delivery models (with options for in-person training as was intended pre-pandemic) could be implemented for future training. Policy and system-level change is required to allow the training to reach its full potential,(2) and these changes are taking place.(3) Continuing attention is needed to ensure quality of training delivery and that evidence-based updates occur.

FIGURE 1

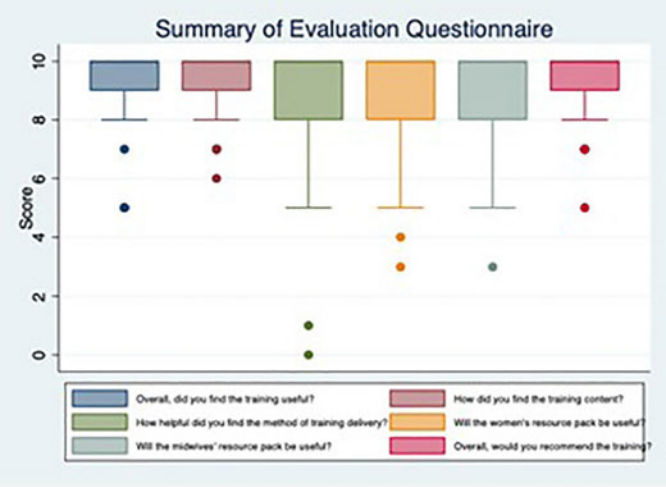

Figure 1: Evaluation Questionnaire results graph - summary of midwives' responses

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AN INTEGRATED APPROACH TO PELVIC AND WOMEN`S HEALTH SERVICES IN SOUTH AFRICA: WHAT ARE THE FACILITATORS AND BARRIERS?

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HYPOTHESIS / AIMS OF STUDY
Pelvic floor disorders are a common, but complex dysfunction which can be managed effectively at a primary care level using conservative treatment. First contact models of care have been shown to be effective in providing diagnostic evaluation and management of many patient conditions, improved access to care and reduction in specialist outpatient waiting lists. Global barriers to implement such models of care include cost of care and limited resources to providing integrated services at a primary care level (1). It requires a coordinated and multidisciplinary care structure which might be hard to implement due to challenges such as limited resources in middle to low income countries such as South Africa. This leads to patients not receiving optimal care and recovery post-interventions.

This study therefore aimed to explore the barriers and facilitators associated with an integrated approach to deliver pelvic and women`s health services within a South African context.

STUDY DESIGN, MATERIALS AND METHODS
In-depth interviews (n = 16) and a focus group (n = 8) were used to explore the opinions of clinicians, researchers, managers, patients and educationalists on the barriers and facilitators associated with an integrated approach to provide optimal pelvic and women`s health services within a diverse healthcare system in South Africa. Content thematic analysis was used to analyze and interpret the data. The data was coded to establish themes and sub-themes. Consequently it was indexed, tabulated and mapped to make links between the themes. The themes were grouped together into predetermined and emerging categories based on similarities in the context of the comments made by the participants.

RESULTS
Interviewees included five included physiotherapists, two urogynaecologists, two patients, three managers, one psychologist, dietitian and urologist, represented clinicians, researchers, postgraduate students, and educationalists. The focus group included health care practitioners within the private and public health care sector, two managers, two educationalists and two researchers in the field or urogynaecology. The mean age and the mean years of experience of the participants were 45.73 ± 14.95 years and 17.31 ± 12.73 years respectively. The major challenges seemed to be a lack of initiative to implement interprofessional collaborative clinics, a fear of compromising quality of patient care, rules and legislation regarding logistical aspects, and limited resources. The following were highlighted as facilitators and benefits of increasing implementation of interprofessional clinics: optimise use of existing resources; improved opportunities for clinical and skills training; outcomes can inform policy; it provides a platform for comprehensive and inclusive research strategies.

INTERPRETATION OF RESULTS
It seems as if the benefits may outweigh the barriers and that an integrated interprofessional model of patient care can lead to improved educational, research and clinical strategies to improve pelvic and women's health services within a South African context. There is evidence that with strategic implementation a pelvic health clinic led by advanced health care practitioners can be an effective model of care for management of urinary incontinence and pelvic organ prolapse, regardless of group or individual initial contact. It is successful in providing good clinical and service outcomes that are well accepted by patients and staff.

CONCLUDING MESSAGE
The concerns that were raised regarding challenges, can be overcome by means of creative planning, education and implementation strategies (2). Further research is needed to explore an optimal model for implementation.

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Funding National Research Foundation **Clinical Trial** No **Subjects** Human **Ethics Committee** Human Research **Ethics Committee** of the University of the Witwatersrand **Helsinki** Yes **Informed Consent** Yes

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AN 18-MONTH LONGITUDINAL QUALITATIVE STUDY OF WOMEN'S EXPERIENCES OF SELF-MANAGEMENT AND CLINIC-BASED CARE WHEN USING A PESSARY FOR VAGINAL PROLAPSE: ACCEPTABILITY, ADHERENCE AND OUTCOME

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HYPOTHESIS / AIMS OF STUDY
To investigate acceptability, adherence to treatment and pathways to effectiveness (quality of life) of a self-management intervention when compared to clinic-based care for women who use a vaginal pessary for pelvic organ prolapse.

STUDY DESIGN, MATERIALS AND METHODS
The study design was a qualitative case study (1) carried out in parallel to a randomised controlled trial. The intervention tested was self-management of a vaginal pessary for women with pelvic organ prolapse. The self-management intervention included a 30 minute teaching session, an information leaflet, a two-week follow up telephone call and a contact telephone number for the local centre. Following ethical approval, purposive maximum variation sampling (based on trial group [self-management or clinic-based care], variance in treating centre, user status [new/ existing pessary users], and age) was used to invite a subsample of women, who had consented to a randomised controlled trial, to take part in the case study. Interested women were sent written information about, and asked to consent to, the case study specifically. The data from each recruited woman formed one case. Women were interviewed at baseline and 18 months after randomisation. Interviews were semi-structured, digitally recorded and transcribed. Where possible, interviews were face to face and either at the participant's home or in the clinic. COVID-19 affected data collection in that no face-to-face interviews could be conducted after March 2020, and all remaining interviews were by telephone. Interviews explored women's experiences of: prolapse symptoms and pessary use, the intervention they received, adherence and outcome. Data analysis followed case study analytic traditions (1) whereby all data from a case were analysed and findings collected together to form a case summary with a focus on understanding a woman's experience of prolapse and pessary use, intervention, adherence and outcome and how these factors interacted. Case summaries were collated by group (self-management and clinic-based care), the groups were then qualitatively compared.

RESULTS
Sample: Thirty-six women, 18 per group, were recruited as planned; 23 women had data at both time points (12 self-management and 11 clinic-based care) and these cases formed the basis of the analysis, with 1392 minutes of interview data recorded. The age range of the recruited women was 49 to 72 years. Twelve women were new pessary users and 11 were existing users. Women were recruited across the 21 UK centres involved in the study.

Acceptability: Self-management was reported to be an acceptable intervention to women whether they received self-management or not. Women reported benefits of pessary self-management for women and health services, and valued the possibilities provided to women who could self-manage their pessary such as flexibility and independence in using the pessary as needed. Acceptability of self-management was supported by provision of a local telephone number for contact in case of concerns.

"I think everything is fine and as I say, if I have a problem, I know there's a number I can call which is…that gives you confidence as well, that you're not totally abandoned." (Case 22, self-management)

Adherence: Adherence varied considerably between individual women. There were examples of women who adhered completely to their self-management or clinic-based intervention throughout the 18 month follow up. There were those who adhered to some extent, and those who did not adhere at all (Table 1). Patterns of adherence to trial group were similar between self-management and clinic-based care.

Intervention adherence varied over time because of multiple contextual factors. Key facilitators of adherence for both trial groups were good general health and a supportive network. For the clinic-based care group a need for reassurance from a trained healthcare professional was a factor positively contributing to adherence. For women in the self-management group the desire to be in control and able to manage the pessary themselves was a positive factor. For example:

"So I was quite happy to go to the hospital because they just had a look to make sure everything was all right and I found that really quite reassuring." (Case 17, clinic-based care)

"It's just been feeling more empowered myself to take care of myself and to not have to go to the hospital as regularly, so every six months. Now, I can go annually. For me, that's just so much easier in terms of my lifestyle." (Case 21, self-management)

A key barrier to adherence was developing bothersome pessary complications.

Table 1: Case study examples of variation in adherence by treatment group

Pathways to Effectiveness (Quality of Life): As with adherence there was considerable variation in prolapse symptoms and quality of life at 18-month follow-up (Table 2). The pessary itself influenced women's quality of life, regardless of trial group. There were women who experienced good quality of life in both groups, with some women in the self-management group stating that their quality of life has improved beyond the symptom control of the pessary; and those with no improvement or / worsening symptoms.

Table 2: Case study examples of variance in quality of life at 18 months

The presence of pessary complications greatly affected quality of life of women using a vaginal pessary for their prolapse. For instance:

"… taking the pessary out in case that was causing or some cause of the urinary infections. So I actually had the pessary removed in March this year and certainly been no worse and I think probably better." (Case 03, clinic-based care)

Self-efficacy (confidence) influenced both adherence and quality of life. Women in the self-management group had different self-efficacy to those in the clinic-based group. For example, women in the self-management group felt more confident in addressing common problems with their pessary, such as discharge or slippage, on their own without the need for additional for appointments.

INTERPRETATION OF RESULTS
The acceptability of self-management makes it an intervention that is appropriate to offer in prolapse health services. A local support telephone number is an important part of the provision of those self-management services. There is an interaction between the context within which women live their lives, her confidence and ability to self-manage her pessary, her adherence and her quality of life outcomes. Recognition of, and understanding about, that interaction forms an integral part of the treatment counselling women need to self-manage their pessary.

CONCLUDING MESSAGE
Women find self-management of a vaginal pessary for prolapse an acceptable intervention. Adherence to vaginal pessary self-management and women's prolapse related quality of life are influenced by contextual factors in women's lives, the absence of pessary complications and a woman's self-efficacy to self-manage a pessary.

FIGURE 1

	Self-management	Clinic-based care
Fully adherent n = 9 (SM) n = 5 (SC)	**Case 21,** Changed pessary independently over the course of the trial	**Case 01,** attended all clinic appointments and did not change her pessary herself for the trial duration
Partially adherent n = 1 (SM) n = 5 (SC)	**Case 24,** changed to surgical pathway after 12 months due to developing bothersome complications	**Case 36,** attended all clinic appointments, but removed/reinserted pessary between these appointments to clean it
Non-adherent N = 2 (SM) N = 1 (SC)	**Case 30,** changed to clinic-based care after teaching appointment	**Case 08,** did not attend any clinic appointments, and self-managed her pessary over the entire trial period

Table 1: Case study examples of variation in adherence by treatment group

FIGURE 2

	Self-management	Clinic-based care
good	Case 78 Symptom control, SM eliminates painfulness of pessary removal, SM allowed her move house without having added worry of needing to arrange pessary care	Case 84 Pessary provided immediate symptom relief, allowing her to empty bladder, sleep through the night and improved sex life, values HCP input during clinic visits
moderate	Case 53 Partial symptom control due to pessary, SM increases wellbeing, but not to optimum level due to persistence of some symptoms	Case 04 Pessary provided symptom control, clinic-based care provided reassurance through visual checks, some discharge
poor	Case 24 Developed complications (bleeding), stopped SM and discontinued pessary use	Case 03 Developed recurring UTIs and discontinued pessary use, QoL better without pessary

Table 2: Case study examples of variance in quality of life at 18 months

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SESSION 3 - PHARMACOLOGY AND LUTS

Abstracts 19-30
09:05 - 10:35, Hall G
Chair: Prof Christopher Henry Fry (United Kingdom)

19 | www.ics.org/2022/abstract/19

CARBON MONOXIDE IN THE BRAIN SUPPRESSES THE MICTURITION REFLEX IN RATS

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HYPOTHESIS / AIMS OF STUDY

It is well known that high concentrations of carbon monoxide (CO) are toxic and affect the human physiological conditions such as oxygen delivery insufficiency of systemic organs and neural disturbances. But, today, CO is also recognized as an endogenous gaseous signaling molecule related to neuromodulator, tissue homeostasis maintenance, cytoprotection, vasomodulation, anti-inflammation and anti-apoptosis [1].

CO is formed during degradation of haem to biliverdin by haem oxygenase (HO) in the body including the lower urinary tract and the brain. There were a few reports showing roles of endogenous CO in the micturition reflex, especially as a relaxation factor in the urethral smooth muscle [2]. On the other hand, roles of CO in the brain in regulation of the micturition reflex remains unclear. In this study, to elucidate roles of brain endogenous CO in regulation of the micturition reflex, we investigated effects of centrally administered CORM-3 (a CO donor) and ZnPP (a non-selective inhibitor of HO) on the rat micturition reflex.

STUDY DESIGN, MATERIALS AND METHODS

Urethane anesthetized (0.8 g/kg, ip) male Wistar rats (350-450 g) were used. A catheter was inserted into the bladder from the bladder dome to perform continuous cystometry. Two hours after the surgery, intravesical instillation of saline at 12 ml/h was started to evaluate intercontraction intervals (ICI) and maximal voiding pressure (MVP). One hour after the start of cystometry, CORM-3 (1 or 10 nmol/rat), ZnPP (10 or 30 nmol/rat) or vehicle was intracerebroventricularly administered. In some rats, CORM-3 (10 nmol/rat) or ZnPP (30 nmol/rat) was intravenously administered through a catheter inserted into the femoral vein. Evaluations of ICI and MVP were continued 120 min after the administration. We also performed single cystometry (saline instillation rate at 12 ml/h) in some rats. After 4-5 times of single cystometry, ZnPP (30 nmol/rat) was intracerebroventricularly administered, then single cystometry was continued for 30 min after the administration. Next, effects of intracerebroventricular pretreatment with CORM-3 (10 nmol/rat) on intracerebroventricularly administered ZnPP (30 nmol/rat)-induced responses were investigated.

RESULTS

Intracerebroventricularly administered CORM-3 dose-dependently prolonged ICI and intracerebroventricularly administered ZnPP dose-dependently shortened ICI (Fig. A and B), without affecting MVP (data not shown). On the other hand, intravenously administered CORM-3 or ZnPP showed no significant effect on ICI or MVP (data not shown). Intracerebroventricularly administered ZnPP significantly reduced single-voided volume (Vv) and bladder capacity (BC) without affecting post-voiding residual volume (Rv) or voiding efficiency (VE) (Table). Intracerebroventricularly administered ZnPP-induced ICI shortening was cancelled by intracerebroventricular pretreatment with CORM-3 (Fig. C).

INTERPRETATION OF RESULTS

CORM-3-induced ICI prolongation was induced by intracerebroventricular, but not intravenous, administration, indicating that exogeneous CO derived from CORM-3 centrally suppressed the micturition reflex. ZnPP-induced ICI shortening was induced by intracerebroventricular, but not intravenous, administration, and intracerebroventricularly administered ZnPP induced reduction in Vv and BC without altering Rv or VE. These results suggest that ZnPP-mediated inhibition of HO in the brain may induce frequent urination through reduction in endogenous CO production. In fact, supplementation of CO by intracerebroventricular pretreatment with CORM-3 cancelled the intracerebroventricularly administered ZnPP-induced ICI shortening, indicating that brain endogenous CO play a suppressive role in regulation of the micturition reflex.

CONCLUDING MESSAGE

Endogenous CO in the brain centrally suppresses the micturition reflex in rats. Thus, brain endogenous CO could be a novel therapeutic target for patients who cannot obtain sufficient therapeutic effects from conventional medications on lower urinary tract dysfunctions.

FIGURE 1

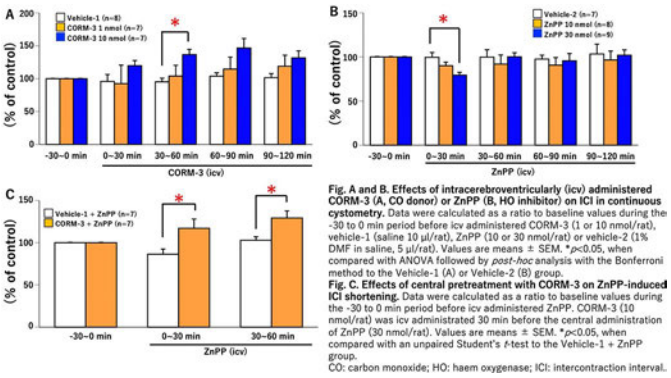

Fig. A and B. Effects of intracerebroventricularly (icv) administered CORM-3 (A, CO donor) or ZnPP (B, HO inhibitor) on ICI in continuous cystometry. Data were calculated as a ratio to baseline values during the -30 to 0 min period before icv administered CORM-3 (1 or 10 nmol/rat), vehicle-1 (saline 10 μl/rat), ZnPP (10 or 30 nmol/rat) or vehicle-2 (1% DMF in saline, 5 μl/rat). Values are means ± SEM. *p<0.05, when compared with ANOVA followed by *post-hoc* analysis with the Bonferroni method to the Vehicle-1 (A) or Vehicle-2 (B) group.
Fig. C. Effects of central pretreatment with CORM-3 on ZnPP-induced ICI shortening. Data were calculated as a ratio to baseline values during the -30 to 0 min period before icv administered ZnPP. CORM-3 (10 nmol/rat) was icv administrated 30 min before the central administration of ZnPP (30 nmol/rat). Values are means ± SEM. *p<0.05, when compared with an unpaired Student's t-test to the Vehicle-1 + ZnPP group.
CO: carbon monoxide; HO: haem oxygenase; ICI: intercontraction interval.

FIGURE 2

Table. Effects of intracerebroventricularly administered ZnPP on urodynamic parameters in single cystometry

	Before icv	After icv 0~30 min (%)
Vv	100.0 ± 0.0	84.2 ± 4.4*
Rv	100.0 ± 0.0	89.4 ± 8.5
BC	100.0 ± 0.0	89.7 ± 4.3*
VE	100.0 ± 0.0	95.8 ± 3.3

Data are calculated as a ratio to baseline values before intracerebroventricular administration of ZnPP (30 nmol/rat) (n=9). Values are means ± SEM. Vv: single-voiding volume, Rv; post-voiding residual volume, BC: bladder capacity, VE: voiding efficacy. *p<0.05, when compared with paired t-test to Before icv. BC: bladder capacity; CO: carbon monoxide; ; Rv: post-voiding residual volume; VE: voiding efficiency; Vv: single-voided volume.

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HYDROGEN SULFIDE PREVENTS CYCLOPHOSPHAMIDE-INDUCED BLADDER DYSFUNCTION IN RATS THROUGH SUPPRESSION OF BLADDER AFFERENT PATHWAYS

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HYPOTHESIS / AIMS OF STUDY
Cyclophosphamide (CYP), a non-specific broad-spectrum anticancer drug, causes serious and uncomfortable side effects in patients including hemorrhagic cystitis (HC). The cystitis is characterized by bladder inflammation and haemorrhage, pelvic pain, and lower urinary tract symptoms (LUTS) such as increased urinary frequency and urgency. These symptoms seriously affect the treatment tolerance and prognosis of patients undergoing chemotherapy with CYP [1]. However, before and during the chemotherapy, there are only symptomatic treatments for HC. Therefore, critical approaches for preventing CYP-induced cystitis are urgently needed.

Hydrogen sulfide (H2S) has recognized as a gasotransmitter and plays key roles in several physiological functions including vasodilation, anti-inflammation, antioxidation, cytoprotection [2]. Therefore, H2S has a possibility to be a promising therapeutic target for CYP-induced cystitis to improve tolerability of chemotherapy with CYP. However, effects of H2S on CYP-induced cystitis have not been investigated yet.

Therefore, in this study, we aimed to evaluate the effects of an H2S donor (NaHS) pretreatment on bladder dysfunction in rats with CYP-induced cystitis and elucidate mechanisms underlying the NaHS-induced effects.

STUDY DESIGN, MATERIALS AND METHODS
Male Wistar rats (290-320 g) were used.

(1) Study 1: Rats were divided into four groups: Vehicle + Saline (n = 8), Vehicle + CYP (n = 9), NaHS 3 + CYP (n = 10), and NaHS 10 + CYP (n = 8). The rats were treated with daily intraperitoneal (ip) injections of vehicle (saline, 1 ml/kg) or NaHS (3 or 10 μmol/kg) in saline solution for 7 days (day 1-7). CYP (150 mg/kg, ip) or saline (5 ml/kg, ip) had been injected two days before the cystometry (day 6).

(2) Study 2: Rats were divided into four groups: CAP(-) + Vehicle + CYP (n = 10), CAP (-) + NaHS 10 + CYP (n = 10), CAP(+) + Vehicle + CYP (n = 16), and CAP(+) + NaHS 10 + CYP (n = 15). Daily administration of vehicle (saline, 1 ml/kg) or NaHS (10 μmol/kg) and single administration of CYP (150 mg/kg, ip) were performed as the same in Study 1. To desensitize capsaicin (CAP)-sensitive afferent nerves, CAP solution containing 25 mg/ml CAP in 10% ethanol, 10% Tween-80 and 80% saline was subcutaneously (sc) injected at 125 mg/kg in divided doses on two continuous days (day 3 and 4): 25 and 50 mg/kg at a 12-h interval on the first day (day 3) and 50 mg/kg on the second day (day 4). Control rats received a corresponding volume of the solvent (10% ethanol, 10% Tween-80 and 80% saline). On day 8, before anesthesia and cystometry, eye wipe test by an eye drop of CAP solution (10 μl of 100 μg/ml) was performed to confirm CAP-induced desensitization of afferent pathways.

Cystometry was performed one day after the final administration of vehicle or NaHS (day 8). Under urethane anesthesia (0.8 g/kg, ip), a catheter was inserted into the rat bladder via the bladder dome. One hour after stabilization, single and continuous cystometry were performed by intavesical instillation of saline at a constant flow rate (4.0 ml/h) via the bladder catheter to measure intravesical pressure. After cystometry, bladder tissues were collected to perform HE staining.

RESULTS
(1) In continuous cystometry, compared to the control group (Vehicle + Saline), in the Vehicle + CYP group, the intercontraction intervals (ICI) and bladder compliance (Comp) were significantly decreased, and the number of non-voiding contractions (NVCs) was significantly increased (Table 1). In the NaHS 3 + CYP group, the number of NVCs was significantly decreased compared to the Vehicle + CYP group (Table 1). In the NaHS 10 + CYP group, ICI and Comp were significantly increased and the number of NVCs was significantly decreased compared to the Vehicle + CYP group (Table 1). In single cystometry, there was no significant difference in post-voiding residual volume (Rv) among four groups (data not shown). Based on these data, we performed histological analysis focusing on the following three groups: Vehicle + Saline, Vehicle + CYP, and NaHS 10 + CYP. In bladder tissues, CYP increased scores of neutrophile infiltration, haemorrhage, and oedema, but these CYP-induced changes were not significantly improved by NaHS pretreatment (Fig. 1).

(2) The number of eye wipes in response to an eye drop of CAP solution was significantly decreased by CAP pretreatment (Fig. 2). In continuous cystometry, CAP showed a tendency to increase ICI in vehicle- and CYP-treated rats (Table 2). NaHS-induced improvement of CYP-induced decreases in ICI and Comp and an increase in the number of NVC was not detected in CAP-treated rats (Table 2). In single cystometry, there was no significant difference in Rv among four groups (data not shown).

INTERPRETATION OF RESULTS
(1) CYP injection significantly decreased ICI and Comp and increased the number of NVCs without increasing Rv, suggesting that CYP successfully induced urinary frequency with low bladder distensibility and detrusor overactivity (DO) in rats. Both doses of NaHS significantly attenuated the CYP-induced increase in NVCs, suggesting that NaHS could suppress the CYP-induced DO. Moreover, NaHS at a dose of 10 μmol/kg also attenuated the CYP-induced decreases in ICI and Comp, indicating that NaHS partially improved the urinary frequency with low bladder distensibility in CYP-treated rats. However, in histological analysis, inflammatory scores increased by CYP were not influenced by NaHS in the bladder, indicating that another mechanism rather than anti-inflammation may be involved in NaHS-induced improvement of bladder dysfunction in CYP-treated rats.

(2) CAP-induced desensitization of bladder afferent pathways is reported to improve DO and hyperalgesia in interstitial cystitis [3]. H2S has a role as a neuromodulator [2], so we investigated mechanisms for NaHS-induced improvement of bladder dysfunction in CYP-treated rats focusing on CAP-sensitive bladder afferent pathways. In this study, CAP pretreatment successfully desensitized afferent pathways evidenced by CAP-induced decreases in the number of eye wipes in response to an eye drop of CAP solution. CAP pretreatment by itself showed a tendency to increase ICI without increasing Rv in vehicle- and CYP-treated rats, indicating that hyperexcitability of CAP-sensitive afferent pathways may be involved in the CYP-induced urinary frequency. In the CAP- and CYP-treated rats, NaHS-induced improvement of decreased ICI and Comp and increased the number of NVCs was not detected. Therefore, NaHS pretreatment may prevent bladder dysfunction (urinary frequency, low bladder distensibility and DO) in CYP-treated rats by suppressing CAP-sensitive bladder afferent pathways.

CONCLUDING MESSAGE
Our present data suggest that pretreatment with NaHS partially improved CYP-induced bladder dysfunction at least through suppression of CAP-sensitive bladder afferent pathways. Therefore, H2S donor pretreatment may be useful for prevention for bladder dysfunction induced by HC, a side effect of CYP chemotherapy.

FIGURE 1

Table 1. Urodynamic parameters in continuous cystometry

Group	ICI (sec)	Comp (ml/cmH_2O)	NVCs
Vehicle + Saline (n=8)	1726 ± 113	0.168 ± 0.015	0.5 ± 0.1
Vehicle + CYP (n=9)	415 ± 38*	0.053 ± 0.005*	8.4 ± 0.8*
NaHS 3 + CYP (n=10)	452 ± 54*	0.050 ± 0.005*	4.3 ± 0.5*#
NaHS 10 + CYP (n=8)	763 ± 73*#	0.092 ± 0.009*#§	4.2 ± 0.7*#

Vehicle + Saline: Wistar rats treated with vehicle (saline, 1 ml/kg/day, ip) and saline (5 ml/kg, ip); Vehicle + CYP: Wistar rats treated with vehicle (saline, 1 ml/kg/day, ip) and CYP (150 mg/kg, ip); NaHS 3 + CYP: Wistar rats treated with NaHS (3 μmol/kg/day, ip) and CYP (150 mg/kg, ip); NaHS 10 + CYP: Wistar rats treated with NaHS (10 μmol/kg/day, ip) and CYP (150 mg/kg, ip). Values are presented as means ± SEM. *P<0.05, when compared with the Bonferroni method (ICI and Comp) or non-parametric Kruskal-Wallis analysis (NVCs) to the Vehicle + Saline group; #P<0.05, when compared with the Bonferroni method (ICI and Comp) or non-parametric Kruskal-Wallis analysis (NVCs) to the Vehicle + CYP group; §P<0.05, when compared with the Bonferroni method to the NaHS 3 + CYP group Comp: bladder compliance; CYP: cyclophosphamide; ICI: intercontraction intervals; NVCs: non-voiding contractions.

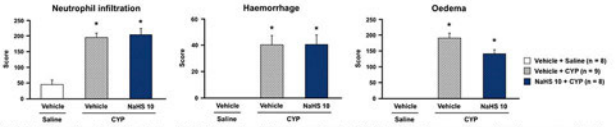

Fig. 1. Histological evaluation of bladder of rats with CYP-induced cystitis. Scores of neutrophils infiltration, haemorrhage and oedema were evaluated. Vehicle (saline, 1 ml/kg/day, ip) or NaHS (10 μmol/kg/day, ip) was pretreated once a day for 7 day. Saline (5 ml/kg, ip) or CYP (150 mg/kg, ip) was pretreated at day 6, and bladder tissues were collected at day 8. Values are means ± SEM. *P<0.05, when compared with non-parametric Kruskal-Wallis analysis to the Vehicle and Saline group. CYP: cyclophosphamide.

FIGURE 2

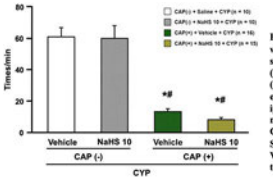

Fig. 2. Effect of CAP pretreatment on CAP-evoked eye-wiping responses. The number of eye wipes were evaluated within one minute after the administration of an eye drop of CAP solution (10 μl, 100 μg/ml). CAP(-) + Vehicle + CYP: Wistar rats treated with solvent of CAP (10% ethanol, 10% Tween 80 in saline, 2 ml/kg, sc), vehicle (saline, 1 ml/kg/day, ip) and CYP (150 mg/kg, ip); CAP(-) + NaHS 10 + CYP: Wistar rats treated with solvent of CAP (10% ethanol, 10% Tween 80 in saline, 2 ml/kg, sc), NaHS (10 μmol/kg/day, ip) and CYP (150 mg/kg, ip); CAP(+) + Vehicle + CYP: Wistar rats treated with CAP (125 mg/kg, sc), vehicle (saline, 1 ml/kg/day, ip) and CYP (150 mg/kg, ip); CAP(+) + NaHS 10 + CYP: Wistar rats treated with CAP (125 mg/kg, sc), NaHS (10 μmol/kg/day, ip) and CYP (150 mg/kg, ip). Values are means ± SEM. *P<0.05, when compared with non-parametric Kruskal-Wallis analysis to the CAP(-) + Vehicle + CYP group; #P<0.05, when compared with non-parametric Kruskal-Wallis analysis to the CAP(-) + NaHS 10 + CYP group. CAP: capsaicin; CYP: cyclophosphamide.

Table 2. Urodynamic parameters in continuous cystometry

Group	ICI (sec)	Comp (ml/cmH_2O)	NVCs
CAP(-) + Vehicle + CYP (n=10)	387 ± 61	0.066 ± 0.012	5.3 ± 0.6
CAP(-) + NaHS 10 + CYP (n=10)	765 ± 73*	0.123 ± 0.007*	3.0 ± 0.5*
CAP(+) + Vehicle + CYP (n=16)	614 ± 75	0.048 ± 0.004#	8.3 ± 1.0#
CAP(+) + NaHS 10 + CYP (n=15)	750 ± 94*	0.077 ± 0.013#	7.6 ± 1.2#

CAP(-) + Vehicle + CYP: Wistar rats treated with solvent of CAP (10% ethanol, 10% Tween 80 in saline, 2 ml/kg, sc), vehicle (saline, 1 ml/kg/day, ip) and CYP (150 mg/kg, ip); CAP(-) + NaHS 10 + CYP: Wistar rats treated with solvent of CAP (10% ethanol, 10% Tween 80 in saline, 2 ml/kg, sc), NaHS (10 μmol/kg/day, ip) and CYP (150 mg/kg, ip); CAP(+) + Vehicle + CYP: Wistar rats treated with CAP (125 mg/kg, sc), vehicle (saline, 1 ml/kg/day, ip) and CYP (150 mg/kg, ip); CAP(+) + NaHS 10 + CYP: Wistar rats treated with CAP (125 mg/kg, sc), NaHS (10 μmol/kg/day, ip) and CYP (150 mg/kg, ip). *P<0.05, when compared with the Bonferroni method (ICI and Comp) or non-parametric Kruskal-Wallis analysis (NVCs) to the CAP(-) + Vehicle + CYP group; #P<0.05, when compared with the Bonferroni method (ICI and Comp) or non-parametric Kruskal-Wallis analysis (NVCs) to the CAP(-) + NaHS 10 + CYP group. CAP: capsaicin; Comp: bladder compliance; CYP: cyclophosphamide; ICI: intercontraction intervals; NVCs: non-voiding contractions.

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INHIBITORY EFFECTS OF VIBEGRON, A Β3-ADRENOCEPTOR AGONIST, ON THE MYOGENIC CONTRACTILE AND MECHANOSENSITIVE AFFERENT ACTIVITIES IN AN OBSTRUCTED RAT BLADDER

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HYPOTHESIS / AIMS OF STUDY

β3-Adrenoceptor (β3-AR) agonists have been widely used to treat overactive bladder syndrome (OAB), and vibegron is a newly approved β3-AR agonist. It has been reported that β3-AR agonists including vibegron can inhibit non-voiding contractions (NVCs) of the hypertrophied bladder in rats with bladder outlet obstruction (BOO) [1]. Moreover, bladder myogenic microcontractions, which may be similar to NVCs, possibly link to the single-unit mechanosensitive afferent activities (SAAs) of Aδ-fiber, and mirabegron, another another β3-AR agonist, inhibit the afferent activities through the suppression of the microcontractions in normal rats [2]. In addition, SAAs of Aδ- and C-fibers were intermittently enhanced by propagation of bladder myogenic microcontractions in BOO rats [3]. In the present study, we investigated the effects of vibegron on bladder function, specifically on NVCs in cystometry (CMG) and bladder mechanosensitive SAAs. These functions are associated with myogenic microcontractions in a male rat model of BOO. Additionally, an immunohistochemical assay can be used to determine the site of β3-ARs expression in the bladder and whether their expressions relate to substance P (SP), a sensory neuropeptide.

STUDY DESIGN, MATERIALS AND METHODS

Male Wistar rats were used (10-12 weeks old). The proximal urethra was tightly ligated with a steel rod (1.1 mm in diameter), then the rod was removed. Ten days after the surgical procedure, CMG and SAA measurements were taken under two distinct conditions.

Single CMG measurements were performed under a conscious-restrained condition. A PE-50 catheter with a cuff was implanted into the bladder three days before the measurements. Saline was instilled into the bladder at a rate of 6 mL/h until micturition occurred, and voided urine was collected. CMG recordings were repeated three times both before and after the intravenous (i.v.) administration of vehicle or vibegron (3 mg/kg). The following parameters were averaged and analyzed: basal pressure, threshold pressure, maximum voiding pressure, mean voided volume, residual volume, bladder capacity, and the mean amplitude and the number of NVCs. NVCs were bladder contractions without micturition, which were characterized by amplitudes greater than 2 cm H2O observed for 3 min preceding micturition.

SAAs measurements were performed under a urethane-anesthetized condition (1.0 g/kg, intraperitoneally). Bilateral L6 dorsal roots were transected via a laminectomy. The fine filaments were dissected from the left L6 dorsal roots and placed across a bipolar electrode for monitoring SAAs. Nerve fibers primarily originating from the bladder were identified by electrical stimulation of the left pelvic nerve and by bladder distension. Nerves with conduction velocities (CV) more than 2.5 m/s were designated as Aδ-fibers and those with CV less than 2.5 m/s as C-fibers. Saline instilled until the intravesical pressure reached 30 cmH2O. The bladder was kept under an isovolumetric condition, allowed to stabilize for 5 min, and then vehicle or vibegron (3 mg/kg) was administered i.v. and recording was performed for 5 min. Mean bladder pressure, number of microcontractions and SAAs were analyzed.

In the separates rats, the expression of β3-adrenoceptor and substance P (SP), a sensory neuropeptide, in the bladder was further evaluated following immunohistochemical procedures.

RESULTS

In the CMG measurements, all numeric values of CMG parameters were unchanged before and after vehicle administration. However, the bladder capacity and number of NVCs were significantly increased and decreased, respectively, following vibegron administration (Table 1 middle line). For comparison between vehicle and vibegron groups, data were converted into relative values after each administration (% of each before administration). In this comparison, the number of NVCs in the vibegron group was significantly decreased compared with that in the vehicle group (Table 1 bottom line).

In the SAAs measurements, in the vehicle group, 22 afferent fibers were detected (Aδ-fibers: n = 11, CV: 6.32 ± 1.49 m/s; C-fibers: n = 11, CV: 1.99 ± 0.10 m/s). In the vibegron group, 19 afferent fibers were detected (Aδ-fibers: n = 10, CV: 4.04 ± 0.69 m/s; C-fibers: n = 9, CV: 1.91 ± 0.19 m/s). Values of mean intravesical pressure and amplitude of microcontractions after vehicle administration were significantly decreased, suggesting the suppression of the intravesical pressure time-dependently under an isovolumetric condition. In contrast, the number of microcontractions and mean firing rates of Aδ-fibers and C-fibers were unchanged before and after vehicle administration, whereas the number of microcontractions and firing rates of Aδ- and C-fibers were significantly decreased following vibegron administration (Figure 1AB). For comparison between vehicle and vibegron groups, data were converted as relative values after each administration (% of each before administration), same as CMG parameters. In this comparison, mean intravesical pressure, the number of microcontractions, and the firing rates of Aδ- and C-fibers in the vibegron group were significantly decreased compared with those in the vehicle group.

Immunohistochemical evaluation was conducted to investigate the expression change of β3-AR in BOO rats. We confirmed that this BOO rat showed hypertrophic smooth muscle regions compared with those in the sham rat. Immunoreactivity (IR) of β3-AR in both sham and BOO rats was stronger in the urothelium- and suburothelium-layers rather than in smooth muscle regions, which were not changed between groups. Moreover, the IR of SP in sham and BOO rats was stronger in the suburothelium layer. These expressions were unlikely different between groups. Merged plates for β3-AR and SP depicting co-expression (yellow) were similarly shown in the suburothelium layer in both groups (Figures 1C).

INTERPRETATION OF RESULTS

Vibegron decreased NVCs and microcontractions, thus suggesting that vibegron can inhibit bladder myogenic contractile activities in BOO rats. Additionally, the present SAAs measurements showed an inhibitory effect of vibegron on the SAAs of Aδ- and C-fibers. Immunohistochemical assays confirmed the co-expression of SP and β3-AR in the suburothelium layer at a small portion, an expression similar between sham and BOO rats. This finding also shows that β3-ARs contribute to the sensory bladder function.

CONCLUDING MESSAGE

These findings are the first to suggest that vibegron can inhibit the mechanosensitive afferent transduction via Aδ- and C-fibers, at least partly by suppressing bladder myogenic contractile activities on OAB associated with BOO.

FIGURE 1

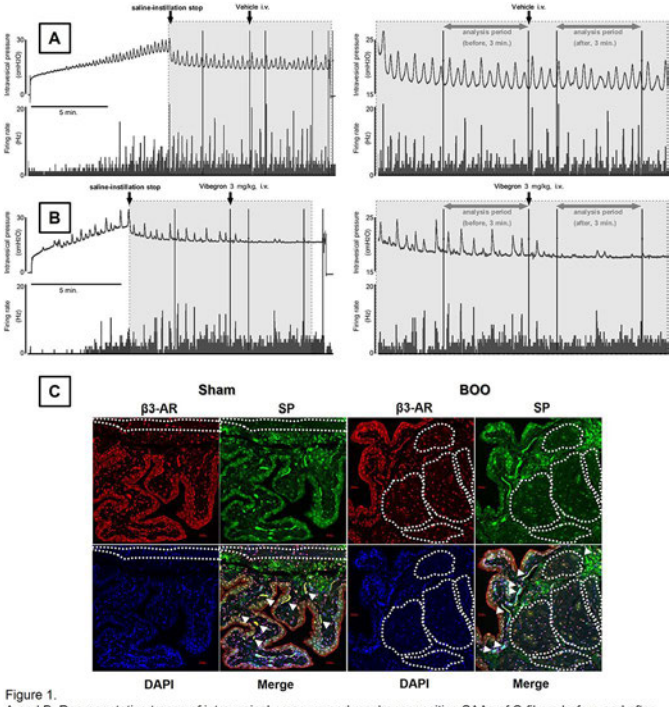

Figure 1.
A and B. Representative traces of intravesical pressure and mechanosensitive SAAs of C-fibers before and after vehicle (A) or vibegron (B) administration under an isovolumetric condition
Each gray-square in left panel is corresponding to the right panel.
C. Representative immunohistochemical stainings (×200) of the urinary bladder in Sham (left) or BOO (right) rat
White circles were indicated as smooth muscle regions.
White arrows were indicated as co-expression of β3-AR and SP.

FIGURE 2

Table 1. Body and bladder weight between groups, and CMG parameters before and after vehicle or vibegron intravenous administration

		Body weight (gram)						Bladder weight at day 10 (mg)	
		at BOO creation (day 0)		at catheterization (day 7)		at CMG (day 10)			
Vehicle (N = 7)		263.3 ± 2.5		266.1 ± 4.5		247.3 ± 6.7		543.1 ± 55.6	
Vibegron (N = 7)		273.6 ± 3.2		257.4 ± 6.3		246.4 ± 8.2		494.1 ± 78.8	
CMG parameters (Numeric values)		Basal pressure (cmH_2O)	Threshold pressure (cmH_2O)	Maximum voiding pressure (cmH_2O)	Bladder capacity (ml)	Mean voided volume (ml)	Residual volume (ml)	NVCs Amplitude (cmH_2O)	NVCs Numbers (times)
Vehicle	Before	8.59 ± 0.54	11.67 ± 0.93	52.06 ± 2.33	1.08 ± 0.19	0.60 ± 0.15	0.48 ± 0.17	7.16 ± 1.33	4.86 ± 0.76
	After	8.28 ± 0.54	12.16 ± 1.24	52.79 ± 4.57	1.11 ± 0.22	0.64 ± 0.15	0.47 ± 0.14	6.74 ± 0.86	4.52 ± 0.84
Vibegron	Before	10.61 ± 1.71	14.64 ± 2.67	60.63 ± 6.34	1.43 ± 0.49	0.57 ± 0.22	0.85 ± 0.57	7.15 ± 1.22	5.10 ± 0.74
	After	9.54 ± 1.30	14.36 ± 2.79	57.32 ± 7.77	1.58 ± 0.49*	0.68 ± 0.28	0.90 ± 0.56	6.56 ± 1.47	2.33 ± 0.64**
CMG parameters (Relative values of after administration)		Basal pressure	Threshold pressure	Maximum voiding pressure	Bladder capacity	Mean voided volume	Residual volume	NVCs Amplitude	NVCs Numbers
		(% of each before administration)							
Vehicle		96.4 ± 2.0	104.7 ± 8.6	100.5 ± 6.8	102.2 ± 6.6	112.5 ± 16.9	123.3 ± 32.6	129.6 ± 39.0	95.0 ± 8.6
Vibegron		91.5 ± 3.5	97.3 ± 2.7	92.9 ± 4.5	115.9 ± 5.7	133.7 ± 23.2	115.8 ± 7.3	80.3 ± 9.8	40.8 ± 8.0##

Values are expressed as mean ± SEM.
*P<0.05, **P<0.01: significant differences from before administration (paired Student's t-test)
##P<0.01: significant difference from vehicle group (Mann-Whitney U-test)

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TMEM16A CHLORIDE CHANNEL ACTIVATOR CAN INCREASE THE VOIDING PRESSURE AND SHORTEN THE INTERCONTRACTION INTERVAL DURING CYSTOMETRY IN RATS WITH METABOLIC SYNDROME INDUCED ACONTRACTILE DETRUSOR

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HYPOTHESIS / AIMS OF STUDY

The pharmacotherapy for acontractile detrusor (AD) is still disappointing. Previous studies have demonstrated the functional role of calcium activated chloride channel (CaCC) on bladder smooth muscle. We investigated the effects of activation of TMEM16A, a CaCC, on detrusor strips and voiding cycle presented in cystometry (CMG) using a model of metabolic syndrome (MetS) induced AD in rats.

STUDY DESIGN, MATERIALS AND METHODS

Fructose feeding rats were fed a fructose rich diet while control animals received standard rat chow for 6 months. Based on the results of cystometric presentation at month 6, rats in NDF group (normal detrusor function) and AD group were selected. We conducted a strategy using a TMEM16A activator (N-(2-methoxyethyl)-N-(4-phenyl-2-thiazolyl)- 2,3,4-trimethoxybenzeneacetamide (Eact)) as a reagent to involve ①Organ bath isometric tension experiments of harvested bladder smooth tissue to construct concentration-response curve (CRC). ②Continuous infusion CMG under anesthesia with replacement of infused physiological saline by Eact solution at different concentrations. The results of CRC and the CMG parameters including maximum bladder voiding pressure (MBVP) and intercontraction interval (ICI) were recorded and compared among control, NDF and AD groups.

RESULTS

①Administration of Eact could induce contractions on isolated rat detrusor in control, NDF, and AD groups. The tension increased as the concentration of Eact increased (Figure 1A). The ED80 for Eact was 1.7x10-5M. ②The reduced MBVP in AD group could be significantly potentiated by intravesical treatment of Eact (≧1X10-4M) in a concentration dependent manner. The MBVP in NDF and control groups could also be significantly enhanced by intravesical treatment of Eact (both ≧1X10-4M) (Figure 1C). The prolonged ICI in UAB group could be significantly shortened by intravesical treatment of Eact (≧1X10-5M) in a concentration dependent manner while the ICI in NDF and control groups could be significantly lengthened (Figure 1D).

INTERPRETATION OF RESULTS

In our organ bath study, rat detrusor contractions could be induced by treatment of Eact in AD group in a concentration dependent manner. In the continuous infusion CMG study, significantly decreased MBVP and increased ICI could be found in AD group which could also be ameliorated by intravesical administration of Eact in a concentration dependent manner. Both in vitro and in vivo studies showed the positive effect of TMEM16A chloride channel activator on bladder contraction in rats with MetS induced AD.

CONCLUDING MESSAGE

This study demonstrated activation of TMEM16A CaCC can “reverse” the decreased voiding pressure and prolonged intercontraction interval of cystometry in rats with MetS induced AD, indicating the novel therapeutic target of TMEM16A CaCC for AD.

FIGURE 1

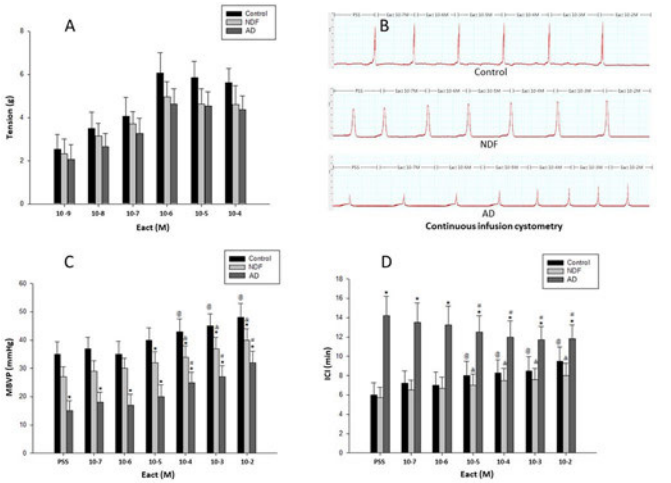

Figure 1. The concentration responses of TMEM16A activator (Eact) on organ bath experiments of bladder smooth muscle (A) and continuous infusion cystometry (B, C, D) in control, NDF and MetS induced AD rats (n=6 in each experiment). NDF: normal detrusor function. AD: acontractile detrusor. MBVP: maximum bladder voiding pressure. ICI: intercontraction interval.
* p< 0.05 when compared with control group. @&# p< 0.05 when compared with baseline CMG using PSS solution in each group.

Figure 1.

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THE SOLUBLE GUANYLATE CYCLASE ACTIVATOR BAY 60-2770 RESTORES PURINOCEPTOR-INDUCED BLADDER CONTRACTIONS IN A RAT MODEL OF CHRONIC PROSTATITIS

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HYPOTHESIS / AIMS OF STUDY

Chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS) is one of the most challenging urological diseases, due to its complex and unclear aetiology and the poor efficacy of current pharmacological treatment options. Phosphodiesterase 5 (PDE5) inhibitors have shown promising effects in the treatment of lower urinary tract symptoms. However, unwanted side effects have led many researchers to focus on alternative drugs that modulate the nitric oxide/cyclic guanosine monophosphate (NO/cGMP) signalling pathway. In the detrusor, NO causes cGMP accumulation and muscle relaxation by activation of the enzyme soluble guanylate cyclase (sGC). Oxidative stress conditions, for instance chronic inflammatory diseases like CP/CPPS, lead to the oxidation of sGC. In it oxidized state, NO is unable to activate sGC. However, sGC activators such as BAY 60-2770 can overcome this and activate the sGC enzyme in a NO independent manner [1].

The aim of the current study was to examine how innate bladder contractility as well as purinergic and cholinergic receptor expression is affected by induction of CP/CPPS and how this, in turn, is impacted by treatment with the sGC activator BAY 60-2770.

STUDY DESIGN, MATERIALS AND METHODS

In the current study, 24 adult male Sprague-Dawley rats (350-500 g; Charles River Laboratories, Calco, Italy) were used. The animals were randomly divided into four groups (n = 6 per group). In group 1 and 2, vehicle (10 µl sterile saline) was injected directly into the dorsal lobe of the prostate, serving as control. In group 3 and 4, rats were intraprostatically injected with zymosan (0.1 mg in 10 µl sterile saline), to create a functional model for CP/CPPS. Thereafter, the rats were allowed to recover for 7 days. On days 8-20, the rats were given daily subcutaneous injections with either dimethylsulfoxide (DMSO; 0.05 ml*day-1; serving as control; Gr1 & Gr3), or BAY 60-2770 (0.5 mg*kg-1*day-1; dissolved in 99.5% DMSO; Gr2 & Gr4). On day 21, the animals were euthanized, their bladder was excised, and ex vivo organ bath experiments were performed in which the contractile responses to electrical field stimulation (EFS), the cholinergic agonist methacholine (MeCh) and the purinergic agonist ATP were examined. Subsequently, the urinary bladder was examined immunohistochemically for purinergic (P2X1 & P2X3) and cholinergic (M3) receptor expression.

Statistical calculations were performed using GraphPad Prism version 9.3.1 (GraphPad Software Inc., San Diego, USA). Two-way ANOVA followed by Bonferroni`s post-hoc test for multiple comparisons was used for statistical comparisons of organ bath data. Immunohistochemical findings were statistically compared using the Kruskal-Wallis test for non-parametric comparisons. Subsequently, Dunn`s multiple comparisons test was used to compare the difference in the sum of ranks between each group. Statistical significance was regarded for p-values < 0.05.

RESULTS

Induction of CP/CPPS did not significantly change the bladder contractile responses to EFS (Fig 1a) or MeCh (Fig 1b). However, induction of CP/CPPS significantly reduced ATP-induced bladder contractions, as compared to controls (Fig 1c). In tissues from animals in which CP/CPPS was induced, treatment with BAY 60-2770 led to significantly increased contractile bladder responses to EFS (Fig 2a) and MeCh (Fig 2b). Further, treatment with BAY 60-2770 restored alterations in ATP-induced bladder contractions caused by induction of CP/CPPS (Fig 2c). There were no significant differences between the groups regarding purinergic (P2X1 & P2X3) or cholinergic (M3) receptor expression in the bladder urothelium or detrusor.

INTERPRETATION OF RESULTS

The current study demonstrated that induction of chronic inflammation in the prostate led to reduced ATP-induced isolated bladder contractions. This finding is consistent with previous in vivo studies on cross-sensitization between the prostate and bladder and the potential effects of CP/CPPS on bladder function [2]. The present study demonstrated no significant differences between the groups regarding purinoceptor (P2X1 and P2X3) expression in the bladder. Thus, these findings indicate that induction of prostatitis leads to alterations in bladder purinoceptor sensitivity and/or down-stream purinergic signaling. The currently demonstrated effect of chronic prostate inflammation on ATP-induced bladder contractions may be of particular interest since it has previously been shown that ATP can act as a modulator of release of other neurotransmitters that have a role in bladder contractility and afferent nerve activity [3].

It has previously been shown that induction of chronic prostate inflammation can lead to reduced MeCh-induced bladder contractions [2]. However, in the current study, the induction of chronic prostatitis did not lead to significant changes in muscarinic receptor-induced bladder contractions. The discordance between the current study and previous studies could be explained by the fact that previous studies had an in vivo set up while the current study utilized an ex vivo organ bath setup to examine receptor-induced bladder contractile responses. The current study was purposely designed to examine the potential effects of CP/CPPS on muscarinic and purinergic contractile responses in the isolated bladder. In an in vivo set up, the alterations in bladder function could also be affected by possible changes in prostate or urethral contractility as well as in afferent and efferent nerve signaling. Further, the present study aimed to examine the effects of sGC activators, which was not investigated in vivo.

The current study showed that after induction of chronic prostate inflammation, treatment with the sGC activator BAY 60-2770 led to increased EFS- and MeCh-induced bladder contractions. Likewise, treatment with BAY 60-2770 led to increased purinergic contractile responses. However, the purinergic responses are small in magnitude in comparison to the cholinergic responses. The observed alterations did not appear to be due to receptor up-regulation since there were no differences between the groups regarding receptor expression. Considering this, the increase in EFS-induced bladder contractions after BAY- 60-2770 treatment observed in animals in which chronic prostatitis was induced is likely due to changes in muscarinic receptor sensitivity and/or down-stream cholinergic signaling.

CONCLUDING MESSAGE

To the best of our knowledge, the current study is the first that examines how contractile properties of the isolated detrusor are affected by induction of CP/CPPS and a subsequent treatment period with a sGC activator. Induction of CP/CPPS led to reduced ATP-induced bladder contractions. This alteration was restored by treatment with the sGC activator BAY 60-2770. Even though further studies are required to better understand the mechanisms behind BAY 60-2770's effects on purinergic and cholinergic responses in the cross-sensitized bladder, the current findings indicate that drugs targeting the NO/cGMP pathway might be a promising option to restore alterations in bladder function due to CP/CPPS.

FIGURE 1

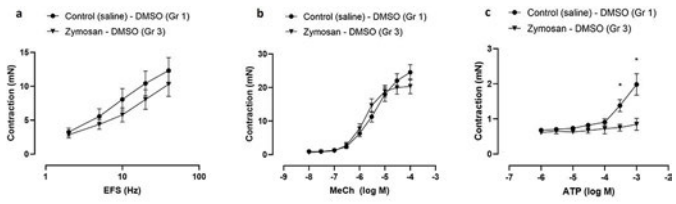

Figure 1. Contractile bladder responses to electrical field stimulation (EFS), methacholine (MeCh), and adenosine 5'- triphosphate (ATP) in Group 1 (intraprostatic saline – s.c. DMSO) and Group 3 (intraprostatic zymosan - s.c. DMSO) during organ bath experiments. Induction of chronic prostate inflammation (Gr 3) did not significantly alter the contractile responses to (a) EFS or (b) MeCh, as compared to controls. (c) Induction of chronic prostatitis caused a significant decrease in bladder contractile responses to ATP compared to controls at higher concentrations of ATP. Values are shown as mean ± SEM. Statistical comparisons were made by two-way ANOVA followed by Bonferroni's test for multiple comparisons, n = 6. * denotes p-value < 0.05.

Figure 1

FIGURE 2

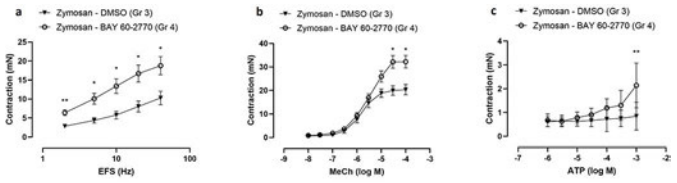

Figure 2. Contractile bladder responses to electrical field stimulation (EFS), methacholine (MeCh), and adenosine 5′- triphosphate (ATP) in Group 3 (intraprostatic zymosan - s.c. DMSO) and Group 4 (intraprostatic zymosan - s.c. BAY 60-2770) during organ bath experiments. (a) Two-week daily subcutaneous treatment with BAY 60-2770 led to significantly increased contractile bladder responses to EFS. (b) Contractile responses to high concentrations of MeCh were significantly higher in Gr 4 compared to Gr 3. (c) Contractile responses to ATP were significantly higher in Gr 4 compared to Gr 3 (1×10^{-3} M, p=0.005). Values are shown as mean ± SEM. Statistical comparisons were made by two-way ANOVA followed by Bonferroni's test for multiple comparisons, n = 6. * denotes p-value < 0.05.

Figure 2

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SOLUBLE GUANYLATE CYCLASE DEPENDENCY OF AQUEOUS NO FUNCTIONAL RESPONSES IN HEALTHY AND INFLAMED RAT URINARY BLADDER

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HYPOTHESIS / AIMS OF STUDY

Functional effects of nitric oxide (NO) have in the urinary bladder been suggested to be mediated through a signaling pathway involving soluble guanylate cyclase (sGC) and cyclic guanosine monophosphate (cGMP), in turn modulating Ca2+-channels (1). The present study examines cGMP-dependent responses to aqueous NO in healthy and inflamed rat urinary bladder (detrusor) smooth muscle preparations.

STUDY DESIGN, MATERIALS AND METHODS

Thirty-six male Sprague-Dawley rats (210–510 g; Charles-River, Calco, Italy) were used, receiving either no treatment (serving as controls) or an intraperitoneal injection with cyclophosphamide (CYP; 100 mg/kg) 60 h before the experiment, in order to chemically induce cystitis. Rats were euthanized with an overdose of pentobarbitone, and the bladders were excised and stored in oxygenated Krebs solution at all times.

Two full-thickness strips, approximately 6×2 mm, excised proximal to the ureters and above the trigone, were prepared from each bladder. The preparations were mounted in 20 mL organ baths filled with Krebs solution (gassed with 5% CO2 in 95% O2 at a temperature of 37°C), stretched to approximately 10 mN, and let to equilibrate for 45 minutes, obtaining a basal tension of about 5 mN. Functional responses were recorded using the MP100WSW data acquisition system and the AcqKnowledge software (Biopac Systems, Goleta, USA).

Argon was used to remove traces of oxygen before pure NO was led through deoxygenated NaOH and water. The production of aqueous NO solution was done as per a published protocol (2), where vials containing, in sequence, pyrogallol (10 mM), NaOH (10 mM), and de-ionized water were set up in an airtight manner. The resulting solutions contained a calculated NO concentration of 2 mM (2).

Functional responses to NO (4, 10, 20, 40 μM) were studied in the absence and presence of the sGC inhibitor ODQ by cumulative addition to the organ baths in methacholine (3 μM) pre-contracted healthy or inflamed bladder strips. Viability was assessed by addition of methacholine (50 μM) or high K+ Krebs solution (124 mM) at the beginning and end of every experiment. Aqueous NO (2 mM) was administered in close proximity of the tissue in the organ bath using a 1000 μL gas-tight Hamilton syringe in volumes of 40, 100, 200 or 400 μL. When employing ODQ, it was added to the baths and let to equilibrate for approximately 20 minutes before adding the NO solution.

Statistical significance was determined by two-way ANOVA followed by Sidak's test for multiple comparisons using the GraphPad Prism 9 software (GraphPad Software Inc., San Diego, USA). p-values < 0.05 were considered statistically significant. Data are presented as mean ± SEM.

RESULTS

Aqueous NO solution (40, 100, 200, and 400 μL, corresponding to final concentrations of 4, 10, 20, and 40 μM in the baths) induced concentration-dependent relaxations in methacholine (3 μM) pre-contracted rat detrusor strips, e.g., ranging from -0.85 ± 0.18 mN to -1.47 ± 0.29 mN in the control group, and -0.84 ± 0.22 mN to -1.42 ± 0.29 mN in the CYP-treated group (Fig 1a, b). The relaxation to NO was statistically significantly abolished in the presence of a high concentration of the sGC inhibitor ODQ (25 μM), and a trend showing a shift towards a contractile response was instead observed, most prominently in the control group.

In contrast, in the presence of a low concentration of ODQ (0.25 μM), the relaxatory responses to NO were not abolished. Instead, a slightly greater NO relaxation was observed ($p = 0.026$ at 10 μM in the CYP-treated group; Fig 1d). The median difference between relaxatory responses in the absence vs. presence of the low concentration of ODQ was 10% in the control group (Fig 1c) and 14% in the CYP group (Fig 1d).

INTERPRETATION OF RESULTS

The present results confirm previous findings and demonstrate that the method to produce aqueous NO solution is robust and can be used to study direct functional nitrergic effects. While no statistical comparisons were presently made between controls and the CYP (inflamed) group, it was evident that both groups displayed relaxatory responses to NO and that the sGC inhibitor, ODQ, abolished these responses. This finding was further strengthened by the lack of effect seen when adding the sGC inhibitor at a lower concentration, displaying a pharmacological concentration dependency of this effect.

The fact that ODQ was shown to block the relaxatory response evoked by NO confirms the hypothesis that nitrergic relaxations in the detrusor to a large extent are mediated through a cGMP-dependent pathway. These findings are in accordance with previous studies where ODQ has been shown to block NO donor responses in the rat urinary bladder (3). Thus, the present results strengthen the conclusion that aqueous NO can be readily produced and used for functional pharmacological studies, acting in a specific manner on sGC. Work remains to further investigate the details of which downstream pathways that are involved. Finally, the current study suggests that the sGC-mediated pathway is important also during cystitis, although further investigations should be conducted to scrutinize possible changes in detail.

CONCLUDING MESSAGE

The present study succeeded in demonstrating that NO in aqueous solution evokes a functional relaxation in rat detrusor strip preparations and that the relaxation is mediated via sGC and the subsequent production of cGMP. Furthermore, this pathway seems to be equally important also in cystitis. However, further studies should assess possible changes in nitrergic signaling in the inflamed urinary bladder.

FIGURE 1

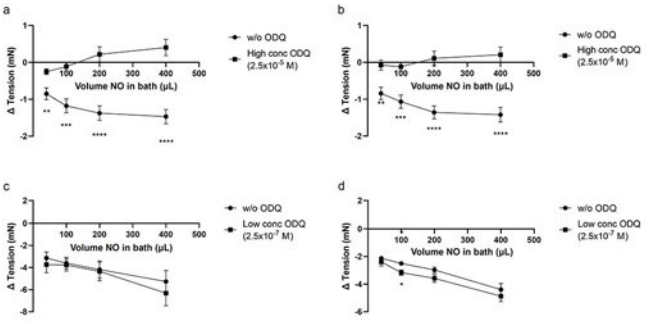

Fig 1. Functional nitrergic responses in the absence (•) and presence (■) of high (a, b) or low (c, d) concentrations of the soluble guanylate cyclase inhibitor ODQ. Responses to cumulatively increasing concentrations of NO (40, 100, 200, 400 μL) in healthy (a, c) and inflamed (b, d) bladder tissues. n=21 (a), n=22 (b) and n=12 (c, d). Vertical bars represent SEM. * denotes p<0.05, ** denotes p<0.01, *** denotes p<0.001, **** denotes p<0.0001.

Fig 1. Functional nitrergic responses

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THE ROLE OF THE MUCOSA IN MEDIATING SPONTANEOUS CONTRACTIONS OF THE PIG URINARY BLADDER

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HYPOTHESIS / AIMS OF STUDY

Normal bladder function requires co-operative interaction of several cell types. Isolated detrusor muscle generates nerve-evoked contractions, regulated by the release of transmitters, as well as spontaneous contractions (SCs), associated with spontaneous action potentials. However, it appears that the mucosa (urothelium and lamina propria) influences spontaneous contractile activity and associated intracellular Ca2+ transients recorded from the bladder wall (1,2). When isolated, the mucosa can also develop spontaneous and agonist-induced contractile activity and when left intact with the detrusor layer, greatly augments the spontaneous contractile activity (3). What is unclear is if the mucosa interacts with the detrusor via release of diffusible agents or through cell-to-cell contact. The aim of this study was to investigate the nature of this interaction by measuring SCs from detrusor preparations with and without an adjacent mucosa, using tissue from a large animal (pig) bladder with an architecture similar to that of the human bladder.

STUDY DESIGN, MATERIALS AND METHODS

Female pig (Sus scrofa domestica ~6-months old) bladders obtained from a local abattoir were placed in cold Krebs bicarbonate (KB) solution (mM: NaCl 118.4, NaHCO3 24.9, KCl 4.7, CaCl2 1.9, MgSO4 1.15, KH2PO4 1.15, glucose 11.7). From each bladder dome, four sets of longitudinally-orientated preparations were prepared. These were: (a) intact (detrusor + mucosa); (b) denuded (detrusor with mucosa removed); (c) mucosa alone; (d) reconstructed (denuded with previously isolated mucosa placed on top). Preparations were tied between a fixed hook and an isometric force transducer, maintained under a fixed (20 mN) load in KB solution at 37°C for 45 min. SCs were recorded and assessed during the final 15-min of the equilibration period. The amplitude (μN/mg tissue) and frequency (number of events in 5-min) of SCs were recorded and compared between the four different preparations. All data are expressed as the medians (25,75% interquartiles), n = number of bladder strips. Statistical analyses were carried out by Kruskal-Wallis rank sum test, followed by Wilcoxon non-parametric tests.

RESULTS

The basal SCs were detected in 100% of mucosa, intact and reconstructed pig bladder strips. However, only 30% of denuded strips demonstrated basal SCs. The amplitude and frequency of basal SCs were significantly smaller in denuded strips vs. all other strip types (Figure 1). The highest amplitude of SCs was detected in mucosa strips (Figure 1A). There was no significant difference in the amplitude or frequency of SCs between intact vs. reconstructed strips, demonstrating that a functional physical connection between the layers was not needed for generation of SCs.

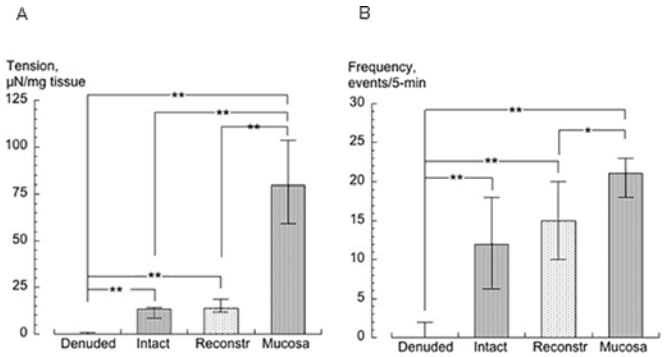
INTERPRETATION OF RESULTS

The contractile properties of the bladder mucosa have been previously described and it is speculated that phasic activity of intact bladder strips may be influenced by this layer (1,2,3). Our study demonstrated that the pig bladder detrusor alone, similar to guinea pig detrusor, has very little intrinsic ability to generate spontaneous activity and the interaction between mucosa and detrusor is required for generation of SCs. Dissecting the mucosa away from the muscle and then reattaching it to the detrusor restores spontaneous activity. This implies that there is a diffusible factor between the mucosa and the detrusor modulating the spontaneous activity and cellular/physical connection between these two layers is not required for generation of SCs.

CONCLUDING MESSAGE

Spontaneous activity of pig bladder originates from the mucosal layer possibly through the release of a diffusible factor which acts on the underlying detrusor to generate SCs. Further studies are needed to identify the source and nature of this diffusible factor.

FIGURE 1



SCs in pig bladder wall preparations. A: amplitude of SCs normalised to preparation weight C: frequency of SCs in denuded, intact, reconstructed (reconstr) & mucosa strips (all n = 9). Data are median (25,75% interquartiles; *p < 0.05, **p < 0.01, Wilcox tests)

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Funding N/A **Clinical Trial** No **Subjects** Animal **Species** Pig **Ethics Committee** Ethical approval was not required as animal tissue was obtained from the local abattoir

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BEST IN CATEGORY PRIZE: FEMALE LOWER URINARY TRACT SYMPTOMS (LUTS) / VOIDING DYSFUNCTION

HISTOLOGICAL AND PHYSIOLOGICAL EVALUATION OF THE EFFECTS OF ADIPOSE-DERIVED STEM CELL SHEETS ON A RAT MODEL OF DETRUSOR UNDERACTIVITY

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HYPOTHESIS / AIMS OF STUDY

Studies focusing on the role of stem cells in bladder regeneration have mostly used bone marrow-derived stem cells. Furthermore, none of the earlier reports have discussed the transplantation of adipose-derived stem cell sheets generated in temperature-responsive culture dishes into rats, the evaluation of physiological functional recovery by cystometry, or confirmation of their long-term viability and differentiation. In this study, we investigated the effects of adipose-derived stem cell (ASC) sheets in a rat model of detrusor underactivity.

STUDY DESIGN, MATERIALS AND METHODS

Mature male syngeneic Lewis rats were obtained for ASC sheet production. To produce GFP-expressing ASC sheets, male Lewis rats [LEW-Tg(CAG-EGFP)1Ys] were used, which express GFP in tissue cells throughout the body under the control of the CAG promoter. ASC sheet transplantation was performed on 10-week-old female syngeneic Lewis rats. The experiments involving animals and genetic recombination were approved by the Research Promotion Organization of Tottori University (32-027, 20-Y-23).

Based on the intervention methods, the experimental animals were subdivided into four groups containing eight animals each: the first group underwent induction of bladder cryo-injury followed by application of ASC sheets to the injury site (cryo-injury + ASC sheet group); the second group underwent bladder cryo-injury induction but did not receive ASC sheets (cryo-injury group); the third group underwent the surgical procedure without cryo-injury induction or application of ASC sheets (sham operation group); and the fourth group did not undergo any treatment (control group).

The engineering of the ASC sheet involved washing of the adipose tissue obtained from inguinal subcutaneous fat tissue of male Lewis rats, followed by dissection into small pieces. ASCs were obtained via centrifugation and filtered through a mesh filter. The cell pellets were seeded into culture dishes. Subsequently, temperature-responsive culture dishes were used to prepare the cell sheets.

In this study, we used a rat bladder cryoinjury model. A cryo-injury procedure was performed on the bladder three days prior to ASC sheet transplantation. A small incision was made in the midline of the lower abdomen in the supine position and an aluminum rod, cooled with dry ice, was placed in contact with the anterior wall of the bladder to induce cryoinjury. This was followed by placing the bladder in the abdominal cavity, and closure of the wound. In the sham operation group, the bladder was similarly exposed, only saline was injected, and no cryo-injury was administered.

Three days after cryo-injury induction, the rats were anesthetized with isoflurane, as described above, and a midline incision was made in the lower abdomen to expose the damaged part of the bladder. In the cryo-injury + ASC sheet group, the ASC sheet was applied to the cryo-injured area. For the cryo-injury and sham operation groups, the bladder was re-exposed, and saline was injected into the bladder; however, the ASC sheet was not applied. Finally, the wound was closed and the operation was completed. Seven days after these surgeries, the rats were euthanized after cystometry, and their bladders were removed for histological and reverse transcription polymerase chain reaction (RT-PCR) analyses.

To confirm the viability and differentiation of ASC sheets, GFP-expressing ASC sheets were prepared from inguinal adipose tissue of male LEW-Tg (CAG-EGFP)1Ys rats using the same method. In accordance with the procedure described above, cryo-injury was induced in 25 female Lewis rats, and three days later, GFP-expressing ASC sheets were transplanted into the bladder. Five rats were euthanized at 3, 7, 14, 21, and 28 days after implantation. The abdomen of euthanized Lewis rats was cut open and observed under a fluorescent stereomicroscope to confirm ASC sheet viability under excitation light. The bladder was removed and fixed in 10% formalin. Double immunofluorescence staining for GFP and vWF was performed.

RESULTS

· Cystometry

The results of cystometry evaluation are shown in Fig. . No significant differences were found in the maximum intravesical pressure, injection volume, and voided volume between the four groups; however, significant differences were evident in the pressure threshold ($P = 0.016$), residual volume ($P = 0.011$), voiding efficiency ($P = 0.020$), and percentage of urine overflow ($P = 0.001$) (Fig. 1).

· Histopathology

Acute inflammatory findings were observed in the cryo-injury group based on histopathological analysis. In contrast, in the cryo-injury + ASC sheet group, chronic inflammation caused by infiltration of inflammatory cells was observed; however, the degree of tissue necrosis was low, and granuloma formation, which occurs during the wound healing process, was also confirmed. Furthermore, the bladder tissue from each group was stained with the anti-vWF antibody, and a comparison of the mean number of capillaries in the 4× field of view was performed between the groups. The number of capillaries was significantly higher in the cryo-injury + ASC sheet group than that in the other groups.

· RT-PCR analysis

The mRNA levels of VEGF and HGF were significantly higher in the cryo-injury + ASC sheet group in comparison to the cryo-injury group ($P = 0.045$ and $P = 0.037$ respectively). The four groups showed no significant differences in bFGF levels, although the mRNA expression was comparatively higher in the cryo-injury + ASC sheet group.

· Immunofluorescence based analysis of GFP

Following application of GFP-expressing ASC sheets, green fluorescence of the sheets was observed under excitation light. In the anterior bladder wall, green fluorescence was observed in all rats up to day 14 (100%) and in four out of five rats on day 21 (80%). At 28 days post-implantation, fluorescence was observed in one of five rats (20%). At every time point, green fluorescence was confined only to the bladder implantation site and was not visible in the other organs. Immunostaining of the removed bladder showed many GFP-positive cells at the ASC sheet application site. On day 3, double immunofluorescence staining showed that GFP-positive cells did not merge with the vWF-positive cells. However, 7 days after sheet transplantation, the GFP-positive cells merged with vWF-positive cells, indicating that the cells had differentiated into blood vessels (Fig. 2).

INTERPRETATION OF RESULTS

Transplantation of ASC sheets after cryo-injury resulted in recovery of bladder contraction at a relatively early stage. Several mechanisms have been proposed for stem cell wound healing, including differentiation, homing, and immunoregulation.[1] A large body of evidence suggests that neovascularization induction is strongly involved in tissue repair and wound healing in ASCs. Recently, it has been reported that ASCs secrete factors such as VEGF, PDGF, IGF, HGF, b-FGF, SDF-1, TGF-β, and GDF11, which promote the differentiation of ASCs and fibroblasts into endothelial cells.[2, 3] Furthermore, this study showed that ASCs marked with GFP differentiated into cells that provided structural elements of the capillary system and survived for up to 28 days after transplantation. As a result, stable blood perfusion to the injured bladder wall is maintained, and acute inflammation is suppressed, suggesting that these combined effects may lead to a relatively early recovery of injured bladder function.

CONCLUDING MESSAGE

Adipose-derived stem cell (ASC) sheets transplanted into the bladder of cryo-injured rats differentiated into blood vessels and restored bladder contractile function seven days after transplantation.

FIGURE 1

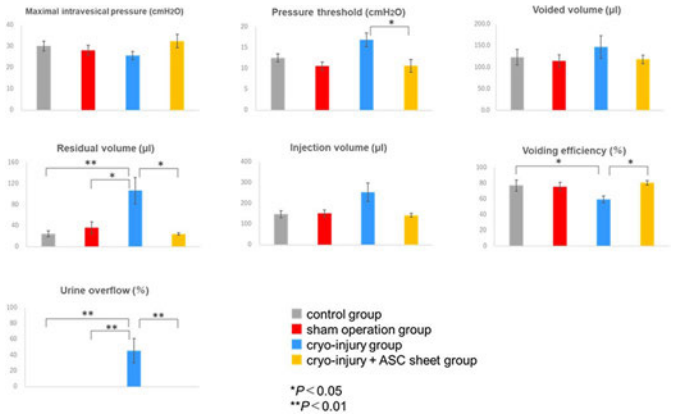
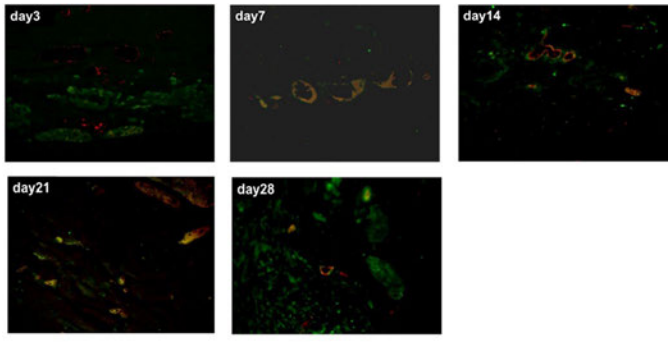


FIGURE 2



ASCs, Adipose-derived stem cells; GFP, green fluorescent protein; vWF, von Willebrand factor

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MAST CELLS IN THE URINARY BLADDERS OF INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME PATIENTS EXPRESS THE MAST CELL RELATED G-PROTEIN COUPLED RECEPTOR X2 (MRGPRX2): POTENTIAL ROLE IN THE PATHOGENESIS OF NEUROGENIC INFLAMMATION.

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HYPOTHESIS / AIMS OF STUDY

Interstitial cystitis/Bladder pain syndrome (IC/ BPS) is a chronic debilitating inflammatory disease of the urinary bladder that significantly affects the quality of life. Recent reports have shown progressive increase in the prevalence and incidence rates of IC/BPS across genders. This places IC/BPS amongst conditions that merit intensive research to bridge the wide gaps between diagnosis and treatment. The pathophysiology of IC/BPS is elusive and rather multifactorial, in which a defect in the bladder urothelium and chronic inflammation of bladder wall are key features. The numbers and activity of mast cells, in addition to the density of the substance P (SP) positive nociceptive sensory nerve endings, are significantly elevated in the bladders of IC/BPS patients. The urothelial barrier defect is associated with increased urothelial permeability, allowing harmful urinary constituents to penetrate the bladder wall and depolarise the nociceptive sensory nerve fibres, which release neuroactive substances including SP, inducing mast cell degranulation and tissue inflammation. However, the responsiveness of mast cells to SP is variable between different tissues depending on the local cellular micro-environment. MRGPRX2 is a recently identified G-protein coupled receptor involved in mast cell responsiveness to SP in different chronic inflammatory conditions, and its expression is associated with increased tissue inflammation. The responsiveness of the bladder mast cells to SP remains poorly understood. This makes theories related to neurogenic inflammation in the pathogenesis of IC/BPS uncertain. Thus, the potential contribution of neurogenic inflammation in the pathogenesis of BPS/IC warrant further investigation.

STUDY DESIGN, MATERIALS AND METHODS

In the present study, we investigated the responsiveness of bladder mast cells to SP through studying the expression of MRGPRX2 on BPS/IC bladder mast cells. Formalin Fixed Paraffin embedded urinary bladder biopsies from 18 IC/BPS patients, in addition to healthy controls from 10 bladder biopsies with non-invasive bladder cancer. These were obtained from the human tissue archive, clinical pathology department, University Hospital Southampton, NHS FT. IC/BPS were diagnosed clinically based on the ESSIC criteria. 4 serial sections, each of 4μm thickness, were cut from each bladder biopsy and stained with antibodies against mast cell-specific proteases tryptase (AA1) and chymase (CC1), as well as anti-MRGPRX2 (Abcam, USA). All staining was performed using an automated autostainer platform. Following microscopic scanning, images from the serial sections were aligned and superimposed using Adobe Photoshop CS6 software. Mast cell quantification and co-expression patterns were studied using Image J software. Statistical differences between the IC/BPS and the control groups were analysed by Mann Whitney U test and unpaired t-tests using GraphPad Prism 9 software.

RESULTS

All of the 18 IC/BPS biopsies consistently co-expressed MRGPRX2 with tryptase and chymase in the lamina propria and detrusor layers of the bladder wall, indicating the potential for bladder mast cells to respond to SP (Figure 1). Tissue resident mast cells are found in 2 subtypes of different protease expression behaviour, mast cells tryptase only (MCT) and mast cell tryptase chymase (MCTC). The average density of the two mast cell subtypes MCT and MCTC in the IC/BPS group was 177 and 167 cells/mm2, respectively. This was significantly higher when compared to the control group. Moreover, the percentage of mast cells that co-expressed tryptase and chymase (MCTC), out of all mast cells (tryptase +ve) in the IC/BPS group averaged at 67%, which was significantly higher compared to the controls ($P < 0.05$). Interestingly, about 66% of the tryptase +ve mast cells (all mast cell) expressed MRGPRX2, which was significantly higher compared to the control group (25%; $P < 0.0001$). Similarly, about 65% of the mast cell stained with tryptase and chymase (MCTC) expressed MRGPRX2, which was significantly higher compared to the controls (30%; $P < 0.0001$) (Figure 2).

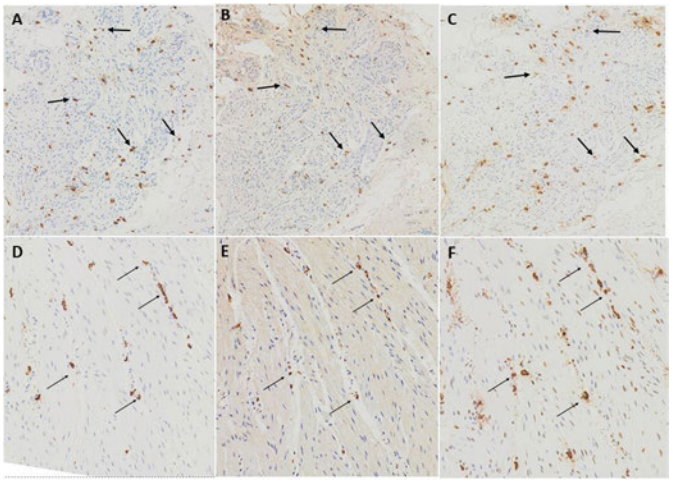
INTERPRETATION OF RESULTS

The densities of the 2 mast cell subtypes in the In IC/BPS biopsies were significantly increased compared to non-IC/BPS controls. Similarly, mast cells consistently expressed MRGPRX2, indicating their responsiveness to the neuropeptide SP. In addition, mast cell numbers and their expression of MRGPRX2 are significantly elevated in IC/BPS bladder biopsies, suggesting potential involvement in the pathophysiology of the chronic inflammation seen in the bladder walls of these patients.

CONCLUDING MESSAGE

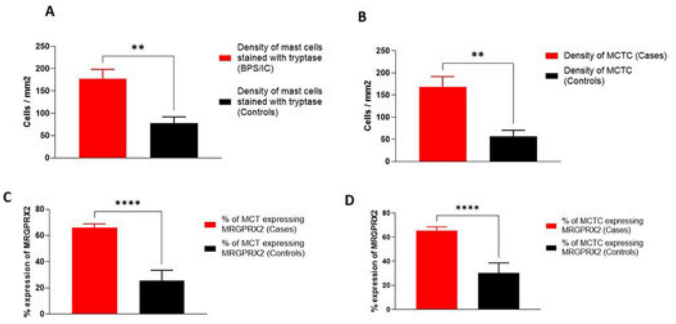
Accordingly, neurogenic inflammation caused by the SP-induced mast cell degranulation is potentially behind the chronic tissue inflammation in IC/BPS patients. Thus, blocking SP-MRGPRX2 signalling could alleviate long-standing bladder inflammation and pain in this group of patients. Moreover, other MRGPRX2 agonists including morphine, antibiotics (e.g. fluoroquinolones and vancomycin), neuromuscular blockers (e.g. Atracurium), and bradykinin B2 receptor antagonists (e.g. Icatibant), may potentially induce mast cell degranulation and subsequent bladder wall inflammation.

FIGURE 1



Each of (A, B and C) and (D, E and F) represent serial sections from one IC/BPS bladder biopsy. Arrows represent mast cell stained with antibodies for chymase (CC1), MRGPRX2 and tryptase (AA1), in sections (A and D), (B and E) and (C and F), respectively.

FIGURE 2



Graphs A, B, C and D represent the differences between IC/BPS and the control urinary bladder biopsies in the density of the mast cell subtypes MCT and MCTC (A and B, respectively) and % expression of MRGPRX2 by MCT and MCTC (C and D, respectively).

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INTEGRATED PERMEABILITY AND PRO-INFLAMMATORY CYTOKINES ANALYSIS OF MEDICAL-GRADE MANUKA HONEY ON CO-CULTURE MODEL SYSTEM RELATED TO PAINFUL BLADDER SYNDROME/INTERSTITIAL CYSTITIS: NOVEL FINDING

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HYPOTHESIS / AIMS OF STUDY

Painful bladder syndrome/Interstitial cystitis (PBS/IC) is a chronic debilitating inflammatory condition of the urinary bladder of complicated poorly-understood pathophysiology accompanied by daytime and/or night-time urinary frequency and urinary urgency, in the absence of bacterial infection. The main cause of PBS/IC is thought to be a persistent bladder inflammation by the deficiency of the glycosaminoglycan covering the urothelium surface that results in the leaky urothelium and subsequent activation of neurogenic inflammation. The use of medicinal honey for wound management has been supported through clinical studies highlighting its antimicrobial activities and anti-inflammatory properties. Our previous studies showed that 4% of Manuka honey (MH) can protect the monolayer primary human urothelial cells viability and inhibited pro-inflammatory cytokines release. The objectives of this study were to determine the effect of MH on the human urothelial-fibroblast cells' co-culture model system permeability and pro-inflammatory cytokines production induced by tumor necrosis factor-alpha (TNF-α).

STUDY DESIGN, MATERIALS AND METHODS

200 µl of the fibroblast cells (FB) (3x10^6 cells/ml) were seeded on the basal side of the transwell insert membrane for 2 hours to adhere. After that, 300 µl (3 × 10^6 cells/ml) of the primary human urothelial cells (HUC) were seeded in the apical compartment of the transwell insert. Cells were co-cultured for 5 days and media was changed every day with HUC medium supplemented with fetal calf serum (FCS, 5% v/v) and Ca2+ (2 mM). The physical barrier was monitored every day (Pre-treatment) by transepithelial electrical resistance (TEER) using an epithelial voltohmmeter (EVOM). On day 5, 20 µl of TNF-α (10 ng/ml) were added to the apical chamber and incubated for 24 h with/without 20 µl of 4% MH pre-treatment. The TEER values will be measured after treatment (post-treatment) and supernatants were collected for cytokine expression assay (Human IL-6 and IL-8 DuoSet, R&D system) following the manufacturer's instructions. Samples were diluted at 1:10 (IL-6) and 1:5 (IL-8) in sample buffer and run in duplicate (n = 6).

RESULTS

TEER values were significantly elevated by 2 to 3 folds when the culture medium was supplemented with fetal calf serum (5% v/v) and Ca2+ (2 mM) compared to unsupplemented (data not shown). The TEER value of this model system was significantly decreased upon 24-hour incubation with TNF-α ($P < 0.01$ vs control). Interestingly, pre-incubation of the model systems with 4% MH has blocked the effects of TNF-α and maintained the urothelial barrier function integrity ($P < 0.01$ vs TNF-α -treated group, Figure 1). Moreover, TNF-α (10 ng/ml) showed significantly induced IL-6 and IL-8 release compared to the control ($P < 0.01$) while pre-treatment with 4 % MH showed significantly decreased expression of IL-6 and IL-8 ($P < 0.01$ vs TNF-α -treated group, Figure 2).

INTERPRETATION OF RESULTS

In the present study, we found that HUC supplemented with FCS (0.5% v/v) and Ca2+ (2 mM) showed significantly increased TEER value compared to un-supplemented similarly to previous studies (1), and TNF-α showed significantly decreased TEER value of epithelial cells (2, 3). TNF-α is a major cytokine secreted by activated mast cells. Mast cells-derived TNF-α has been shown to induce IL-6 and IL-8 release from urothelial cells and significantly increased in urine from PBS/IC patients. Our data suggest that urothelial cells are responsive to inflammatory stimuli (TNF-α) by releasing IL-6 and IL-8 and may participate in the pathology of inflammatory urinary tract disease including PBS/IC. As novel findings, this is the first study of the beneficial effects of Manuka honey on human urothelial cells and human fibroblast cells co-culture model system induced by TNF-α related to an in vitro model of PBS/IC and inflammation diseases. Further studies, which take these into animal models, will need to be undertaken.

CONCLUDING MESSAGE

Taken together, these results suggest that MH could protect the urothelial barrier function of PBS/IC patients. These results provide another strong evidence supporting the potential anti-inflammatory effect of MH when used as an intravesical therapeutic agent in the bladders of PBS/IC patients and established a novel in vitro clinically relevant model to assess the efficacy of MH in therapeutic agent for the treatment of bladder conditions including PBS/IC, with a future view (outside the scope of the current study) to assessing efficacy in a full clinical trial.

FIGURE 1

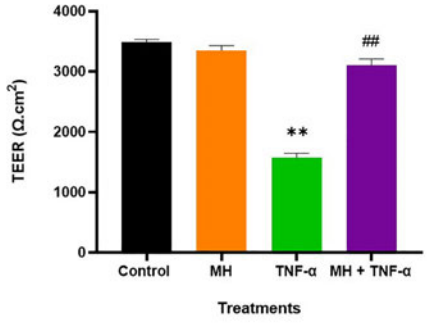

Figure 1. The integrity of TNF-α on the HUC and fibroblast co-culture model barriers was monitored by measuring the TEER value. HUCs were cultured on the apical side and FB cells were cultured on the basolateral side of Snapwell insert in the medium supplemented with FCS (5% v/v) and Ca^{2+} (2 mM). At day 5, TNF-α (10 ng/ml) were added in the apical chamber and incubated for 24 h with/without 4% MH pre-treatment and measured at day 6 (post-treatment). Data are expressed as means ± SEM. **P<0.01 compared to control cultures and ## P<0.01 compared to TNF-α groups.

Figure 1

FIGURE 2

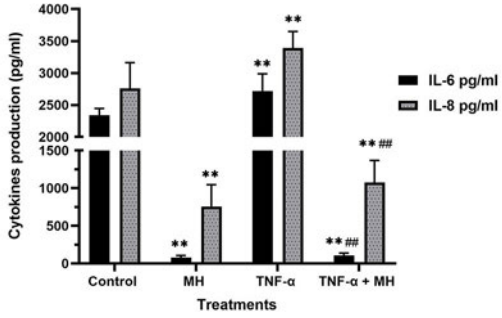

Figure 2 Effects of TNF-α (10ng/ml) for 24 hours on co-culture system with/without 4% MH (w/v) pre-treatment for 30 minutes on IL-6 and IL-8 expression. Data are expressed as means ± SEM. **P<0.01 compared to untreated control and ## P<0.01 compared to TNF-α groups.

Figure 2

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PRETREATMENT WITH 5-AMINOLEVULIC ACID HAS A POTENTIAL TO PROTECT CYCLOPHOSPHAMIDE-INDUCED BLADDER DYSFUNCTION IN RATS

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HYPOTHESIS / AIMS OF STUDY

Cyclophosphamide (CYP) is one of the most widely used chemotherapeutic agents, and the metabolite acrolein is excreted in urine and accumulates in the bladder to produce toxic effects on the bladder wall, resulting in hemorrhagic cystitis (HC). HC may be fatal despite treatment options such as hydration, clot extraction via cystoscopy, continuous bladder irrigation, and cystectomy. Administration of 2-mercaptoethane sodium sulphonate (mesna) and hyperhydration are the two most frequently used methods to prevent HC, but they are not always effective and cannot be used in all patients. Chemotherapy with CYP is often limited by urotoxicity and requires new drugs against the HC. Because CYP-induced HC is mediated by an inflammatory process, new compounds with anti-inflammatory properties may be beneficial in reducing side effects during CYP therapy.

5-Aminolevulinic acid (5-ALA) is a natural amino acid that originally exists in the body. 5-ALA is metabolized to protoporphyrin IX (PpIX) and by the insertion of a ferrous ion into PpIX, heme and hemeproteins are produced. These 5-ALA-derived molecules play important roles in the energy generating function of mitochondria [1], so simultaneous administration of 5-ALA and sodium ferrous citrate (5-ALA/SFC) reportedly improves mitochondrial function by upregulating the expression of hemeproteins involving in respiratory chain complexes and increases the expression level of heme oxygenase-1 (HO-1), a cytoprotective molecule showing anti-oxidative stress and anti-inflammatory effects [2].

Mitochondrial metabolic pathways are important modulators of inflammatory pathways and mitochondrial dysfunction is implicated in aging and pathologies including type 2 diabetes, neurodegeneration, cancer, and inflammatory disorders. Such cellular senescence is thought to be partly attributable to mitochondrial dysfunction and the associated increase in production of reactive oxygen species, and one of the etiologies of lower urinary tract dysfunction (LUTD) is thought to be increased oxidative stress due to mitochondrial dysfunction in the bladder. Inflammation and mitochondrial dysfunction may therefore provide therapeutic targets for LUTD. In this study, therefore, we investigated effects of 5-ALA/SFC pretreatment on bladder dysfunction in CYP-treated rats.

STUDY DESIGN, MATERIALS AND METHODS

At 13–15 weeks old, male Wistar rats were randomly divided into four groups as follows: (1) Vehicle-1 + Vehicle-2 group (V1 + V2); (2) Vehicle-1 + CYP group (V1 + CYP); (3) low 5-ALA/SFC + CYP group (ALA100 + CYP); and (4) high 5-ALA/SFC + CYP group (ALA300 + CYP). In each rat, Vehicle-1 (saline, 10 ml/kg/day) or 5-ALA/SFC (low: 100 and 157 mg/kg/day; high: 300 and 471 mg/kg/day) was orally administered once daily for 7 days. On Day 6, Vehicle-2 (saline, 5 ml/kg) or CYP (150 mg/kg) was administered intraperitoneally.

On Day 8 (one day after the last administration of 5-ALA/SFC or Vehicle-1), under urethane anesthesia (0.8 g/kg, ip), cystometry (saline, 4 ml/h) was performed via a catheter inserted into the bladder from the bladder dome. After cystometry, bladder tissues were collected to perform hematoxylin and eosin staining, ELISA and real-time PCR.

RESULTS

CYP significantly shortened intercontraction intervals (ICI), decreased bladder compliance (Comp), and increased the number of non-voiding contractions (NVCs) (Table 1) without altering post-voided residual volume (Rv) (data not shown). These CYP-induced changes in ICI and the number of NVCs were significantly attenuated by pretreatment with 5-ALA/SFC at higher doses, and there was no significant difference in Comp between V1 + V2 and ALA300 + CYP (Table 1). Therefore, histological and in vitro analyses of bladder tissues were performed in three groups as follows: V1 + V2, V1 + CYP, and ALA300 + CYP.

In histological analysis, CYP increased pathological scores (neutrophil infiltration, bleeding and edema) in the bladder, and pretreatment with higher doses of 5-ALA/SFC significantly improved CYP-induced increases in neutrophil infiltration/bleeding scores (Fig. 1). In vitro analysis, CYP increased protein levels of myeloperoxidase (MPO), a marker of neutrophil infiltration, in the bladder, however, there was no significant difference in the MPO levels between V1 + V2 and ALA300 + CYP (Fig. 2). CYP administration showed no significant change in HO-1 mRNA levels in the bladder, while the HO-1 levels were significantly higher in ALA300 + CYP than those in V1 + V2 (Fig. 2).

INTERPRETATION OF RESULTS

CYP injection significantly shortened ICI, decreased Comp, and increased the number of NVCs without changing Rv, suggesting that CYP successfully induced urinary frequency with low bladder distensibility and detrusor overactivity (DO) in rats. Pretreatment with 5-ALA/SFC at higher doses significantly attenuated the CYP-induced changes in ICI and the number of NVCs, and the CYP-induced decrease in Comp was not detected in ALA300 + CYP. These data suggest that 5-ALA/SFC pretreatment could improve the urinary frequency, decreased bladder distensibility, and DO in CYP-treated rats.

In histological and in vitro analyses of rat bladder tissues, CYP significantly increased histological scores of neutrophil infiltration, bleeding and edema, and MPO protein levels, indicating that CYP successfully induced HC. These CYP-induced changes in scores of neutrophil infiltration and bleeding were significantly attenuated by pretreatment with 5-ALA/SFC at higher doses, and the CYP-induced increase in the MPO levels was not detected in ALA300 + CYP. These data indicate that 5-ALA/SFC pretreatment could partially improve the bladder inflammation induced by CYP. In addition, CYP administration tended to increase HO-1 mRNA levels, but not significantly, in the bladder, while the HO-1 levels were significantly higher in ALA300 + CYP than those in V1 + V2. Because HO-1 is reported to show anti-oxidative stress and anti-inflammatory effects [3], our present data indicate that pretreatment with 5-ALA/SFC improved the bladder inflammation perhaps via the increased HO-1.

CONCLUDING MESSAGE

Our present data suggest that pretreatment with 5-ALA expects protective effects on bladder dysfunction in CYP-induced HC by partially improving bladder inflammation perhaps via HO-1 up-regulation. Therefore, 5-ALA pretreatment might be useful for prevention of CYP-induced urinary side effects during chemotherapy.

FIGURE 1

Table 1. Urodynamic parameters in cystometry.

Group	V1+V2 (n=10)	V1+CYP (n=9)	ALA100+CYP (n=9)	ALA300+CYP (n=10)
ICI (sec)	1166 ± 426	321 ± 109**	339 ± 122**	733 ± 345*†
Comp (ml/cmH_2O)	0.036 ± 0.018	0.016 ± 0.006**	0.016 ± 0.006**	0.027 ± 0.011
NVC	0.80 ± 1.03	25.4 ± 24.9*	18.6 ± 21.1	4.00 ± 7.44†

V1+V2: Wistar rats treated with Vehicle-1 (saline, 10 ml/kg/day, po) and Vehicle-2 (saline, 5 ml/kg, ip); V1+CYP: Wistar rats treated with Vehicle-1 and CYP (150 mg/kg, ip); ALA100+CYP: Wistar rats treated with 5-ALA/SFC (100/157 mg/kg/day, po) and CYP (150 mg/kg, ip); ALA300+CYP: Wistar rats treated with 5-ALA/SFC (300/471 mg/kg/day, po) and CYP (150 mg/kg, ip). Data are shown as mean ± SD. *P < 0.05, **P < 0.01, when compared with the Mann–Whitney U-test with Bonferroni correction to the V1+V2 group; †P < 0.05, when compared with the same test to the V1+CYP group. CYP: cyclophosphamide; 5-ALA: 5-aminolevulinic acid; SFC: sodium ferrous citrate; ICI: intercontraction interval; Comp: bladder compliance; NVC: the number of non-voiding contractions.

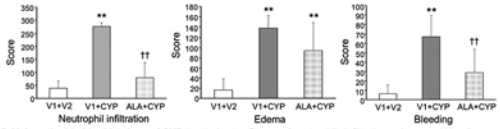

Fig. 1. Effects of 5-ALA on the bladder histology of CYP-treated rats. Scores of neutrophils infiltration, edema and bleeding were evaluated. CYP-induced changes in urodynamic parameters were partially attenuated by pretreatment with higher doses of 5-ALA/SFC (300/471 mg/kg/day, po). Therefore, histological evaluation and molecular analysis shown in Fig. 2 were performed in three groups, V1+V2, V1+CYP, and V1+ALA (higher dose of 5-ALA/SFC were pretreated) groups. Vehicle-1 (V1, saline, 10 ml/kg/day, po) or 5-ALA/SFC was pretreated once a day for 7 days. Vehicle-2 (V2, saline, 5 ml/kg, ip) or CYP (150 mg/kg, ip) was pretreated at day 6, and bladder tissues were collected at day 8. Data are shown as mean ± SD. **P < 0.01, when compared with non-parametric Kruskal-Wallis analysis to the V1+V2 group. ††P < 0.01, when compared with the same test to the V1+CYP group. CYP: cyclophosphamide; 5-ALA: 5-aminolevulinic acid; SFC: sodium ferrous citrate.

FIGURE 2

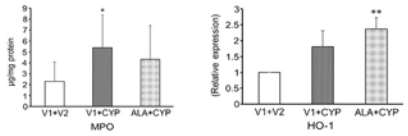

Fig. 2. Effects of 5-ALA on protein levels of MPO and mRNA levels of HO-1 in the bladders of CYP-treated rats. Concentrations of MPO, as a marker of neutrophil infiltration, in whole bladder tissues were measured by ELISA. In addition, quantitative real-time PCR was performed to measure the mRNA levels of HO-1. Vehicle-1 (V1, saline, 10 ml/kg/day, po) or 5-ALA/SFC (300/471 mg/kg/day, po) was pretreated once a day for 7 days. Vehicle-2 (V2, saline, 5 ml/kg, ip) or CYP (150 mg/kg, ip) was pretreated at day 6, and bladder tissues were collected at day 8. Data are shown as mean ± SD. *$P < 0.05$, **$P < 0.01$, when compared with the Mann–Whitney *U*-test with Bonferroni correction to the V1+V2 group. CYP: cyclophosphamide; 5-ALA: 5-aminolevulinic acid; SFC: sodium ferrous citrate ; MPO: myeloperoxidase. HO-1: heme oxygenase-1.

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GLANDULAR GROWTH, FIBROSIS AND LOWER URINARY TRACT SYMPTOMS INDUCED BY SELECTIVE DEFICIENCY OF CYTOCHROME B5 REDUCTASE IN THE MOUSE PROSTATE

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HYPOTHESIS / AIMS OF STUDY

Benign prostatic hyperplasia (BPH) and enlargement is a highly prevalent condition amongst elderly men and is frequently associated with lower urinary tract symptoms (LUTS). The aetiology of BPH-LUTS is multifactorial and is believed to result from concurrent physiological and metabolic alterations that arise with age. Cytochrome B5 reductase type-3 (CYB5R3) is an oxidoreductase that regulates pathways in the mitochondria, endoplasmic reticulum and nitric oxide-cyclic GMP signalling through its actions on soluble guanylate cyclase. Downregulation of CYB5R3 activity has been associated with oxidative stress, inflammation, and metabolic dysfunction [1], all of which progressively increase through natural aging. We hypothesized that selective knockdown of CYB5R3 in the prostate would induce metabolic dysfunction comparable to advance age resulting in a BPH-LUTS phenotype. To address this hypothesis, we generated a conditional CYB5R3 knockout mouse and performed 4-hydroxytamoxifen (4-OHT, active metabolite of tamoxifen) injections into the prostate lobes. The voiding activity of mice was monitored over 12 weeks and prostate after which tissues were examined for morphological changes by histology. The purpose of this study was to generate an animal model of BPH-LUTS by mimicking the cellular dysfunctions associated with aging selectively within the prostate.

STUDY DESIGN, MATERIALS AND METHODS

Generation of CYB5R3 conditional knockout mouse. A mouse with loxP sites flanking exon3 of the CYB5R3 gene [2] (CYB5R3flox/flox) was crossed with a mouse expressing the tamoxifen inducible Cre recombinase under the β-actin promoter (CAG-Cre, Jackson laboratories, stock#:004682) to generate the conditional CYB5R3flox/flox + CAG-Cre (CYB5R3 KO) mouse (Fig 1A). Both mouse strains were based on a C57Bl/6 background. At 8-12 weeks of age, male CYB5R3 KO and age matched CYB5R3 wildtype (WT) mice were used for 4-OHT prostate injections. Mice were anesthetized with isoflurane and using sterile surgical conditions a lower midline incision was made to expose the prostate glands and urinary bladder. Each lobe was bilaterally injected with 2-5 µl of 0.5 mg/ml 4-OHT (dissolved in ethanol/CremophorEL/saline) using a 32-gauge insulin syringe (Fig 1B). The incisions were sutured, and mice were given prophylactic ampicillin (100 mg/kg, SQ, 7 days) and ketoprofen (3 mg/kg, IM, 3 days) during the recovery period.

Voiding assessments. Voiding activity was initially analyzed by two-hour urine spot tests starting one week prior to 4-OHT injections and performed weekly thereafter for 6 weeks. At 8 weeks after surgery, weekly 24-hour metabolic cage assessments were performed for 13 weeks after injections. Metabolic cages (Columbus Instruments Inc.) were maintained in a climate-controlled cabinet on 12-hour light/dark cycles.

Histology and immunofluorescence. Following completion of voiding assessments, mice were humanely sacrificed for tissue collection. Prostate tissues were fixed in 10% neutral buffered formalin and processed for paraffin embedding, sectioned 3-4 µm thick and processed for Van Gieson staining and immunofluorescence. Slides were imaged using an Olympus BX63 microscope and analysis performed using FIJI ImageJ software.

Data and statistical analysis. Data are expressed as mean ± standard deviation. Pairwise comparisons were performed using Student's t-test where the null hypothesis was rejected at $p < 0.05$.

RESULTS

Prostate CYB5R3 KO mice exhibit urinary frequency and reduced voided volumes. CYB5R3 KO and WT mice (N = 4 each) began showing differences in voiding behaviour at 10-12 weeks following 4-OHT injections with KO mice exhibiting increased voiding frequency (Fig 1C) and decreased voided volumes (Fig 1D). There were no differences in total voided volumes (Fig 1E) or total water intake (Fig 1F) between KO and WT mice. Additionally, there were no significant differences in body weight (Fig 2A) over the entire observation period nor changes in blood pressure monitored by weekly tail cuff plethysmography (not shown), indicating there were little to no systemic effects of 4-OHT injections.

CYB5R3 KO have increased prostate collagen deposition and glandular growth. Gross examination of the tissues from CYB5R3 KO and WT mice showed no significant differences in bladder or seminal vesical wet weights (Fig 2A). Van Gieson staining (Fig 2B-2D) showed increased collagen deposition (pink) within the convergence point of the urethra, prostate glands, seminal vesicles, and ductus deferens, all of which are surrounded by skeletal muscle of the external urethral sphincter (EUS). Moreover, there was increased number of glandular structures further congesting the area (Fig 2D). Immunofluorescence of prostate sections from KO mice when compared to those of WT (Fig 2F versus 2E) exhibited decreased CYB5R3 (red) localization to the prostate glandular epithelium of the lateral lobes surrounding the EUS (outlined with a dotted white line) and increased α-smooth muscle actin (green) around glands and in foci within the interstitial space (Fig 2F, white arrows).

INTERPRETATION OF RESULTS

CYB5R3 knockdown in the prostate resulted in increased urinary frequency and voided volumes which correlated with increased fibrosis and glandular growth within the prostate, without signs of outlet obstruction. These observations closely match with voiding features seen with aged male mice [3] suggesting disruption of local cellular metabolic processes are a major contributor of BPH-LUTS pathophysiology that precedes outlet obstruction.

CONCLUDING MESSAGE

Understanding of the mechanisms that drive development of BPH-LUTS are still lacking and use of aged rodent models can be cost prohibitive and highly variable. Selective CYB5R3 KO may represent a useful animal model to study the milieu of the aging prostate.

FIGURE 1

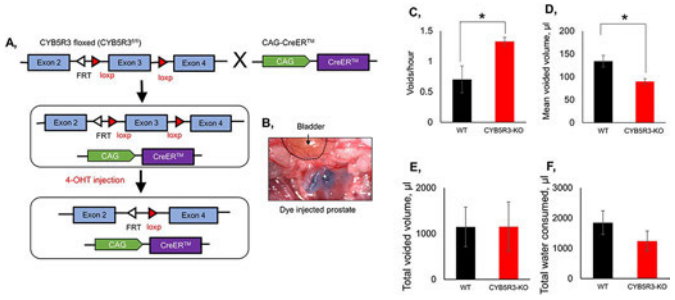
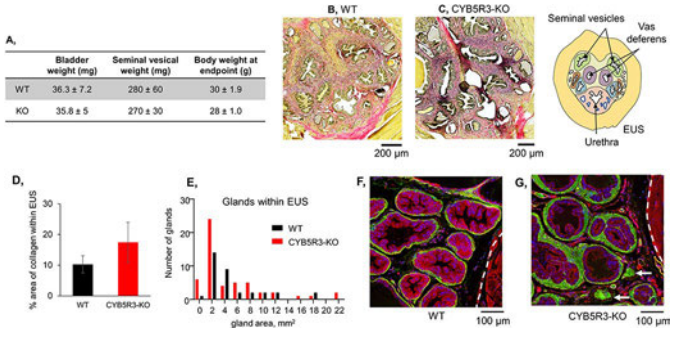


FIGURE 2



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3. Zabbarova et al., Benign prostatic hyperplasia/obstruction ameliorated using a soluble guanylate cyclase activator. J Pathol., 256(4):442-454, 2022.

Funding National Institutes of Health (R01DK098361) **Clinical Trial** No **Subjects** Animal **Species** mouse **Ethics Committee** University of Pittsburgh Institutional Animal Care and Use Committee

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SESSION 5 - MALE LOWER URINARY TRACT SYMPTOMS

Abstracts 53-64
11:00 - 12:30, Hall D
Chair: Dr John PFA Heesakkers (Netherlands)

53 | www.ics.org/2022/abstract/53

MANAGEMENT MODALITIES OF PRIMARY BLADDER NECK OBSTRUCTION IN YOUNG ADULT MEN: A SYSTEMATIC REVIEW AND META-ANALYSIS

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HYPOTHESIS / AIMS OF STUDY
Unlike the elderly population, where the predominant cause of bladder outlet obstruction is a benign enlargement of the prostate, many young males have primary bladder neck dysfunction/obstruction (PBNO). This systematic review was done to critically appraise the various evidence available in the literature for the presenting symptoms, diagnosis, and management modalities for PBNO.

STUDY DESIGN, MATERIALS AND METHODS
The review was registered in PROSPERO with registration number CRD42021216042. This review included the following subjects:

- Human male subjects
- Age 18-50 years
- Primary bladder neck obstruction on invasive urodynamic evaluation

A systematic search of the PubMed, Embase and Cochrane Central Register of Controlled Trials databases was performed to identify relevant studies published in the English language. The Methodological index for non-randomized studies was used for risk assessment of bias in this review.

RESULTS
MINORS scale was modified according to the studies in this review. Intermediate risk of bias was present in 3 studies and low risk of bias in 7 studies.

a) The difference in IPSS between baseline and after 12 months: (Figure 1)

The pooled estimate in the sub-group of medical treatments is -7.69, whereas, for the sub-group of surgical treatments, it is found to be -17.70.

b) Difference in Qmax between baseline and after 12 months: (Figure 2)

The pooled estimate in the sub-group of medical treatments is 4.54, whereas for the sub-group of surgical treatments it is found to be 7.74.

c) Difference in PVR between baseline and after 12 months:

The pooled estimate in the sub-group of medical treatments is -31.49, whereas for the sub-group of surgical treatments it is found to be -156.00.

INTERPRETATION OF RESULTS
This review summarises the effect of alpha-blocker therapy on IPSS, Qmax, and PVR at 3 months and 12 months. Although it improves the IPSS and Qmax at 3 months and 12 months the results are more significantly in favor of surgical treatment at 12 months. Therefore, alpha-blockers improve the parameters in the short term but the effects are not sustained until long. Transurethral incision of bladder neck (TUIBN)/Bladder neck incision (BNI) is considered the gold standard treatment option for PBNO. The long-term success rate is more statistically significant than that achieved with medical management. The natural history of PBNO is not known. A subset of patients with severe obstructive patterns may experience long-term repercussions due to delays in diagnosis, ineffective diagnosis, or therapy. Long-standing obstruction, in any case, can lead to reflux, hydroureteronephrosis, impaired functioning of the detrusor muscle, and eventually renal impairment.

CONCLUDING MESSAGE
PBNO is not an uncommon diagnosis among young men with LUTS. It needs careful evaluation with videourodynamics and appropriate early management. Behavioral therapies along with alpha-blockers and Onabotulinum toxin A are successful in the short term, but bladder neck incision is the only technique found to have long-term results.

FIGURE 1

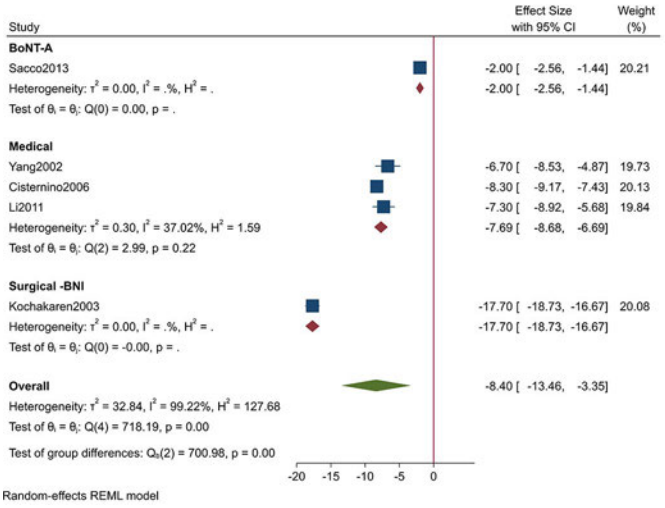

Figure 1: Difference in IPSS between baseline and after 12 months

FIGURE 2

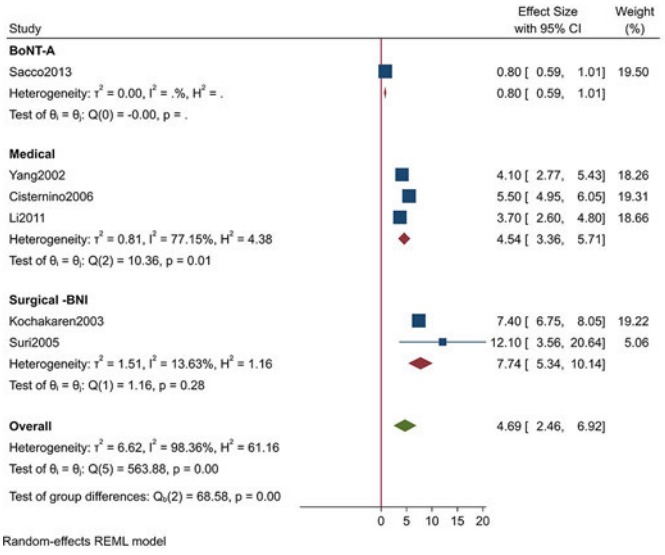

Figure 2: Difference in Qmax between baseline and after 12 months

Funding None **Clinical Trial** No **Subjects** None

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SHIFT CHANGE OF THE ACTIVATED COMPLEMENT PATHWAY IN THE FIBROTIC PROCESS ASSOCIATED WITH PROGRESSION OF BENIGN PROSTATIC HYPERPLASIA

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HYPOTHESIS / AIMS OF STUDY

In a previous study, benign prostatic hyperplasia (BPH) was reported to show a histological transition from smooth muscle-dominant type to fibrous-dominant type as it becomes more severe. Severe BPH patients with fibrous-dominant type could have the resistance to oral medication. However, the mechanism of BPH fibrosis and the influence on lower urinary tract symptoms (LUTS) by tissue fibrosis remained unresolved. On the other hands, we reported that complement activation by an autoimmune reaction was associated with the growth process of BPH. Therefore, we hypothesized that activation of complement pathways might be also associated with the fibrous process of BPH with progression. In this study, to clarify the mechanism of BPH fibrosis with progression and the influence on LUTS by tissue fibrosis, we analyzed the histological severity and the expression of complement components using human fibrous BPH tissues.

STUDY DESIGN, MATERIALS AND METHODS

The subjects were 56 histological BPH patients who underwent prostate needle biopsy due to high PSA levels in our institutions (mean age 68.6 ± 6.5 years). BPH patients were divided into two histological groups, fibromuscular type and fibrous type, by hematoxylin-eosin and elastica-Masson staining. Complement expression function analysis was performed by immunohistochemical staining using C3, factor B, and C5b-9 antibody, and the occupancy ratio of the stained region was calculated. In addition, the correlation between these histological changes of BPH and IPSS scores was analyzed.

RESULTS

Twenty-seven cases (48.2%) were classified as fibromuscular type, and 29 cases (51.8%) were classified as fibrous type. The proportion of fibrous components was significantly lower in the fibromuscular type than in the fibrous type (fibromuscular type 36.0 ± 12.9%, fibrous type 61.1 ± 11.7% ($p < 0.01$)). Abundant infiltration of inflammatory cells was observed in the fibromuscular type ($p = 0.03$). In the expression analyses of complement components, factor B was not significantly different between the two groups, whereas C3 (fibromuscular type 10.7 ± 8.2%, fibrous type 16.4 ± 12.7%) and C5b-9 (fibromuscular type 15.9 ± 6.2%, fibrous type 17.6 ± 9.2%) were significantly upregulated in the fibrous type compared to the fibromuscular type ($p = 0.04$, $p = 0.04$). The IPSS-3 score in the fibrous type was significantly higher compared to that in the fibromuscular type ($p = 0.04$).

INTERPRETATION OF RESULTS

Generally, the histological findings of BPH shows a histological transition from the fibromuscular type to the fibrous type during the fibrous process of BPH. In this study, we analyzed the time-dependent change of the expression of complement components and LUTS including voiding and storage symptoms using human fibrous BPH tissues. In these analyses could clarify the mechanism of BPH fibrosis by the complement pathway activation. First, as the histological findings of BPH show a histological transition to fibromuscular type, the activated complement pathway made the shift change to complement alternative pathway activation with the abundant infiltration of inflammatory cells. Secondly, as the histological findings of BPH show a transition from fibromuscular type to fibrous type, the activated complement pathway made the shift change to the complement late pathway. These results suggested that shift change to complement late pathway activation was involved in the progression of fibrous BPH. Furthermore, the deterioration of LUTS associated with the progression of BPH fibrosis was predominant in voiding symptoms, suggesting that the complement pathway might be a therapeutic target for voiding symptoms.

CONCLUDING MESSAGE

The shift changes of the activated complement pathway from complement alternative pathway to complement late pathway was associated with the fibrous process of BPH as the histological findings were made a transition to the fibrotic stage including fibrous and fibromuscular type.

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Funding None **Clinical Trial** No **Subjects** Human **Ethics Committee** Fukushima Medical University **Ethics Committee Helsinki** Yes **Informed Consent** Yes

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EFFECT OF ROUTINELY PREOPERATIVE URETHRAL DILATION TO PREVENT URETHRAL STRICTURE AFTER TRANSURETHRAL RESECTION OF THE PROSTATE FOR BENIGN PROSTATIC HYPERPLASIA

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HYPOTHESIS / AIMS OF STUDY

Urethral stricture is one of the postoperative complications after transurethral resection of the prostate for benign prostatic hyperplasia and urethral dilation is simple and effective procedure to treat urethral stricture. However, there are no studies that have evaluated the relationship between preoperative urethral dilation and the incidence of post-transurethral resection of the prostate urethral stricture. Thus, we retrospectively investigated the effect of routinely urethral dilation just before surgery on preventing urethral stricture after transurethral resection of the prostate for benign prostatic hyperplasia.

STUDY DESIGN, MATERIALS AND METHODS

From January 2010 to December 2018, a total of 651 patients who underwent transurethral resection of the prostate for benign prostatic hyperplasia was included in this study. We divided into two groups: Group A (295 patients, routinely urethral dilation before transurethral resection of the prostate) and B (356 patients, control group). We used a 26Fr resectoscope sheath, 30-degree telescope, and bipolar resectoscope. Urethral dilation was performed immediately before insertion of resectoscope sheath and 28Fr dilator was used. Urethral stricture after transurethral resection of the prostate was assessed by cystoscopy. Each patient was evaluated at 1 month, 3 months, and 6 months after transurethral resection of the prostate. The effect of urethral dilation was assessed based on International Prostate Symptom Score (IPSS), peak urine flow rate, voiding volume, and post-void residual urine.

RESULTS

There were no significant differences of clinical variables, such as prostate volume, serum prostate specific antigen (PSA), age, operation time, and duration of catheterization between two groups ($p > 0.05$). However, peak urine flow rate was significantly different between group A and B (19.87 ± 9.12 vs 16.18 ± 9.79, $p = 0.047$). The incidence of urethral stricture after transurethral resection of the prostate was 4.06% (12/295) and 8.71% (31/356) in group A and B, respectively ($p = 0.032$).

INTERPRETATION OF RESULTS

As you see in Table 1, there were no significant differences of clinical variable between two group, except the incidence of urethral stricture after surgery. The mean duration of the urethral stricture after transurethral resection of the prostate was 137.5 ± 102.9 days. In all patients who had urethral stricture, the mean lengths of stricture was 8.1 ± 7.6 mm and the sites of stricture were bladder neck (18/43), urethral meatus (21/43), and bulbous urethra (4/43).

CONCLUDING MESSAGE

This study demonstrated that the preoperative urethral dilation decreased the incidence of urethral stricture after transurethral resection of the prostate. We suggested that the routinely preoperative urethral dilation is simple and effective way to prevent urethral stricture after transurethral resection of the prostate for benign prostatic hyperplasia.

FIGURE 1

Table 1. Comparison of the clinical variables between the two groups.

Variables	Group A (n=295)	Group B (n=356)	p-value
Age (yrs)	71.51±8.59	69.52±7.41	0.692
BMI (kg/m^2)	22.87±4.12	23.01±3.97	0.278
PSA (ng/mL)	5.18±4.97	4.87±5.15	0.612
Prostate volume (cc)	56.19±29.13	54.64±25.67	0.571
Preoperative variables			
IPSS	18.46±8.62	17.95±7.98	0.652
QoL	3.87±1.54	3.79±1.31	0.915
Preoperative uroflowmetry			
Qmax (mL/s)	9.13±7.24	10.16±6.97	0.104
Voiding volume (cc)	246.87±97.59	238.12±86.54	0.243
PVR (cc)	67.29±87.51	71.08±79.59	0.187
Operation time (mins)	59.67±31.59	56.51±35.19	0.487
Duration of catheterization (days)	3.19±1.52	3.38±1.48	0.097
Resected prostate volume (cc)	29.87±19.45	27.12±8.08	0.173
Urethral stricture (%)	12 (4.06)	31 (8.71)	0.032

BMI, body mass index;PSA, prostate specific antigen;IPSS, International prostate symptom score;QoL, Quality of life;PVR, post-void residual urine

Funding No source of funding **Clinical Trial** No **Subjects** Human **Helsinki** Yes **Informed Consent** Yes

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PREDICTIVE FACTORS OF POSTOPERATIVE URINARY RETENTION AFTER OPEN INGUINAL HERNIA REPAIR

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HYPOTHESIS / AIMS OF STUDY
Open inguinal hernia (IH) repair is one of the most common general surgery operations. It can be conducted under general, spinal or local anesthesia. Postoperative urinary retention (POUR) is a common complication after inguinal hernia repair, ranging from 0-40% depending on the type of anesthesia used, reaching higher percentages when the operation is performed under regional anesthesia [1]. Despite the high rates of POUR, open inguinal hernia repair under spinal anesthesia remains popular among surgeons, anesthesiologists and patients. The aim of this study is to investigate the perioperative risk factors of POUR in patients undergoing elective open inguinal hernia repair under spinal anesthesia.

STUDY DESIGN, MATERIALS AND METHODS
This is a prospective study, enrolling male patients elder than 50 years old, eligible for IH repair. Exclusion criteria were emergency surgery, benign prostatic hypertrophy under medication, history of open or endoscopic lower urinary tract surgery, neurological conditions under medication, ASA Score ≥ 3, IH repair under general or local anesthesia. All patients were submitted to open inguinal hernia repair with mesh placement. Possible factors of POUR that were recorded were age, comorbidities, previous abdominal operations, Body Mass Index (BMI), International Prostate Symptom Score (IPSS), nocturia, preoperative Anxiety Visual Analog Scale score (A-VAS), recurrent hernias, postoperative Pain Visual Analog Score (P-VAS), perioperative use of intravenous (IV)/spinal opioids, perioperative administration of IV fluids, intraoperative administration of atropine, European Hernia Society (EHS) hernia Classification, operation duration, type of hernia, posterior wall reinforcement and hernia sac size. Postoperative urinary retention was defined as the inability to void urine up to 8 hours after surgery. Statistical analysis has been performed according to multivariate analysis for non-parametric samples and a cut-off value for statistical significance of 0.05 with SPSS v26 (IBM Corp. 2017. IBM SPSS Statistics for Windows. Armonk, NY: IBM Corp.).

RESULTS
141 consecutive male patients have been enrolled in this study with a mean age of 63.5 years. The incidence of postoperative urinary retention was 36.1% (51 patients). All patients with POUR were catheterized using a foley catheter. Catheter removal was successful 24 hours after surgery in 46 patients (90.2%), in 3 patients (5.9%) the catheter was removed 48 hours after surgery, while 2 (3.9%) patients required prolonged catheterization. Studied parameters which reached statistical significance at multivariate analysis, were comorbidities, IPSS score, nocturia, posterior wall reinforcement (PWR), preoperative high A-VAS score and intraoperative use of atropine. At the logistic regression model (OR 95%CI) only comorbidities ($p = 0{,}04$), PWR ($p = 0{,}006$) and high A-VAS score ($p = 0{,}043$) were found to be statistically significant. 49% of the patients had no comorbidities, 28% had one, 20% patients had two and 3% patients had more than two. The most common condition under medication was arterial hypertension (53/72). Most common causes of anxiety among patients with high A-VAS score were anxious personality (12/29), operation (8/29) and anesthesia (4/29).

INTERPRETATION OF RESULTS
In our study we found a high incidence of POUR comparing to literature [1]. We attribute our results to the fact that we only included males over 50 years old, all repairs were performed under spinal anesthesia and we set a small time interval from surgery to urinary retention diagnosis. Perioperative parameters that were identified as prognostic factors of POUR in our study were IPSS and nocturia, intraoperative use of atropine, comorbidities, posterior wall reinforcement and preoperative high A-VAS score.

Comorbidities were identified as a predictive factor of POUR. In our study we included patients with a low ASA score and mild systemic diseases such as arterial hypertension, dyslipidemia and hyperuricemia but under medication with a variety of drugs, making it impossible to identify any specific drug that could predispose to POUR.

Posterior wall reinforcement is usually performed in patients with large direct hernias to reinforce the repair and/or to facilitate mesh placement. Suturing of the trasversalis fascia to the Cooper ligament before mesh placement is not superior to tension free techniques and it increases the possibility of urinary retention and should be avoided [1].

According to our results preoperative anxiety leads to increased rates of POUR. This is to the best of our knowledge the first study to investigate preoperative anxiety as a predictive factor of POUR. The use of Anxiety VAS score is an easy and accurate way to preoperatively identify patients who are in danger of developing postoperative urinary retention. According to the existing literature a patient was considered anxious with 51mm or more on the VAS scale [2]. In this group of patients, a different approach should be used, such as thorough explanation of the procedure and anesthesia technique along with premedication in order to reduce anxiety levels or even a different anesthetic approach.

CONCLUDING MESSAGE
Postoperative urinary retention after open inguinal hernia repair is more likely to be present in male patients with comorbidities, high Anxiety VAS score and posterior wall reinforcement. Further investigation with studies on larger series and less limitations are needed to obtain clear messages and guidelines.

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2. Facco E, Zanette G, Favero L, et al. Toward the validation of visual analogue scale for anxiety. Anesth Prog. 2011, 58:8 13. 10.2344/0003-3006-58.1.8

Funding Koukoulis G, Bouliaris K, and Tepetes K received a research grant from Greece and the European Union (European Social Fund-ESF) through the Operational Programme «Human Resources Development, Education and Lifelong Learning 2014- 2020 to conduct this study. **Clinical Trial** Yes **Registration Number Clinical Trial**s number NCT03976934 https://www.clinicaltrials.gov/ct2/show/NCT03976934 **RCT** No **Subjects** Human **Ethics Committee** Scientific Council of General Hospital of Larissa **Helsinki** Yes **Informed Consent** Yes

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THE ROLE OF DETRUSOR ULTRASTRUCTURAL STUDY IN PREDICTING LONG TERM VOIDING OUTCOMES OF MALE PATIENTS WITH HYPOCONTRACTILE BLADDERS WHO UNDERWENT TRANSURETHRAL RESECTION OF THE PROSTATE (TURP)

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HYPOTHESIS / AIMS OF STUDY
It is known that satisfactory voiding function requires both adequate detrusor contractility and an unobstructed outflow tract. It has been demonstrated that impaired detrusor contractility can reduce the success of transurethral resection of the prostate (TURP). Due to the limitations of urodynamic studies in diagnosis of hypocontractile detrusor (HCD), detrusor ultrastructural studies have been proposed as a method of assessing detrusor failure. Our previous ultrastructural studies (1) showed that features such as the 'myohypertrophy pattern' were associated with poorer voiding outcomes after TURP. The objective of this study is to report on the longer term voiding outcomes in men with hypocontractile bladders who have had TURP, and correlate voiding outcomes with detrusor ultrastructure studies.

STUDY DESIGN, MATERIALS AND METHODS
Patients who had urodynamic diagnosis of bladder outflow obstruction or evidence of impaired detrusor contractility and were selected to undergo TURP at a single centre as part of their treatment, were included in the study. Detrusor biopsies were obtained at cystoscopy and processed for analysis by transmission electron microscopy. Detrusor ultrastructural features such as myohypertrophy pattern (cell size, irregularity), degenerative features and elastosis were scored by consensus and observers were blinded to clinical and urodynamic data. Postoperative voiding outcomes were correlated with ultrastructural features. Longer term follow up (mean 16 years) was conducted and reviewed in the context of initial voiding outcomes and ultrastructural features.

RESULTS
Seventeen patients were recruited for the study, 12 with hypocontractile detrusor on urodynamic studies and 5 with bladder outlet obstruction (BOO) on urodynamic studies. In the HCD group of patients, the mean postvoid residual urine (PVR) measurement was 930ml (range 400ml to 1600ml). Postoperatively all BOO patients voided, three HCD patients voided immediately, three HCD patients had delayed recovery of voiding, and six patients failed to void. Ultrastructural studies of the 12 patients with HCD showed severe degeneration in nine patients (75%), severe collagenosis in ten (83%), myocyte size variability in ten (83%) and severe fascicle derangement in nine (75%). Voiding outcome after TURP was significantly associated fascicle derangement ($p = 0.03$), degeneration ($p < 0.05$), collagenosis ($p = 0.01$) and elastosis ($p = 0.005$). At longer term follow up (mean 16 years), three patients had deceased, and an additional two were lost to follow up. There was association between successful initial post TURP voiding outcome and rate of subsequent catheter freedom, with poorer voiding outcome and detrusor ultrastructural features of hypocontractile detrusor associated with subsequent urinary retention and requirement for long term catheterisation.

INTERPRETATION OF RESULTS
Detrusor ultrastructural features of fascicle derangement, degeneration, collagenosis and elastosis appear to be associated with impaired detrusor contractility and are associated with poorer voiding outcomes after transurethral resection of the prostate in the short term as well as on longer term follow-up (mean 16 years).

CONCLUDING MESSAGE
Detrusor biopsy with ultrastructural analysis may be a useful diagnostic and prognostic tool in men with urinary retention considering surgical treatment options in the short term and long term.

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Funding Royal Australasian College of Surgeons Research Scholarship **Clinical Trial** Yes **Public Registry** No **RCT** No **Subjects** Human **Ethics Committee** Sydney Local Health District Human Research **Ethics Committee Helsinki** Yes **Informed Consent** Yes

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INCONTINENCE IN THE MALE OLDER POPULATION: A CROSS-SECTIONAL MULTISITE PREVALENCE STUDY

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HYPOTHESIS / AIMS OF STUDY
Population aging leads to an increase in the number of men 65 years or older with various nursing care problems, such as incontinence. When talking about incontinence, nursing research and practice mostly focus on women. Therefore, incontinence in the male population is still underreported. We defined urinary incontinence (UI) as any involuntary loss of urine without any involuntary loss of fecal material (1) . Fecal incontinence was defined any involuntary loss of fecal material without any involuntary loss of urine (1). And double incontinence, as an involuntary loss of urine and fecal material (2). The aim of this study was to report the prevalence, type of incontinence and used interventions with regard to UI, FI and DI in men 65 years or older.

STUDY DESIGN, MATERIALS AND METHODS
This is a secondary data analysis of the "Nursing Care Quality" measurement in Austria (3). We used data from the years 2014, 2015 and 2016 from hospitals and geriatric institutions. We included data of men 65 years or older, to assess the prevalence, type of incontinence and used interventions. Descriptive statistics as well as X2 tests and Mann-Whitney U-Test was used for data analyses.

RESULTS
Of all men 65 years or older (N = 3686), 75% were continent (n = 2764), 11.7% (n = 430) were UI; 2.8% (n = 105) were FI and 10.5% (387) were DI. DI men 65 years or older had statistically significantly more medical diagnoses (3.7; SD 2.1) than UI men 65 years or older (3.2; SD 1.9) or FI men (3.1; SD 2). Besides, they were significantly more often bedfast (45.5%) or immobile (32.6%) compared to UI men 65 years or older (6.3%; 2.8%) or FI men 65 years or older (34.3%; 23.8%). Adjustment of clothing was performed statistically significantly more often in UI men 65 years or older (55.7%) compared to FI men or DI men 65 years or older (39.3%; 46.3%). Medication itself or the evaluation of medication was used statistically significantly more often in the group of DI men 65 years or older (12.9%; 11.6%) than in UI men or FI men 65 years or older (7.7%; 8.1% vs. 1.9%; 2.9%). We also identified statistically significant differences in the use of absorbent products such as pads between UI, FI and DI men 65 years or older (42.8%; 46.7%; 54.8%).

INTERPRETATION OF RESULTS
This study revealed that although incontinence in men is a neglected topic in the international literature, one fourth of the men 65 years or older are affected by either UI, or FI or DI.

CONCLUDING MESSAGE
Based on the results we conclude that within men 65 years or older specific focus should be placed on the prevention of FI in older men, as well as on the revision of medication as one crucial treatment strategy.

FIGURE 1

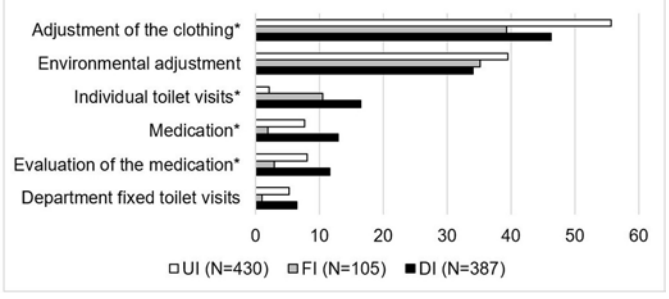

Figure 1. Percentage of nursing interventions in UI/FI/DI residents (multiple answers possible) *p < 0.05

FIGURE 2

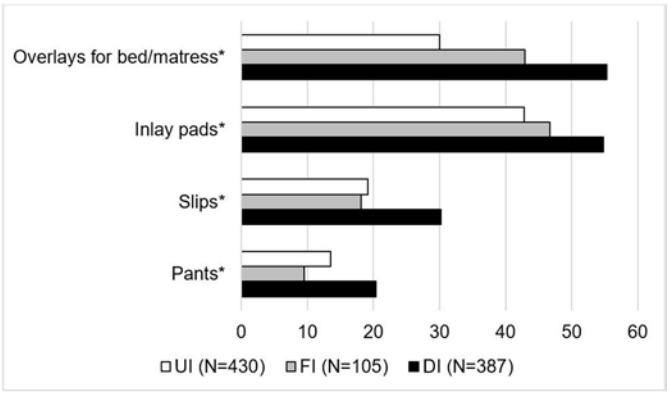

Figure 2. Percentage of used aids in UI/FI/DI residents (multiple answers possible) *p < 0.05

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Funding None **Clinical Trial** No **Subjects** Human **Ethics Committee** **Ethics Committee** of the Medical University of Graz **Helsinki** Yes **Informed Consent** Yes

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ARTIFICIAL URINARY SPHINCTER CUFF SIZES AND SAFE INSTRUMENT/CATHETER PASSAGE

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HYPOTHESIS / AIMS OF STUDY

The artificial urinary sphincter (AUS) is the gold standard for males with urinary incontinence. It is generally a safe procedure with a high degree of satisfaction. However, there is a lifelong risk of infection and erosion. AUS cuffs are commonly placed around the bulbar urethral area. There is always a risk of trauma and erosion of cuffs with catheterization or endoscopy. At this time there is little guidance as to which size catheters or scopes can pass through each AUS cuff sizes safely. The goal of this study was to determine which size of catheters/scopes can pass through different cuff sizes safely.

STUDY DESIGN, MATERIALS AND METHODS

All AUS cuff sizes available (3.5 cm up to 6.0 cm), catheter sizes between 12Fr- 22Fr and scope sizes 19Fr flexible /rigid, 21Fr-26Fr rigid scopes were examined. We used deflated assembled cuffs and 3 different blind observers to measure the free space left between the wall of the cuff and the catheter/scope to be sure that there was consistency. We created a scale from 1 to 3 to determine the ease of passage for each catheter/scope. We also had an MRI radiologist examine bulbar urethra thickness in 20 male patients to determine the average thickness without the bulbospongiosus muscle. Using our average bulbar urethral thickness, we were able to estimate how much free space remained within the urethral lumen and how easy and safe it was to pass each catheter/scope.

RESULTS

For 3.5 cm cuffs, 12Fr catheters pass easily and safely, 14Fr-16Fr catheters and 19Fr flexible/rigid scopes can pass through with some mild risk of trauma. Larger catheter/scope sizes cannot pass through without significant risk of trauma.

For 4.0 cm cuffs, 12Fr-14Fr catheters pass easily and safely. 16Fr-18Fr catheters and 19Fr-21Fr rigids/flexibles scopes can pass with some mild risk of trauma. Larger catheter/scope sizes cannot pass through safely.

For 4.5 cm cuffs, 12Fr-18Fr catheters and 19Fr flexible/rigid scopes pass easily and safely. 20Fr-22Fr catheters and 21Fr rigid scopes can pass with some mild risk of trauma. Larger catheter/scope sizes cannot pass through safely.

For 5.0cm cuffs, 12Fr-22Fr catheters and 19Fr-21Fr flexible/rigid scopes can pass easily and safely. 22Fr-26Fr scopes can pass with some mild risk of trauma.

For 5.5cm cuffs, all catheters/scopes can pass easily and safely. However, the 26Fr rigid scope can pass with some mild risk of trauma.

For 6cm cuffs, all catheters/scopes examined can pass easily and safely.

INTERPRETATION OF RESULTS

Our recommendations are divided in 3 distinct categories. First, there is the catheters and scopes that can pass easily and can be used safely without an increased risk of trauma and erosion. The others are the ones that they can pass through with a mild risk of trauma and erosion. They should be used only if needed, carefully and if possible, on direct visualization. Finally, the catheters and scopes with difficult passage and higher risk of trauma and, obviously, we don't recommend using them. We should state that our recommendations are extremely safe and prudent. Although we suggest not using some catheters and scopes for different cuff's size, it is possible in clinical practice that some can still be used. We think it'll put the AUS cuffs at higher risk and we suggest that urologists use their clinical judgment.

CONCLUDING MESSAGE

Our study can guide urologists in the management of patients with an AUS who need urethral catheters or endoscopy. These recommendations are based on the measurements of our study along with bulbar urethral thickness. In general, greater caution is needed with smaller cuff sizes (3.5-4.5 cm). Our recommendations, with minimal urethral compression, are purposely conservative and safe to avoid trauma and erosion of the AUS cuffs.

FIGURE 1

TABLE 2: Catheter passage with every cuff size

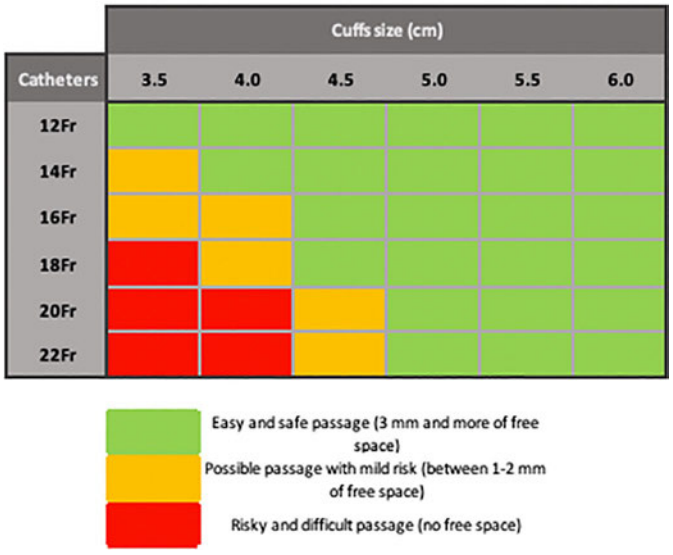
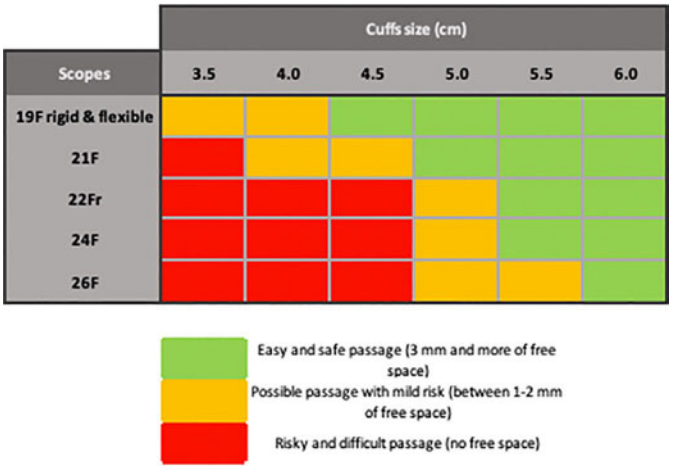


FIGURE 2

TABLE 3: Scope passage with every cuff size



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EFFICACY, SAFETY AND REOPERATIONS OF ARTIFICIAL URINARY SPHINCTER IN ELDERLY MALE PATIENTS: A LARGE MULTICENTRIC STUDY

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HYPOTHESIS / AIMS OF STUDY

Since 1973, the artificial urinary sphincter (AUS) has emerged as the gold standard treatment in moderate to severe male stress urinary incontinence (SUI).

Although urinary incontinence is known to worsen the condition of elderly patients, many surgeons are still hesitant about placing an AUS in these patients.

At this time, literature is scarce, making therapeutic decision difficult and patient information poor.

The main objective was to assess the efficacy of male AUS in elderly patients, defined as 75 years old (yo) or more.

Secondary we sought to determine the role of age over 75yo in safety and reoperation-free survival after AUS placement. We evaluated risk factors that may influence efficacy and reoperation-free survival specifically in the population over 75yo. Finally, we assessed the factors of erosion.

STUDY DESIGN, MATERIALS AND METHODS

The charts of all male patients who underwent AUS implantation between 1991 and 2020 at 13 centers were retrospectively reviewed. The AMS-800 AUS (Boston Scientific™) was used in all cases. Patients with neurogenic SUI as well as with bladder neck implantation were excluded for the sake of population homogeneity. We compared patients over 75yo at AUS placement and patients under 75.

Our primary endpoint was AUS efficacy assessed by the postoperative social continence, defined as the use of 0 to 1 pad per day.

We secondary reported postoperative complications and reoperations (revisions, replacements, explantations and overall). A revision was defined as a reoperation consisting in replacement or repositioning of one or several components of the device.

We performed a survival analysis using Kaplan-Meier curves and Cox proportional hazard models to assess predictive factors of revisions, replacements or explantations. Predictive factors of continence were assessed using a logistic regression.

RESULTS

A total of 1233 patients met the inclusion criteria with 330 patients over 75yo (26.8%).

Regarding the characteristics of population, groups differed on comorbidities (BMI, Charlson index, ASA score, antiplatelet/anticoagulant drugs intake), but also on radiation exposure (40.5% among more than 75yo vs 31.5%), preoperative 24h pad-test (400.0mL vs 300.0mL for the youngest group), and etiologies of incontinence. Indeed although radical prostatectomy remained the first etiology in both groups (77.5% of the eldest vs 88.6%), focal therapies and endourology affected more patients in the older group (15.4% vs 6.6%).

Concerning operative outcomes, we did not find any difference on surgical approach, pressure regulating balloon size, cuff size or intraoperative complications. Only cuff position showed a higher rate of transcorporeal position among the elderlies (13.1% vs 5.5%, $p < 0.001$).

Social continence was achieved for 74.4% of the patients over 75yo, with no significant difference compared to the other group (80.1%, $p = 0.114$).

We observed significantly earlier complications among elderly patients (18.8% vs 12.6%, $p = 0.014$) but their Clavien-Dindo grade was significantly lower ($p = 0.025$).They presented only 11.8% of Grade $\geq$ 3b complications (vs 28.4%). There was no difference on median hospital stay duration (3 days for both groups, $p = 0.901$).

We observed similar overall reoperation rates in both groups (38.2% and 34.8%, $p = 0.299$) but explantation rate was higher among the patients over 75yo (31.7% vs 22.6%, $p = 0.002$). We also found a larger proportion of infections and erosions in the elderly patients (57.8% vs 41.9%, $p = 0.003$).

After a median followup of 24 and 19 months according to the group, the estimated median overall reoperation-free survival was 5 years for the patients over 75 years, and 6 years for the patients under 75 years, with no significant difference ($p = 0.076$).

The over 75yo group survival curve showed a tendency for early (< 1year) reoperations. Also, we found a significantly worse explantation-free survival curve for the elderly group ($p < 0.0001$). Otherwise we did not find any difference between revision-free and replacement-free survivals.

Among the predictive factors of social continence (age over 75, center annual caseload, Charlson index, history of pelvic radiation, history of incontinence surgery, perineal surgical approach, cuff size, transcorporeal cuff position and post focal therapies/endourology incontinence), only the incontinence etiology was significant. Therefore, post endourology or focal therapies incontinence is associated with worse functional results (OR = 0.36, [0.15-0.92], $p = 0.03$).

In the Cox model risk factors of early reoperations were annual caseload and transcorporeal cuff position (HR = 1.06 [1.02-1.1], $p = 0.009$ and HR = 2.66 [1.49-4.7], $p < 0.001$, respectively).

INTERPRETATION OF RESULTS

Our results appear to be in accordance with literature.

Indeed we did not find any impact of age on functional results after an AUS implantation. [1]

Also we found a larger number of postoperative complications in elderly patients but most of them were low grade and didn't affect hospital stay duration. [2]

There was similar reoperation-free survival in both groups [3] with nonetheless a tendency for early explantations in the group over 75yo, probably due to more frequent infections and erosions.

We identified high annual caseload as a risk factor of early reoperations. This finding might be explained by a selection bias of expert centers - and a tendency to choose early reoperation when it's needed.

Transcorporeal cuff position was a risk factor of early reoperations. There was not enough data to know if it was a matter of erosion or urethral atrophy leading to persistent SUI. It could be a confusion bias as patients are offered transcorporeal cuff position because of their history (multioperation, radiation exposure, fragile urethra).

We identified post-endourology or post-focal therapies incontinence as a risk factor of poor post-operative continence. This finding is difficult to discuss given the group heterogeneity.

Our study is not without limitations. Indeed we have few long-term postoperative urodynamic data and questionnaires scores. We also lack information about population characteristics -like cognitive status, dexterity or immune impairment.

CONCLUDING MESSAGE

AUS implantation in male patients over 75 years old appears to be an effective option to treat SUI with few early postoperative risks.

Yet we observed higher rates of early (2 years) explantations among elderly patients, probably due to the increased rate of device erosions and infections.

These findings would improve patients information and therapeutic decision-making.

FIGURE 1

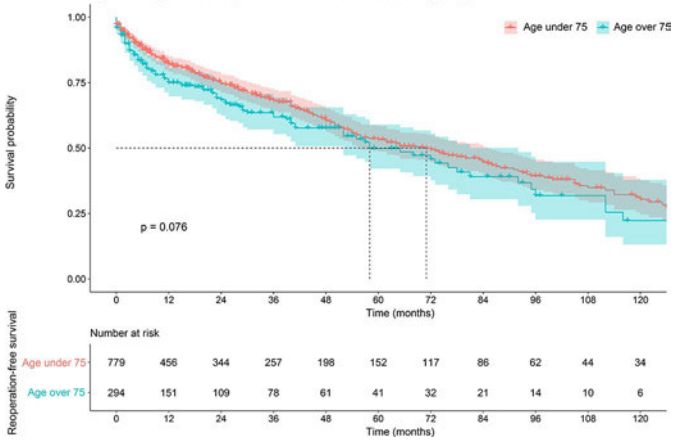
	Age < 75 (n=903)	Age ≥ 75 (n=330)	*p* value
Institution caseload per yr (median [IQR])	9.0 [6.0, 14.0]	10.0 [7.0, 14.0]	0.478
Surgical approach (n (%))			
Perineal	572 (65.7)	203 (63.4)	0.517
Penoscrotal	299 (34.3)	117 (36.6)	
Cuff position (n (%))			**<0.001**
Bulbar	842 (94.5)	279 (86.9)	
Transcorporeal	49 (5.5)	42 (13.1)	
Pressure regulating balloon size, mmHg (n (%))			0.923
51-60	10 (1.3)	4 (1.4)	
61-70	727 (98.1)	283 (98.3)	
71-80	4 (0.5)	1 (0.3)	
Cuff size, mm (median [IQR])	45.0 [40.0, 45.0]	45.0 [40.0, 45.0]	0.428
Intra-operative complication (n (%))	6 (0.8)	4 (1.4)	0.600
Social continence (n (%))	446 (80.1)	148 (74.4)	0.114
Early postoperative complication (n (%))	95 (12.6)	54 (18.8)	**0.014**
Clavien-Dindo classification (n (%))			**0.025**
Grade 1	45 (47.4)	23 (45.1)	
Grade 2	19 (20.0)	15 (29.4)	
Grade 3a	4 (4.2)	7 (13.7)	
Grade 3b	27 (28.4)	6 (11.8)	
Grade 4-5	0 (0.0)	0 (0.0)	
Hospital stay, days (median [IQR])	3.0 [2.0, 4.0]	3.0 [2.0, 4.0]	0.901
Overall reoperation rate (n (%))	314 (34.8)	126 (38.2)	0.299
Revision rate (n (%))	140 (16.9)	41 (13.1)	0.141
Replacement rate (n (%))	90 (13.3)	32 (12.4)	0.791
Explantation rate (n (%))	183 (22.6)	97 (31.7)	**0.002**
Reoperation indication (n (%))			**0.003**
Erosion and/or infection	129 (41.9)	74 (57.8)	
Mechanical failure	69 (22.4)	21 (16.4)	
Non mechanical failure	91 (29.5)	21 (16.4)	
Other	19 (6.2)	12 (9.4)	
Follow up time, months (median [IQR])	24.0 [6.0, 60.0]	19.0 [5.0, 48.0]	**0.011**

Table 1. Surgical characteristics, postoperative outcomes, and reoperations

Revision was defined as any reoperation for replacing or repositioning one or several device components. Mechanical failure was defined as any fluid loss or defect of any components of the device. Non mechanical failure was defined as recurrence or persistence of SUI despite a normally functioning device. The other causes of failure included pump or balloon malposition.

FIGURE 2

Figure 1. Kaplan Meier reoperation-free survival curve according to age



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LONG TERM FUNCTIONAL OUTCOME AND COMPLICATIONS OF ADVANCE®/ADVANCE XP® MALE SUBURETHRAL SLINGS IN THE MANAGEMENT OF POST-PROSTATECTOMY INCONTINENCE: MULTICENTER PROSPECTIVE TEN-YEAR FOLLOW-UP STUDY

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HYPOTHESIS / AIMS OF STUDY
The AdVance®/AdVance XP ® suburethral transobturator male slings are considered an option for the treatment of male stress urinary incontinence (SUI) post-radical prostatectomy (1).

According to 6th International Consultation on Incontinence the male slings are an acceptable surgical approach with several-year follow-up data supporting their safety and efficacy in men with mild to moderate degrees of SUI.

To our knowledge, there are no articles about more than 10 years of follow-up related to male urethral slings.

The aim of our paper is to evaluate the effects on the urethral bulb after ten years of compression/mobilization. We focused on the eventual deterioration of continence in those cured by surgery and later complications such urethral sling erosion(2).

STUDY DESIGN, MATERIALS AND METHODS
An observational, prospective, multicenter study

Inclusion period: we considered initially 111 patients with SIU after radical prostatectomy treated with ADVANCE®/ADVANCE XP male suburethral slings before February 2012.

Patients included: fulfilling 10 years of follow-up until February 2022.

Patients with 24-h Pad test <400 g, continents at night and at rest who also resulted in positive "repositioning test" were considered for sling (1). Exceptionally, 24-h Pad test >400g were accepted in patients who rejected artificial sphincter. Patients were only considered after failed pelvic floor rehabilitation.

Exclusion criteria: patients without complete follow-up were excluded. The presence of urodynamic detrusor overactivity or previous surgery was not considered as contraindication.

Preoperative assessment: continence was assessed by means of the 24-hour pad weight test and Patient-reported outcome measures (PROMs) with the International Consultation on Incontinence Questionnaire Short Form (ICIQ-UI SF). A preoperative urodynamic assessment, according to the International Continence Society criteria, and flexible cystoscopy were performed in all cases. Urgency was defined as the complaint of a sudden compelling desire to pass urine which is difficult to defer.

Written informed consent and negative urine cultures before surgery were mandatory before surgery. Preoperative antibiotic prophylaxis was administered in all cases.

Surgical technique: surgery has been previously described (3). Briefly, the bulbospongiosus muscle is incised in its longitudinal axis and the central tendon it is sectioned distally. A helical rounded tip needle is introduced along the lateral edge of the pubic ramus, pointing towards, and coming out at the uppermost corner between the urethral bulb and inferior pubic ramus. The edge of the proximal fap of the sling should be located at the origin of the central tendon previously marked. Postoperatively, urinary catheter is leaved in place for 48 h and then the patient is discharged.

Follow-up: outcome was assessed at 3 month after surgery. The primary outcome was a pad count, with cure defined as no longer requiring pads; all other cases were defined as failures.

Follow-up was carried out once every 3 months during the first year and once every 6 months thereafter, in parallel to the oncological follow-up (PSA, 24h-PW and ICIQ-UI SF). Surgical complications (<90 days) were evaluated according to Clavien-Dindo classification. The reintervention rate was considered as any case requiring invasive treatment. The loss of continence was defined as the need for pads in a patient initially cured. Patient characteristics, peri-operative data, complication, and revision rate were analyzed prospectively.

Statistics: data analysis was performed using Stata (version 13.1, StataCorp, College Station, TX). Categorical variables were summarized using frequencies and percentages and analyzed using the Chi-squared test. Continuous variables were analyzed using means, medians, and standard deviations. We examined continuous variables used Student's t test and One-way analysis of variance adjusted for multiple comparisons, if necessary. The Wilcoxon test was used to analyze variables with non-normal distributions. All tests were two-sided, and p values less than 0.05 were considered statistically significant. A binary logistic model including all significant covariates was used to validate the results.

Ethical Approval: all procedures involving human participants were performed in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.

The data from this study are based on "Fundación IVO Registry for Patients Undergoing Sling or Artificial Urinary Sphincter After Prostate Cancer Treatment", which has been registered with ClinicalTrials.gov, Identifier: NCT02901392.

RESULTS
One hundred and eleven patients underwent surgery before February 2012. Twenty-four did not complete the minimum follow-up. Therefore, finally the study group was 87 patients. Median follow-up was 136.6 months (range:121.9-170.5).

Baseline patient characteristics: with a median age of 66 years (range: 52-83), 27 patients had undergone an open retropubic radical prostatectomy, 12 patients robotic and 48 patients laparoscopic prostatectomy. No incontinence surgery was previously performed in any patient. Median 24h-Pad test was 199 grams (range: 15-600). Seventeen patients (19.54%) presented preoperative urgency. Urodynamic study was performed in 53 patients: 23 patients-detrusor overactivity, 5 patients-low bladder compliance and 25 without findings in cystometry.

Postoperative complications: there were not intra-operative complications. A total of 19 early postoperative complications were reported (21.83%): 8 patients presented perineal-scrotal pain (Clavien I) and 11 patients with acute urinary retention (Clavien II). To date, there are no reports of recurrent anastomotic stricture, urethral sling erosion or any other recognized late complications.

Cure rate: 59 patients were considered cured (67.81%).

Surgery requirement during follow-up: no patient in this series required surgical review during follow-up.

Loss of continence during follow-up: Of the 59 patients initially cured, 17 patients (28.81%) lost continence during follow-up (Figure 1). Five of 59 patients loss continence before 3 years (8.47%), 9 of 59 patients before 5 years (15.25%) and 16 of 59 patients before 10 years (27.12%).

INTERPRETATION OF RESULTS
These results demonstrate the effectiveness of suburethral mesh in the treatment of SUI after prostatectomy.

It is a surgery with a low risk of complications, especially serious complications.

This is a multicenter study with a long follow-up (more than 10 full years) and therefore its results are reliable.

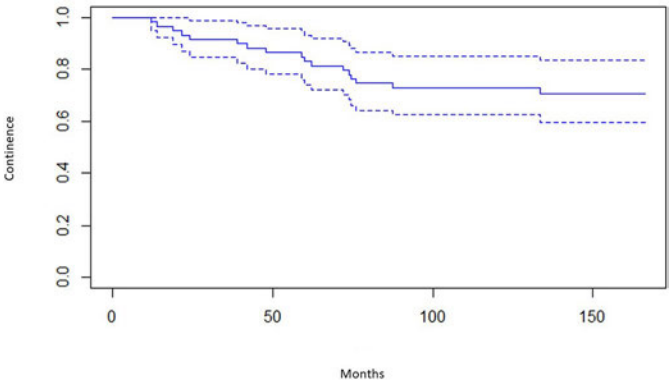
Initial results remain relatively stable during follow-up. Therefore, continuous compression/mobilization of the bulbar urethra maintains its effectiveness.

This long-term compression/mobilization does not translate clinically into a risk of urethral erosion or late complications

CONCLUDING MESSAGE
The AdVance®/AdVance XP ® Male Sling System is a safe and effective treatment for men with SUI after radical prostatectomy.

Understanding relative rates of male slings during long term follow-up can help clinicians better counsel SUI patients of surgical risks, thus promoting informed decision making and appropriate patient expectations

FIGURE 1



Loss of continence during follow-up

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ANALYZING OUTCOMES OF THE ADJUSTABLE TRANSOBTURATOR MALE SYSTEM (ATOMS) FOR POST-PROSTATECTOMY INCONTINENCE AND ITS RELATIONSHIP WITH OVERACTIVE BLADDERS AND RADIOTHERAPY WITH THE HELP OF URODYNAMICS

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HYPOTHESIS / AIMS OF STUDY
First developed in 2008, the Adjustable Transobturator Male System (ATOMS) has recently gained popularity in the post-prostatectomy incontinence (PPI) scene, touting advantages such as surgical simplicity and post-operative adjustability, among others (1). The present study aims to explore this device as a potential treatment option for PPI. With the help of preoperative urodynamic testing, this study also includes a subgroup analysis of patients suffering from concomitant overactive bladder (OAB) as well as those having received prior radiotherapy before device installation.

Primary outcome was dryness rate, 24-hour pad-count change compared to baseline and results from the patient global impression of improvement (PGI-I) questionnaire. Secondary outcome was the frequency of postoperative adverse events, as well as the effects of concomitant OAB and prior radiotherapy on the device effectiveness and safety.

STUDY DESIGN, MATERIALS AND METHODS
This was a single-center retrospective study. All implantations of the third generation Adjustable Trans Obturator Male System for post-prostatectomy incontinence were performed by one surgeon between June 2015 and March 2021. Prior to ATOMS implantation, all patients underwent a thorough work up including questionnaires, bladder diary, pad weight test, pad count, urodynamic study and cystoscopy.

Pre-operative urinary incontinence severity was defined as <2 pads per day (PPD), 2-4 PPD, and >4 PPD with regards to 24-h pad-count and/or <200g, 200-400g, and >400g regarding the 24-h pad-test (24h-PT) to classify mild, moderate, and severe incontinence, respectively. Dryness was defined as requiring 0 or 1 PPD postoperatively. Patients considered "improved" or "very much improved" were defined as having a reduction in the number of pads per day by $\geq$ 50% or $\geq$ 75%, respectively. Finally, significant patient satisfaction was defined by "much better", and "Very much better" PGI-I results.

The obtained data was compiled in Microsoft® Excel® format (v.16.59, 2022) and was converted to SPSS v.26 (IBM Corp. Armonk, N.Y., USA) for analysis.

RESULTS
Medical records of 91 patients were analysed. The median patient age for this group was 71 years with a mean follow-up of 29.9 months (SE 1.8; range 12 - 67). Pre-operative pad per day median was 4 (IQR 6-3; range 1-10), and pre-operative 24-hour pad test was 358 g (IQR 607-256; range 34-1592). This classified most patients as being either moderately (n = 24; 36.9%) or severely (n = 40; 61.5%) incontinent pre-operatively.

Post-operatively, median PPD at final follow-up was 1.0 (IQR 2-0; range 0-5; $p < 0.001$), with an overall improvement being noted in 56 (86.2%) patients. Within these 56 patients having improved, 43 (76.7%) of them were "very much improved" and of them 42 (75.0%) were dry. Patient satisfaction rate was 87.7% (n = 57). With regards to complication rates, eight (12.3%) patients experienced complications of any Clavien-Dindo grade, of which four were a grade III due to one device migration (1.5%), as well as three explantations due to persistent leakage (4.6%). It is interesting to note that all four patients having undergone ATOMS explantation requested to have a reimplantation of the same device.

In our subgroup analysis, patients having received prior radiotherapy (n = 22, 33.8%) had a lower improvement rate (73% vs 93%; p = 0.03) as well as a lower dryness rate (45.5% vs 74.4%; p = 0.02) than those having not received radiotherapy. Radiotherapy recipients also required more post-operative device adjustments (median 3.5 vs 2; p = 0.01) and had a higher total instilled volume (median 18.3mL vs 13mL; p = 0.01). There were no other statistically significant differences found in this subgroup analysis. Notably, differences in complication rates at any Clavien-Dindo grade, as well as the rate of patient satisfaction were statistically insignificant (Figure 1).

Eighteen (27.7%) patients presented with concomitant detrusor overactivity during preoperative urodynamic testing, with clinical overactive bladder being found in 16 patients (24.6%). Patients presenting with detrusor overactivity with clinical urgency symptoms alongside their post-prostatectomy incontinence had no pre-operative differences when compared with patients who had detrusor overactivity with no clinical OAB symptoms. Post-operatively, also no statistically significant difference was found in ATOMS outcomes in patients with detrusor activity with clinical OAB symptoms or in those without (Figure 2).

INTERPRETATION OF RESULTS
The AMS800, which is the most frequently implanted artificial urinary sphincter, may be considered the gold standard surgical treatment for post-prostatectomy incontinence (2). However, the ATOMS may be an excellent alternative. Our study demonstrates that the ATOMS is a safe and effective device in the treatment of post-prostatectomy incontinence, even when the majority of our patients presented with moderate to severe incontinence. We also found that the success rate of the ATOMS implantation seems to be unaffected by the presence of concomitant overactive bladder. Furthermore, in patients having received prior radiotherapy, dryness and improvement rates were less, and these patients required more adjustments and volume instillation.

CONCLUDING MESSAGE
Utilization of the ATOMS device in the treatment of post-prostatectomy incontinence seems safe and effective. Results concluded from this study proves the demand for more robust studies and opens the door for the opportunity to undertake a prospective, non-inferiority pilot project which directly compares the effects of the Artificial Urinary Sphincter versus the Adjustable Trans Obturator Male System in the treatment of male urinary stress incontinence.

FIGURE 1

	No prior radiotherapy (n=43, 66.2%)		Prior radiotherapy (n=22 , 33.8%)		p Value*
Median preoperative 24-h pad-test, g (SE)	374	(36.7)	330	(73)	0.31[1]
Preoperative incontinence severity					
Mild incontinence (%)	1	(2.3)	0	(0)	0.20[2]
Moderate incontinence (%)	15	(34.9)	9	(40.9)	0.20[2]
Severe incontinence (%)	27	(62.8)	13	(59.1)	0.20[2]
Median preoperative PPD (IQR)	4	(6-3)	5.0	(6 - 4)	0.34[1]
Median postoperative PPD (IQR)	1	(2.5-0)	1.1	(4.25-0.5)	0.19[1]
Median pad change (IQR)	3	(5-2)	3	(4.63-2)	0.42[1]
Dryness after final adjustment (%)	32	(74.4)	10	(45.5)	0.02[2]
Improvement after final adjustment (%)	40	(93)	16	(72.7)	0.03[2]
Very much improved after final adjustment (%)	32	(74)	11	(50)	0.03[2]
Patient satisfaction (%)[4]	40	(93)	17	(77.3)	0.06[2]
Median number of adjustments (IQR)	2[b]	(3-1)	3.5[c]	(5-1)	0.01[1]
Median total volume instilled, mL (IQR)	13[b]	(16-10)	18.3[c]	(22-11)	0.01[1]
Postoperative Complication of any grade (%)	4	(9.3)	1	(4.5)	0.33[2]
Grade I (%)	3	(7.0)	0	(0)	-
Grade II (%)	1	(2.3)	0	(0)	-
Grade III (%)	0	(0)	1	(4.5)	-

* p values < 0.05 are considered statistically significant.
[1] p value calculated using the Wilcoxon rank sum test
[2] p value calculated using the Fischer exact test
[b] Includes the 38 patients (88.4%) who required ≥ 1 adjustments
[c] Includes the 22 patients (100%) who required ≥ 1 adjustments
[4] Significant patient satisfaction was defined by "*Much better*", and "*Very much better*" PGI-I results.

Figure 1: Comparison of ATOMS outcomes in patients having received prior radiotherapy versus those who have not on several parameters.

FIGURE 2

	Patients with Detrusor Overactivity on Urodynamics				
	Without Clinical OAB Symptoms (n=7, 39%)		With Clinical OAB Symptoms (n=1, 61%)		p Value[a]
Median preoperative 24-h pad-test, g (SE)	253	(573-212)	314	(481-59)	0.70[1]
Preoperative incontinence severity					
Mild incontinence (%)	0	(0)	0	(0)	-
Moderate incontinence (%)	2	(26.8)	4	(34.6)	-
Severe incontinence (%)	5	(71.4)	7	(63.6)	-
Median preoperative PPD (IQR)	5	(8-3)	5	(6 - 3)	0.55[1]
Median postoperative PPD (IQR)	1	(4-0)	1	(2-0)	0.89[1]
Median pad change (IQR)	2	(5-1.5)	3	(4-2)	0.58[1]
Dryness after final adjustment (%)	2	(28.6)	4	(36.4)	0.37[2]
Improvement after final adjustment (%)	5	(71.4)	8	(72.7)	0.40[2]
Very much improved after final adjustment (%)	4	(57.1)	7	(63.6)	0.36[2]
Patient satisfaction (%)[d]	5	(71.4)	9	(81.8)	0.38[2]
Median number of adjustments (IQR)	2[b]	(4-0)	2[c]	(4-1)	0.52[1]
Median total volume instilled, mL (IQR)	13[b]	(20-6)	12[c]	(20-11)	0.59[1]
Postoperative Complication of any grade (%)	1	(0)	1	(4.5)	0.50[2]
Grade I (%)	0	(0)	0	(0)	-
Grade II (%)	0	(0)	0	(0)	-
Grade III (%)	1	(14.3)	1	(9.1)	-

[a] p values < 0.05 are considered statistically significant.

[1] p value calculated using the Wilcoxon rank sum test

[2] p value calculated using the Fischer exact test

[b] Includes the 9 patients (81.8%) who required ≥ 1 adjustments

[c] Includes the 6 patients (85.7%) who required ≥ 1 adjustments

[d] Positive patient satisfaction was defined by "*Much better*", and "*Very much better*" PGI-I results.

Figure 2: Comparison of ATOMS outcomes in patients presenting with detrusor overactivity with clinical symptoms versus those who do not on several parameters.

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Funding None **Clinical Trial** No **Subjects** Human **Ethics Committee** CÉR CIUSSS Estrie - CHUS **Helsinki** Yes **Informed Consent** Yes

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ADVERSE EFFECTS ON LOWER URINARY TRACT SYMPTOMS AND DYSFUNCTIONS AFTER CARBON-ION RADIOTHERAPY FOR PROSTATE CANCER PATIENTS

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HYPOTHESIS / AIMS OF STUDY

Radiation therapy (RT) is one of the treatment strategies for localized prostate cancer. Among the radiation therapies, carbon-ion radiotherapy (CIRT) has biological and physical advantages over RT using conventional X-rays. Carbon ion beams show an estimated three-fold higher relative biological efficacy than X-rays and have been reported good clinical outcomes for CIRT for localized prostate cancer [1]. On the other hand, radiation-induced urinary toxicities to the bladder and urethra can occur after CIRT, which adversely affect the patient's quality of life. However, there are no reports using objective assessments of urinary toxicities before and after CIRT. The purpose of this study is to clarify changes in lower urinary tract symptoms/dysfunctions before and after CIRT in patients with prostate cancer.

STUDY DESIGN, MATERIALS AND METHODS

We obtained the consent of a prospective study on the assessment of lower urinary tract symptoms/dysfunctions before and after CIRT in patients scheduled to undergo CIRT for prostate cancer. The eligibility criteria for this study were: (i) histological diagnosis of prostate adenocarcinoma, (ii) cT1b-3bN0M0 according to the 7th UICC classification, and (iii) performance status 0–2. Of these, 46 patients had completed CIRT by the end of March 2022, and statistical analysis was performed on 27 patients, excluding 13 patients whose data was not collected and 6 patients who withdrew their consent. Patients were classified using the D'Amico risk group classification, with 11 patients in the intermediate-risk group and 16 patients in the high-risk group. All patients received neoadjuvant androgen deprivation therapy (ADT) for 4-6 months prior to CIRT. CIRT was performed once a day, 4 days a week for 3 weeks, with a total dose of 51.6 Gy(RBE). We evaluated lower urinary tract symptoms using the International Prostate Symptom Score (IPSS), Quality of Life (QOL) Score, and Overactive Bladder Symptom Score (OABSS). We also performed objective evaluations using frequency-volume charts (FVC), uroflowmetry (UFM), and post-void residual urine volume (PVR) measurement. These assessments were performed the following 3 times: before ADT, after 4-6 months of ADT (= just before CIRT), and immediately after CIRT. Of the 27 patients, four were taking α1 blockers, two were taking PDE5 inhibitors, and two were taking β3 adrenergic receptor agonists, before the start of ADT. One patient had a history of transurethral resection of the prostate. Statistical analysis was performed by paired t-test.

RESULTS

The table shows the values of each parameter before ADT, before CIRT, and after CIRT. IPSS-2 (frequency),4 (urgency),5 (weak stream),7 (nocturia), IPSS-total score, and QOL score were significantly increased after CIRT compared to before ADT. OABSS-1 (daytime frequency) and OABSS-total scores were also significantly increased after CIRT. FVC showed no changes in 24-hour urine volume, the number of nocturnal voids, or the nocturnal polyuria index, but the number of daytime voids was significantly increased after CIRT. In UFM, maximum flow rate (Qmax), average flow rate (Qave), and voided volume (VV) were significantly decreased after CIRT compared to before ADT. There was no significant change in PVR.

INTERPRETATION OF RESULTS

This is the first report to investigate lower urinary tract symptoms/dysfunctions before and after CIRT using objective evaluations by FVC and UFM. Not only the patient's subjective complaints, but also objective evaluations showed an increase in the number of daytime voids, a decrease VV, and a decrease of the urinary stream. In a similar situation, there are few reports on the management of lower urinary tract symptoms after RT. One randomized study showed that tadalafil may be a good candidate for the management of lower urinary tract symptoms after low-dose-rate brachytherapy [2], however, there are no reports for that after CIRT. The limitations of this study are the small number of cases and the short observation period. The future task is to continue the evaluation for a long time after CIRT and accumulate the number of cases and clarify the treatment method for improving lower urinary tract symptoms/dysfunctions after CIRT.

CONCLUDING MESSAGE

We objectively clarified changes in lower urinary tract symptoms/dysfunctions before and after CIRT in patients with prostate cancer.

FIGURE 1

n=27	before ADT	pre-CIRT	after-CIRT	
IPSS-1	0.78±0.22	0.67±0.17	1.04±0.29	
IPSS-2	1.70±0.28	1.74±0.30	2.48±0.36	**
IPSS-3	1.41±0.34	1.59±0.36	2.07±0.37	
IPSS-4	0.78±0.19	0.89±0.24	1.44±0.30	*
IPSS-5	1.81±0.34	1.67±0.34	2.96±0.37	**
IPSS-6	0.70±0.24	0.74±0.24	1.22±0.28	
IPSS-7	1.63±0.22	1.78±0.22	2.15±0.22	*
IPSS-total	8.78±1.27	9.04±1.25	13.41±1.59	**
IPSS-QOL	2.96±0.32	3.19±0.37	3.89±0.32	**
OABSS-1	0.59±0.11	0.56±0.10	0.85±0.07	*
OABSS-2	1.67±0.19	1.59±0.18	2.00±0.19	
OABSS-3	1.26±0.29	1.11±0.28	1.59±0.33	
OABSS-4	0.48±0.17	0.41±0.17	0.93±0.25	
OABSS-total	4.00±0.59	3.63±0.55	5.37±0.62	*
urine volume per day (mL)	1903.7±130.6	1840.0±119.4	1803.9±128.1	
average voided volume (mL)	238.1±16.1	221.6±14.2	176.9±12.6	**
total number of voids	8.56±0.66	8.67±0.50	10.89±0.77	**
number of daytime voids	7.15±0.49	7.44±0.40	9.15±0.66	**
number of nocturnal voids	1.41±0.26	1.22±0.19	1.74±0.27	
NPI (%)	36.2±2.2	35.1±2.1	33.3±2.8	
Qmax (mL/s)	14.4±1.5	13.0±1.4	10.8±1.2	*
Qave (mL/s)	8.4±0.9	7.7±0.8	6.3±0.6	**
VV (mL)	195.9±28.5	161.5±19.6	117.9±12.8	**
PVR (mL)	42.7±8.0	29.9±4.6	52.2±9.9	

*P<0.05, **P<0.01

IPSS: international prostate symptom score, OABSS: overactive bladder symptom score

NPI: nocturnal polyuria index

Qmax: maximum flow rate, Qave: average flow rate

VV: voided volume, PVR: post-void residual urine volume

Table: The values of each parameter before ADT, before CIRT, and after CIRT

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Funding None **Clinical Trial** Yes **Public Registry** No **RCT** No **Subjects** Human **Ethics Committee** The institutional review board of Kanagawa Cancer Center (approval number: 2020-62) **Helsinki** Yes **Informed Consent** Yes

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INTRAOPERATIVE QUANTITATIVE URETHRAL INDOCYANINE GREEN FLUORESCENCE ANGIOGRAPHY PREDICTS RECOVERY FROM URINARY INCONTINENCE AFTER ROBOT-ASSISTED RADICAL PROSTATECTOMY

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HYPOTHESIS / AIMS OF STUDY
We previously demonstrated that benign prostate hyperplasia (BPH) and erectile dysfunction (ED) could be associated with poor preoperative urethral function in men by evaluating the relationship between these factors and preoperative maximum urethral closure pressure1. Atherosclerosis and pelvic ischemia due to metabolic syndrome are involved in the pathophysiology of BPH and ED development. Therefore, we hypothesized that atherosclerosis and pelvic ischemia may be involved in the relationship between poor preoperative urethral function and BPH/ED.

This study aimed to evaluate the relationship between urethral blood flow analyzed using intraoperative indocyanine green (ICG) angiography and clinical factors such as prostate volume and erectile function, and postoperative urinary incontinence after robot-assisted radical prostatectomy (RARP).

STUDY DESIGN, MATERIALS AND METHODS
This was a single-center prospective study that enrolled 50 consecutive male patients who underwent RARP for prostate cancer between November 2020 and February 2022. RARP was transperitoneally performed by two experienced surgeons using the da Vinci Xi system. ICG was intravenously administered at a dose of 0.15 mg/kg before resection of the urethra. The urethral blood flow was observed using the firefly fluorescence system. A quantitative analysis of ICG angiography was performed using movie analysis software (Hamamatsu Photonics K.K., Japan). Briefly, three regions of interest (ROI) were selected in the urethra, and time curves of ICG fluorescence intensity were drawn. The urethral blood flow at the three ROIs of the urethra was measured and average was calculated. To assess the validity of the intraoperative ICG angiography method, we analyzed the correlation between urethral blood flow and abdominal arterial sclerosis, which was evaluated by calculating the abdominal aorta calcification index (ACI) on computed tomography (CT). To calculate the ACI, the aorta was divided into 12 areas in each slice of the CT scan. An area with calcification was scored as 1, whereas an area without calcification was scored as 0. The total calcification score in all slices was then calculated as2: ACI = (total score for calcification in each slice)/ (12 x [the number of slices]) x 100.

In addition, we calculated the 24-hour urine loss rate immediately after urethral catheter removal, which was defined as the urinary incontinence volume divided by the voided volume added to the urinary incontinence volume. We evaluated the relationships between intraoperative urethral blood flow and the 24-hour urine loss rate, and between intraoperative urethral blood flow and the following clinical factors: age, prostate volume, International Index of Erectile Function-5 (IIEF 5) score, and nerve-sparing surgery.

RESULTS
Urethral blood flow was significantly negatively correlated with ACI ($r = -0.479$, $p = 0.001$), demonstrating the validity of the intraoperative ICG angiography method. Moreover, urethral blood flow was significantly higher in the high IIEF 5 group (≧ 12 scores) or small prostate-volume group (< 40 mL) ($p = 0.02$) compared to the low IIEF 5 group (< 12 scores) or large prostate-volume group (> 40mL) ($p < 0.001$). However, there was no significant difference in age between the two groups. Furthermore, urethral blood flow was significantly higher in patients who underwent nerve-sparing surgery than in those who did not ($p = 0.01$). Moreover, there was a significant negative correlation between intraoperative urethral blood flow and the 24-hour urine loss rate ($r = -0.649$, $p < 0.001$) (Fig. 1). Multiple linear regression analysis was performed to predict urethral blood flow based on IIEF5 scores, prostate volume, and nerve-sparing surgery. A significant regression equation was found (Table1).

INTERPRETATION OF RESULTS
These results indicate that: (1) the method of our intraoperative ICG angiography is valid, as shown by a significant correlation between abdominal arterial sclerosis and urethral blood flow obtained by intraoperative ICG angiography; (2) BPH and ED are involved in poor urethral blood flow; (3) nerve-sparing surgery preserves urethral blood flow; (4) patients with high urethral blood flow have a low 24-hour urine loss rate immediately after the removal of the urethral catheter.

CONCLUDING MESSAGE
Urethral blood flow may be associated with arterial sclerosis and pelvic ischemia. High intraoperative urethral blood flow may facilitate early recovery from postoperative urinary incontinence after RARP.

FIGURE 1

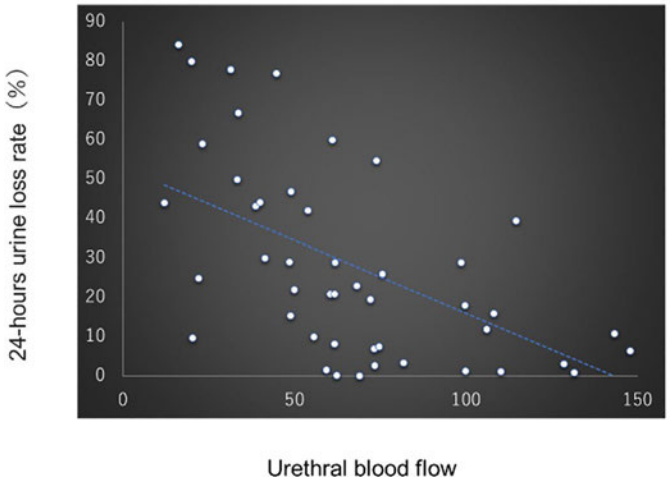

Fig. 1

FIGURE 2

	β	p - value	95% confidential intervals
IIEF5	0.82	0.003	0.94 ～ 4.29
Prostate volume	0.20	0.04	-0.82- ～ -0.01
Nerve-sparing surgery	10.23	0.01	5.27 ～ 46.57

Table 1

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Funding None. **Clinical Trial** Yes **Public Registry** No **RCT** No **Subjects** Human **Ethics Committee** The Aichi Medical University **Ethics Committee Helsinki** Yes **Informed Consent** Yes

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SESSION 6 - PELVIC ORGAN PROLAPSE

Abstracts 65-76
11:00 - 12:30, Hall K
Chair: Dr Heidi Wendell Brown (United States)

65 | www.ics.org/2022/abstract/65

DIFFERENT TECHNIQUES FOR THE SURGICAL REPAIR OF PELVIC ORGAN PROLAPSE (POP) CAN MODIFY THE UROGENITAL HIATUS? A CLUSTER RANDOMIZED TRIAL

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HYPOTHESIS / AIMS OF STUDY
The aim of this study was comparing the effect of two surgical techniques for POP on the urogenital hiatus: vaginal hysterectomy versus hysteropexy.

STUDY DESIGN, MATERIALS AND METHODS
The trial was conducted between 2010 to 2015.

Women with symptomatic uterovaginal prolapse POP-Q stage ≥ 2 requiring surgery who attended the pelvic floor clinic of our hospital were recruited. Patients with co-existing concomitant incontinence surgery were included. Women with language barriers, neoplasms, autoimmune or hematological diseases, anormal uterine bleeding, ultrasound uterine/ovarian findinds were excluded.

All participants signed an informed consent, the study was approved by the Ethics Committee of our hospital.

Follow-up visits were made at 12, 36 and 60 months, respectively. In all the visits gyneco-logical examination, POP-Q and ultrasound were performed and validated QoL surveys were answered.

Two surgery groups were designated:

1. Vaginal hysterectomy with anterior vaginal colporrhaphy and perineal body repair with Vicryl stich

2. Hysteropexy with TFS® mesh to arcus tendineus, parametrium and uterosacral, anterior vaginal colporraphy and perineal body repair with Vicryl stich

Posterior vaginal colporrhaphy was performed when appropriate, suburethral/TVT mesh were applied to correct stress urinary incontinence if appropriate.

The main objective was analyzing whether the urogenital hiatus area could be modified with POP surgery, and a secondary objective was to observe whether there was any difference depending on the surgical technique used. We have not show in this abstract the validated QoL surveys results.

We compared all the patients, regardless of the surgical technique used, analyzing the POPQ before surgery, at 12, 36 and 60 months with the area of the urogenital hiatus to the Valsalva: one group with a hiatal area ≤ 25 cm 2 and another group with hiatal area > 25 cm 2.

The hiatal area measured before surgery, 12, 36 and 60 months has also been compared depending on whether a vaginal hysterectomy or a hysteropexy has been performed.

Patients were assigned by computer-generated randomized table.

The patients could not be masked because they were different surgical techniques.

We used the Student't / Wilcoxon distribution as appropriate and data were analyzed with the statistical method Stada version 14.1

One patient was recruited but did not undergo surgery, another died after the third year, another had dementia after the first year, 13 did not attend all controls, and 3 dropped out of the study. A final total of 41 patients were included in the hysteropexy group and 33 in the vaginal hysterectomy group.

In 2015 we stopped the trial due to lack of supply of TFS® by the distributor. We continue with the follow-up of the patients up to 5 years as designed.

RESULTS
Table 1 shows the demographic characteristics of the study patients.

Table 2 shows the results obtained

INTERPRETATION OF RESULTS
Analyzing the hiatal area to Valsalva, we found no significant results between the presence of > 25 cm 2 hiatal area and the presence of a higher degree of POP before and after surgery.

We also found no significant differences between the different surgical techniques and the hiatal area before and after surgery.

Yes, both surgical techniques reduce the hiatal area after surgery

CONCLUDING MESSAGE
In our study, a hiatal area > 25 cm 2 is not a predictive factor for POP-Q stage before and after corrective surgery.

Both vaginal hysterectomy and hysteropexy, both accompanied by perineal body repair, reduce the size of the urogenital hiatus area in our study

FIGURE 1

	Treatment group nº	
	Hysteropexy n=41	Hysterectomy n=33
Age, mean (SD), y	62,48 (8,61)	63,66 (9,73)
Race nº/total (%)		
White	41 (100)	32 (96,96)
Asian	0	1 (3,04)
Parity, median	2,15 (2)	2,26 (2)
BMI, mean (SD)	26,75 (3,27)	28,78 (5,43)
Postmenopausal nº/total (%)	9 (21,95)	7 (21,21)
Current smoker nº/total (%)	2 (4,87)	2 (6,06)
Stress urinary Incontinence nº/total (%)	14 (34,14)	7 (21,21)
POP-Q stage		
2	21 (47,72)	14 (42,42)
3	19 (43,18)	19 (57,57)
4	1 (2,27)	0 (0)
nº/total (%)		

Table 1

Table 1

FIGURE 2

Mean values of POP-Q score at different moments in time (groups made according to hiatal area Valsalva maneuver)			
	Valsalva ≤ 25 cm ²	Valsalva > 25 cm ²	p-value
POP-Q 0	2.37 ± 0.50 (n=19)	2.59 ± 0.50 (n=56)	0.098
POP-Q 12	0.74 ± 0.87 (n=19)	0.98 ± 0.84 (n=53)	0.273
POP-Q 36	1.05 ± 0.85 (n=19)	1.19 ± 0.86 (n=42)	0.580
POP-Q 60	1.17 ± 0.79 (n=18)	1.46 ± 0.78 (n=41)	0.200
Mean hiatus area at peak Valsalva maneuver at different moments in time (groups are made according to the surgical technique used)			
	Vaginal hysterectomy	Hysteropexy	p-value
Hiatus area 0	29.47 ± 5.43 (n=32)	28.24 ± 5.58 (n=39)	0.352
Hiatus area 12	25.13 ± 4.33 (n=33)	24.74 ± 6.02 (n=40)	0.755
Hiatus area 36	23.78 ± 5.17 (n=27)	23.55 ± 5.00 (n=34)	0.861
Hiatus area 60	21.30 ± 4.01 (n=24)	21.85 ± 3.94 (n=33)	0.608

Data are mean ± SD

Table 2

Table 2

Funding nothing **Clinical Trial** Yes **Public Registry** No **RCT** Yes **Subjects** Human **Ethics Committee** Comité de Ética del Parc de Salut Mar, Barcelona, Spain **Helsinki** Yes **Informed Consent** Yes

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POSTOPERATIVE COMPLICATIONS AND PELVIC ORGAN PROLAPSE RECURRENCE FOLLOWING COMBINED PELVIC ORGAN PROLAPSE AND RECTAL PROLAPSE SURGERY COMPARED TO PELVIC ORGAN PROLAPSE ONLY SURGERY

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HYPOTHESIS / AIMS OF STUDY
Women with both vaginal prolapse and rectal prolapse likely represent a patient population with more severe pelvic floor dysfunction. Postoperatively, these patients may be at increased risk of complications as well as prolapse recurrence. In this study, the first primary objective was to compare the <30-day postoperative complications in women undergoing combined pelvic organ prolapse (POP) and rectal prolapse (RP) surgeries to those undergoing POP-only surgery and to determine preoperative predictors of <30-day complications. The second primary objective was to compare POP recurrence in women undergoing combined POP+RP surgery to those undergoing POP-only surgery and to determine predictors of POP recurrence.

STUDY DESIGN, MATERIALS AND METHODS
This was a multicenter, retrospective cohort study at five academic hospitals and part of the AUGS-SGS Fellows Pelvic Research Network. Patients undergoing combined RP+POP surgery were matched by age, POP stage by leading compartment and POP procedure to those undergoing POP-only surgery from March 2003 and March 2020. Primary outcome measures were <30-day complications separated into Clavien-Dindo (CD) classes as well as 1) subsequent POP surgeries and 2) POP recurrence defined as patients who complained of vaginal bulge symptoms postoperatively. Data and percentages are presented for the combined surgery group followed by POP-only surgery group.

RESULTS
Two hundred and four women underwent combined surgery for RP+POP and 204 women underwent surgery for POP only. Average age (59.3+1.0 vs 59.0+1.0) and parity (2.3 vs 2.6) was similar in each group and most women were Caucasian (75.5% vs 76.0%). A higher proportion of combined patients had lower BMIs (25.3+0.4 vs 26.8+0.3, $p<0.001$), were more likely to be current smokers (13.2% vs 4.4%, $p<0.001$), were diagnosed with a connective tissue disorder (9.3% vs 2.0%, $p<0.001$) and had a psychiatric diagnosis (37.2% vs 16.2%, $p<0.001$). Average follow-up time was 307.2+31.5 days for the combined cohort and 487.7+49.9 days for the POP-only cohort.

A majority (68.1%) underwent abdominal POP repair while 31.9% underwent transvaginal POP repair only. The proportion of patients undergoing open versus minimally-invasive surgical (MIS) abdominal POP repair was similar between groups (30.9% vs 30.2% and 69.1% vs 69.8%). More anti-incontinence procedures (36.8% vs 57.8%, $p<0.001$) and hysterectomies (39.7% vs 48%, $p=0.09$) were performed at the time of surgery in the POP-only cohort.

One hundred and nine patients (26.7%) had at least one 30-day complication. The proportion of patients who had a complication in the combined group and POP-only group was similar (27.0% vs 26.0%, $p=0.82$). CD scores were similar between the groups (10.3% vs 9.3% Grade 1, 11.8% vs 12.3% Grade 2, 3.9% vs 4.4% Grade 3, 1.0% vs 0% Grade 4, 0.5% vs 0% Grade 5). Combined patients were less likely than POP-only patients to develop postop UTIs and urinary retention, but were more likely to be treated for wound infections and pelvic abscesses. Both groups had a similar number of patients who underwent reoperations for bleeding and mid-urethral sling release, although fewer combined patients underwent reoperation for small bowel obstruction. One patient in the combined group developed colonic perforation after combined sacrospinous hysteropexy and Delorme repair and subsequently died.

After adjusting for combined vs POP-only surgery, patients who had anti-incontinence procedures (aOR=1.85, 95% CI 1.16, 2.94, $p=0.02$) and perineorrhaphies (aOR=1.68, 95% CI 1.05, 2.70, $p=0.02$) were more likely to have <30-day postoperative complications.

Twelve patients in the combined group and 15 patients in the POP-only group (5.9% vs 7.4%, $p=0.26$) had subsequent POP repair. In the combined group, 10 patients (4.9%) underwent one repair and 2 patients (1.0%) underwent two repairs. All patients who had recurrent POP surgery in the POP-only group had one subsequent POP repair. Twenty-one patients in the combined surgery and 28 patients in the POP-only group (10.3% vs 13.7%, $p=0.26$) reported recurrent POP.

On multivariable analysis adjusted for number of prior POP repairs, combined vs POP-only group and perineorrhaphy at the time of surgery, patients were more likely to have a subsequent POP surgery if they had had 2 or more prior POP repairs (aOR=6.06, 95% CI 2.10, 17.5, $p=0.01$). A multivariable model for predicting recurrent POP was created by adjusting for combined vs POP-only group (aOR=0.65, 95% CI 0.35, 1.22), minimally-invasive (MIS) POP repair (aOR=0.57, 95% CI 0.31, 1.06), perineorrhaphy (aOR=0.51, 95% CI 0.24, 1.08) and multiparity (aOR=0.83, 95% CI 0.26, 2.69). Risk factors were not statistically significant but the overall model did indicate that these variables may be significant in predicting which patients are more at risk of recurrent POP (p-value 0.04 and AUC 0.66).

INTERPRETATION OF RESULTS
In our cohort of patients, 26.7% of patients had at least one <30-day complication and the proportion of patients with a postoperative complication was similar between the combined group and POP-only group. Most of these complications were minor requiring antibiotics or foley catheter placement. Patients in the POP-only group were more likely to develop postoperative UTIs (5.4% vs 6.9%) and urinary retention (4.4% vs 7.4%), which may be attributable to the higher number of anti-incontinence procedures performed in this group. Patients in the combined group were more likely to be treated for wound infections (2.5% vs 2.0%) and pelvic abscesses (1.5% vs 1.0%). Some studies suggest that operating time > 180 minutes and increased intraoperative blood loss are risk factors for postoperative infections. Surgical time and blood loss are more likely to be elevated in combined procedures where surgeons dissect and repair both the pelvic organs and the rectum.

Anti-incontinence procedures and perineorrhaphies were both risks factors for developing <30-day complications. As previously discussed, patients may be at increased risk for urinary retention and UTIs after anti-incontinence procedures. Perineorrhaphies may increase the risk of wound infection or wound cellulitis as stitches are placed between the vagina and rectum.

In both groups, a similar number of patients reported symptomatic POP recurrence (10.3% vs 13.7%) and underwent subsequent POP surgery (5.9% vs 7.4%). Although fewer patients reported postoperative vaginal bulge symptoms and had subsequent POP surgery in the combined group, the average follow up time was 180 days less compared to the POP-only group. If these patients had been followed for a longer time period, it is possible that more patients would have complained of symptomatic recurrent POP and undergone POP surgery. In this cohort, the only significant risk factor for having a subsequent POP surgery was a history of 2 or more prior POP repairs. On multivariable analysis, protective factors for subsequent POP surgery which approached significance included undergoing a combined POP+PR repair, undergoing an MIS POP repair, having a perineorrhaphy at the time of surgery and multiparity. Patients who have combined surgery may have significant improvement in their pelvic floor support by suspending both the rectum and the pelvic organs. This double reinforcement may outweigh the higher risk of prolapse recurrence that can occur with more severe pelvic floor dysfunction.

CONCLUDING MESSAGE
In conclusion, in this retrospective cohort study, patients undergoing combined POP+RP surgery had a similar risk of <30-day postoperative complications compared to patients undergoing POP-only surgery. Combined pa-

tients also had a similar risk of recurrent POP and subsequent POP surgery compared to patients undergoing POP-only surgery.

Funding AUGS-SGS Fellows Pelvic Research Network **Clinical Trial** No **Subjects** Human **Ethics Committee** Institutional Review Board **Helsinki** Yes **Informed Consent** No

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IS ABSORBABLE SUTURE SUPERIOR TO PERMANENT SUTURE FOR SACROCOLPOPEXY

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HYPOTHESIS / AIMS OF STUDY

Permanent suture has been widely used for attaching mesh to the vagina in the operation, which is to confirm the mesh securely to providing stable repair with a as much as possible lower failure rate. However, in a published study(1) of sacrospinous ligament suspensions, they used permanent suture and obtained an incredible suture-related complications including suture erosion, persistent vaginal bleeding and granulation tissue generation. In this situation, they had to remove the suture. More horrible thing is that the permanent suture exist a long time, and one of the included study above observed 2 permanent suture erosion into the bladder occurring more than 30 weeks after surgery(2). The choice of suture materials become a question and in recent years, absorbable suture have started to be used in sacrocolpopexy. Thus, we performed the first meta-analysis to investigate the priority of absorbable sutures and permanent sutures. The aims of this study were to compare surgical results and suture-related complications after sacrocopolpexy (SCP) with absorbable suture (AS) vs permanent suture (PS).

STUDY DESIGN, MATERIALS AND METHODS

We systematically searched PubMed, Embase, clinicalTrial.gov, and Cochrane Library Central Register of Controlled Trials for articles that compared AS with PS for SCP. The primary outcomes were surgical success rate and suture related complications (suture exposure/erosion, mesh erosion and suture removal). Review Manager 5.3 (Cochrane Collaboration, Oxford, UK) was applied to conduct all analyses.

RESULTS

Four articles involving 689 patients were eventually included. The total success rates of the two group were 96.6% and 93.9%.Our findings demonstrated that AS had similar surgical success rates in comparison with PS (RR = 1.03; 95% CI, 0.97-1.09) and no significant differences in failure rates were noted between two groups (RR = 0.53; 95% CI, 0.22-1.26) . Subgroup analyses in patients with anatomic failure revealed no statistical differences in recurrent posterior prolapse (RR = 0.33; 95% CI, 0.06-2.02) , as well as in recurrent apical or anterior prolapse (P = 0.78, P = 0.68, respectively). However, Our finding demonstrated that AS indicated a lower risk in suture exposure/erosion (RR = 0.20; 95% CI, 0.06-0.61) , suture removal (RR = 0.19; 95% CI, 0.04-0.84) and retreatment (RR = 0.44; 95% CI, 0.14-1.35) . These results confirmed our hypothesis that AS is as effective as PS with a better security. Interestingly, the mesh erosion in the two had no statistical differences (RR = 1.00; 95% CI, 0.51-1.94) .

INTERPRETATION OF RESULTS

Our finding observed that the success rate is similar between the two materials (RR = 1.03; 95% CI, 0.97-1.09) and there was also no differences in failure rate (RR = 0.53; 95% CI, 0.22-1.26) . Subgroup analyses demonstrated no statistical differences in recurrent apical prolapse, anterior prolapse or posterior prolapse (P = 0.78, P = 0.68, P = 0.23) . The total success rates of the two group were 96.6% and 93.9% and that were consistent with published studies.

The function of the suture is to attach the mesh from the vagina to the anterior longitudinal ligament covering the sacral promontory. Thus, the corrections of looking for the exact anatomical site is necessary. In the abstract, in case of a stable scar is formatted with sufficient time provide by suture materials and then we could obtain solid apical support. The apical support is the most likely to be derived from scarring of the vaginal apex to the anterior longitudinal ligament rather than depending on suture longevity. Absorbable materials such as polydioxanone dissolves at an average of 3 months and is completely dissolved at 6 months. After the suture completely dissolved, the apical support will still in the place with a newly established anatomical structure. Under this situation, after 6 months, it is unlikely that PS has any benefit over the scarring that remains in place. The average duration of studies included was 6 months. Our finding demonstrated that AS indicated a lower risk in suture exposure/erosion (RR = 0.20; 95% CI, 0.06-0.61) , suture removal (RR = 0.19; 95% CI, 0.04-0.84) and retreatment (RR = 0.44; 95% CI, 0.14-1.35) . These results confirmed our hypothesis that AS is as effective as PS with a better security. Interestingly, the mesh erosion in the two had no statistical differences (RR = 1.00; 95% CI, 0.51-1.94) . For the mesh materials, it needs more technical support to improve affinity.

CONCLUDING MESSAGE

The current data presented that AS had similar success rate, less exposure/erosion, less suture removal and less retreatment compared with PS, which supported that AS is as effective as PS, but with better security.

FIGURE 1

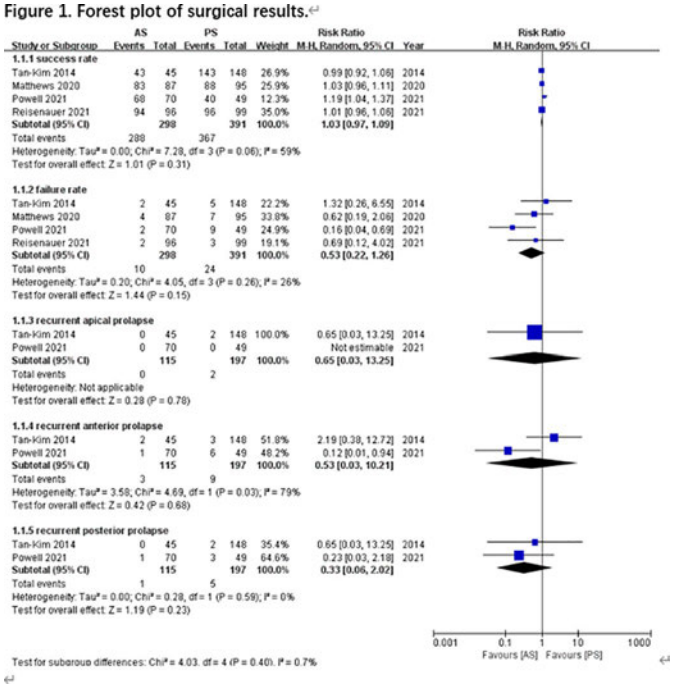

Figure 1. Forest plot of surgical results.

FIGURE 2

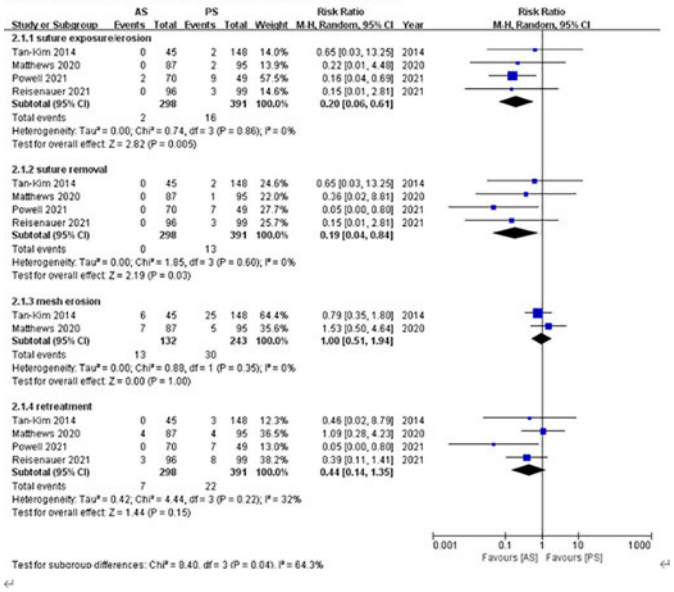

Figure 2. Forest plot of suture-related complications.

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POSTOPERATIVE URINARY RETENTION AND LENGTH OF CATHETERIZATION AFTER SURGERY FOR PELVIC ORGAN PROLAPSE (POP): A 5 YEAR EXPERIENCE.

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HYPOTHESIS / AIMS OF STUDY
Incomplete emptying of the bladder is one of the most common unwanted side effects of Pelvic Organ Prolapse (POP) surgery. The incidence varies widely between studies. Routine transurethral catheterization is the standard procedure after POP surgery. There is increasing trend of short period of catheterization following after uncomplicated vaginal hysterectomy. Early removal of catheter may lead to retention of urine due to reflex pain in the operation site and overfilling of the bladder after prolapse surgery which might have a negative effect on surgical outcome. On the contrary, prolonged catheterization increases the chance of urinary tract infection; prevents early ambulation, prolongs hospital stay and also adversely impacts post-operative wellbeing.

Although several trials addressed the issue of the duration of catheterization after surgery, there is no consensus on how best to minimize complications of prolonged catheterization and practices vary. There was not enough evidence to show that any policy was better than the other.

At our institute the practices vary from 24-72 hours of indwelling catheterization (IDC) after POP surgery .In this study we will review 5 year experience of urinary retention in patients undergoing POP surgery with relation to duration of catheterization at our institute.

STUDY DESIGN, MATERIALS AND METHODS
A retrospective study was conducted at the urogynaecology department between January 2013 to December 2017. All patients who were between 30-80 years and underwent Pelvic organ prolapse surgery were included in the study,exclusion criteria were

• Concurrent UTI/surgery SUI

• Urethral abnormalities

• Diabetic neuropathy

• Women for whom complicated surgical procedure was anticipated (Patient with long standing prolapse with severe fibrosis).

• Iatrogenic bladder injury

• Prolapse surgery associated with plan of bladder or vault Suspension or repair by mesh

In all cases, pre-operative evaluation or examination under anesthesia was documented to define the type and grade of POP. Patients with complete medical records were reviewed and data on the type of surgery, duration of surgery, blood loss, anesthesia type, duration of catheterization, and urinary retention were recorded. Two groups were formed, group A - retention postoperatively and group B - without urinary retention. The duration of catheterization was compared between the two groups.

RESULTS
Postoperative urinary retention occurred in 11.4 % of the study subjects (19/166).Overall, our study examined the association with retention and demographic characteristics for women receiving pelvic organ prolapse surgery at a tertiary care center. Demographic characteristics of our study sample are described in Table 1.The mean age of patients was 55.8 ± 12.2 years and the mean body mass index (BMI) was 28.6 ± 6.2 kg/m2. The mean duration of surgery was approximately two and a half hours with a mean blood loss of 345 ± 305 ml.The study reported that the duration of the indwelling catheter was significantly associated with postoperative urinary retention ($p = 0.013$) (Table 2). The lowest rate of postoperative retention was found in patients who were catheterized for at least 48 hours. Upon stratification, it was found that duration of surgery was significantly associated with postoperative urinary retention ($p = 0.012$). Furthermore, it was revealed that the majority of the underweight patients, i.e. 3 (75%) suffered from postoperative retention ($p < 0.001$) (Table 3).

INTERPRETATION OF RESULTS
The mean age of patients was 55.8 ± 12.2 years and the mean body mass index (BMI) was 28.6 ± 6.2 kg/m2. The study reported that the duration of the indwelling catheter was significantly associated with postoperative urinary retention ($p = 0.013$). The lowest rate of postoperative retention was found in patients who were catheterized for at least 48 hours.

Upon stratification, it was found that the duration of surgery was significantly associated with postoperative urinary retention ($p = 0.012$).

CONCLUDING MESSAGE
Postoperative urinary retention is a common condition encountered following pelvic surgery, which contributes to significant patient discomfort and anxiety. Our study revealed that the optimum duration of catheterization is 48 hours which could improve the patient outcome.

FIGURE 1

Tables

Table 1. Demographics of the Study Participants

Parameter	Mean	Std. Deviation
Age in years	55.8	12.2
Weight in kg	66.5	14.1
Height in cm	151.1	16.7
Body Mass Index in kg/m^2	28.6	6.2
Parity	4.0	2.3
Duration of surgery in hours	2.4	0.7
Intraoperative blood loss ml	345.0	305.7

Table 2. Association between Duration of Indwelling Catheter and Postoperative Urinary Retention

Duration of Indwelling Catheter	Post-operative Urinary Retention		P-value
	Yes	No	
24 hours	5 (26.3%)	14 (73.7%)	0.013
48 hours	7 (6.4%)	102 (93.6%)	
72 hours	7 (18.4%)	31 (81.6%)	

Table 3. Risk Factors of Postoperative Retention Among Patients

Parameters	Post-operative Urinary Retention		P-value
	Yes	No	
Age Group			
Less than or equal to 45 years	1(3.1%)	31(96.9%)	0.082
More than 45 years	18(13.4%)	116(86.6%)	
Parity			
0-1 Children	0(0%)	9(100%)	0.538
2-3 Children	10(12.3%)	71(87.7%)	
4 or more	9(11.8%)	67(88.2%)	
Duration of Surgery			0.012
1 to 2 hours	13(18.8%)	56(81.2%)	
More than 3 hours	6(6.2%)	91(93.8%)	
Type of Anesthesia			
General	13(9.6%)	122(90.4%)	0.114
Spinal	6(19.4%)	25(80.6%)	
Febrile Illness			
Yes	-	3 (100%)	0.693
No	19 (11.7%)	144 (88.3%)	
Body Mass Index			
Below 18.5	3 (75%)	1 (25%)	0.001
18.5—24.9	6 (15%)	34 (85%)	
25.0—29.9	5 (7.9%)	58 (92.1%)	
30.0 and Above	5 (8.5%)	54 (91.5%)	

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Funding non funded **Clinical Trial** No **Subjects** Human **Ethics Committee** ethics review board **Informed Consent** No

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COMPARISON OF VAGINAL SACROSPINOUS HYSTEROPEXY AND VAGINAL HYSTERECTOMY WITH APICAL FIXATION AS A PRIMARY SURGERY FOR PELVIC ORGAN PROLAPSE: RETROSPECTIVE COMPARISON OF PERIOPERATIVE OUTCOMES OVER A 18-YEAR-PERIOD

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HYPOTHESIS / AIMS OF STUDY
Various surgical procedures for female pelvic organ prolapse (POP) exist. One of the most frequently performed surgical management of symptomatic POP consists of vaginal hysterectomy (vag. HE) with apical fixation. However, uterine-preserving procedures such as vaginal sacrospinous hysteropexy (SSHP) have become an increasingly utilized surgical option for the primary treatment of POP. To assess the efficacy of primary SSHP in comparison to primary vag. HE with apical fixation we compared perioperative complications rates and outcomes.

STUDY DESIGN, MATERIALS AND METHODS
A retrospective data analysis was conducted. Women who received a surgical treatment by primary SSHP (study group) for symptomatic POP at our tertiary hospital from November 2004 up to December 2021 were eligible for inclusion. All included patients were matched 1:1 by age and BMI with a patient, who received a primary vaginal hysterectomy (control group) with apical fixation by either uterosacral ligament suspension (USLS) or sacrospinous ligament fixation (SSLF). Clinical information including confirmation of pelvic organ prolapse stage of 2 or higher according to the Pelvic Organ Prolapse Quantification system (POP-Q system) [1], clinical assessment of pelvic floor muscles scored according to the Oxford scale [2] and operative records were obtained from the patients' electronic hospital chart. All patient records were anonymized and de-identified prior to analysis. Only non-emergency patients and patients with planned elective reconstructive pelvic floor procedures were included. Emergency cases, all non-urogynaecologic issues or malignant results, as well as patients with previous pelvic floor surgeries were excluded. Postoperative complications were assessed through the standardized classification of surgical complications according to Clavien-Dindo [3].

Descriptive statistics were performed using contingency tables with absolute and relative distribution for categorial variable with mean and standard deviation or median and interquartile ranges for continuous variables. Endpoints were analyzed using Chi-square-test/Fisher-exact-test (categorial variables) and Mann-Whitney U-test/Kruskal-Wallis-test (continuous variables). A p-value < 0.05 was considered statistically significant. Analysis was performed using SPSS® (IBM, Armonk, NY, USA, Version 27).

RESULTS
A total of 154 patients were included with 77 patients in each group. There were no statistically significant differences in menopausal stage, parity, vaginal births, caesarean sections, nicotine consumption, urinary stress incontinence, overactive bladder, Oxford scale score, diarrhea, obstipation, or fecal incontinence between the two study groups. Furthermore, there was no statistically significant difference in preoperative POP-Q stage, nor in concomitant performed colporrhaphies between the two groups. Both groups also showed no statistically significant difference in preoperative health issues such as: cardiovascular disease, high blood pressure, diabetes, diseases of the respiratory system, neurological disease, orthopedic issues, metabolic diseases, or renal problems.

The SSHP group showed a significantly shorter mean operation time (67.0 vs 97.1 min; $p < 0.001$), fewer hospitalization days (2.94 vs 4.87 days $p < 0.001$) and less intraoperative blood loss (SSHP: 120.00 ml vs. vag. HE: 186.18 ml; $p = 0.035$) in comparison to the control group. Neither group had any intraoperative complication, nor an intraoperative conversion to other surgical management options. Regarding postoperative complications no statistically significant difference was found, with 2 patients experiencing grade 3b complications (one in each group) as categorized by the Clavien-Dindo classification.

Furthermore, we assessed the postoperative difference between the study and control group for issues such as urinary tract infections, de-novo incontinence, residual urine, voiding disorders, vaginal infection, infection of the wound, bleeding, required blood transfusions and pain – no statistically significant differences were found for any of these issues.

INTERPRETATION OF RESULTS
Our findings align with previously published studies that point towards SSHP being a safe alternative to vag. HE with apical fixation. In this study SSHP was associated with shorter operating time, shorter hospital stays and less intraoperative blood loss, while retaining similar short-term outcomes.

CONCLUDING MESSAGE
These results demonstrated that sacrospinous hysteropexy is an effective and safe alternative to vaginal hysterectomy with apical fixation for patients who wish to retain their uterus.

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PELVIC ORGAN PROLAPSE SURGERY: COMPARISON OF SACROCOLPOPEXY VERSUS LATERAL COLPOSUSPENSION

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HYPOTHESIS / AIMS OF STUDY
In recent years minimally invasive transperitoneal procedures of pelvic organ prolapse (POP) surgery are rising compared to traditional transvaginal techniques. Although sacrocolpopexy (SC) is the most common approach, different techniques have showed similarly success. In this regard, lateral colposuspension (LCS) could be compared as alternative to SC for the treatment of anterior and apical vaginal POP.

Purpose of this study was to compare anatomical and functional outcomes of the two techniques.

STUDY DESIGN, MATERIALS AND METHODS
A retrospective analysis involving two Italian centres was performed. Anatomical and functional outcomes of LCS (group A) versus SC (group B) were compared. Before the surgery, all patients underwent a medical interview, urogenital examination, urine analysis/ urine culture and invasive urodynamics.

Laparoscopic approach was used in group A, while laparoscopic or robot-assisted surgery was performed in group B.

After the surgery, patients were visited at 1, 3 and 6 months, then yearly. Outcomes included clinical staging of POP and stress urinary incontinence (SUI) classified by POP-Q system and Valsalva stress test, respectively. Recurrent (persistent and/or de novo) POP was defined significant if greater than stage I. Persistent or de novo constipation and overactive bladder (OAB) were defined as bowel symptoms and urinary urgency/frequency/nocturia/dysuria after surgery.

RESULTS
One-hundred and thirty eight women have been included in the study: 42 patients in group A, and 96 in group B. No preoperative differences in terms of anterior POP ($p = 0.88$) in both groups, on the contrary apical and posterior POP were different ($p = 0.0008$ and $p < 0.0001$, respectively). SC showed overall better results in terms of recurrent (de novo/persistence) POP (overall $p < 0.0001$, persistence $p < 0.0001$, de novo $p = 0.022$) although a higher rate of constipation was recorded ($p = 0.001$). POP recurrence is more frequent in LCS for all types of POP, particularly at the apical level ($p = 0.0003$). Nevertheless, the persistence/de novo rate of significant POP (POP-Q > 1) was not different between the groups ($p = 0.07$, $p = 0.46$). No post-operative change in term of de novo/recurrence symptoms OAB or SUI was documented ($p = 0.5$, $p = 0.9$). Mean follow-ups of 10.47 ± 4.52 months (1-24) of group A versus 33.6 ± 28 months (range 3-113) of group B were statistically different ($p > 0.0001$). Uni- and multi-variable cox-regression analysis and Kaplan-Meier survival curves revealed that SC had a more durable outcome over time than LCS, regardless of age, BMI, POP-Q, previous pelvic surgery, previous hysterectomy, and different follow-up numbers.

INTERPRETATION OF RESULTS
Even if LCS has the known advantage to treat successfully apical compartment with low rate of complications, this study shows that POP recurrence is more frequent in LCS for all types of POP, particularly at the apical level ($p = 0.0003$). Although patients were different at the baseline, the integrated analysis pointed out that SC has a longer POP recurrence-free time than LCS.

CONCLUDING MESSAGE
SC has better long-term anatomical results compared to LCS which presents a higher POP recurrence rate for all types of POP, particularly at the apical level. However, LCS is a suitable option in case of difficult access to the retroperitoneum/sacrum bone and represents a fast and safe procedure with low risk of organ injury.

Funding no **Clinical Trial** No **Subjects** Human **Ethics Committee** University of Foggia **Helsinki** Yes **Informed Consent** Yes

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THE INFLUENCE OF PREGNANCY, PARITY, AND MODE OF DELIVERY ON THE RISK OF URINARY INCONTINENCE AND PROLAPSE SURGERY – A NATIONAL REGISTER STUDY

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HYPOTHESIS / AIMS OF STUDY

The subsequent need for surgery for stress urinary incontinence (SUI) and pelvic organ prolapse (POP) may be a more valid outcome to assess childbirth as a risk factor for pelvic floor dysfunction than reports based purely on pelvic floor symptoms. It is also interesting to examine whether changes during pregnancy and after delivery were transient or if they persisted over time.

The aim of this study, therefore, was to examine the relationship of parity, mode of delivery, and pregnancy to the absolute and relative risk of surgery for POP and SUI, using nulliparous women not affected by childbirth as reference.

STUDY DESIGN, MATERIALS AND METHODS

We collected information from the Swedish National Quality Register of Gynecological Surgery (GynOp). All women who had SUI or POP surgery from 2010 to 2017 and were ≥45 years of age were eligible for the study (n=59,415). The total cohort was stratified according to parity and mode of delivery into three groups: nulliparous women, women with all deliveries by acute or elective caesarean sections (CS), and women with ≥1 vaginal delivery (VD). Women were also stratified by the number of births (0, 1, 2, 3, ≥4). Data were registered prospectively and consecutively, including a preoperative evaluation (with postal- or web-based questionnaires) and based on hospital records from admission, surgery, discharge, and a questionnaire completed 1-year postoperatively. The reference group consisted of all women ≥45 years of age (n=2,309,765) from the Total Population Register (TPR) of Statistics Sweden. Information in the Swedish Medical Birth Register (MBR) was used to determine the rate of women with caesarean and vaginal deliveries and their respective parity based on women born in 1960.

Surgical codes for POP and SUI surgery were based on the International Classification of Diseases, 10th revision. Continuous variables were presented as mean and standard deviation. Categorical data were presented as number, percentage, and 95% confidence interval (CI). Fisher´s exact test and the Mann-Whitney U test were used for categorical and continuous variables for pairwise comparisons. Results are presented as the mean difference for continuous variables and as the difference in percentages for categorical variables, 95% CI and P-value. The absolute risk (AR, per thousand = ‰) of having surgery for POP or SUI was calculated by dividing the number of UI or POP surgeries in GynOp by the number at risk in the reference population presented with a 95% CI. An observed/expected ratio was calculated, and the method of Ulm1 was used to assess the CI of the relative risk (RR) when comparing proportions between groups in GynOp with the respective proportions in the general female population ≥45 years. Statistical significance was set at P<0.05. Statistical analyses were performed using SAS 9.4 (SAS Inc, Cary, NC, USA).

RESULTS

There was 20,488 SUI and 39,617 POP surgeries from 2010 to 2017. Among women with SUI surgery, 93.1% had ≥1 vaginal delivery, 2.6% had ≥1 CS, and 4.3% were 0-para. In women with POP surgery 97.8% had ≥1 vaginal delivery, 0.4% ≥1 CS, and 1.9% were 0-para. Compared with the proportion in the general female population aged ≥45 years, the VD-group was overrepresented in GynOp by the RR 1.22 (95% CI, 1.21-1.24) in women with SUI surgery, and by RR 1.28 (95% CI, 1.27-1.29) with POP surgery, both P<0.001. The reverse applied to the 0-para and CS groups that were equally underrepresented by RR 0.31 (95% CI, 0.29-0.33) and RR 0.26 (95% CI, 0.24-0.28), both P<0.001, respectively for SUI surgery, and by RR 0.14 (95% CI, 0.13-0.15) and by RR 0.004 (95% CI, 0.031-0.043), both P<0.001 respectively for POP surgery.

The AR of POP surgery was lowest in CS delivered women [0.09‰ (95% CI, 0.08-0.11)]. In women with ≥1 vaginal births, POP surgery was >23 times higher [AR 2.11‰ (95% CI 2.09-2.13)]. There was a consistent cumulative increase of AR for POP and SUI surgery with parity in women with vaginal births. This trend was not observed in women with all their deliveries by CS and was in addition on par with the AR of surgery in 0-para women (Figure 1). The first VD carried the highest increase of AR for POP surgery (x6) and SUI surgery (x3). The second vaginal birth added the lowest AR for POP surgery (about 1/4 of the risk at first birth) and for SUI surgery (about 1/10 of the risk compared with the first VD) (Figure 2 A+B).

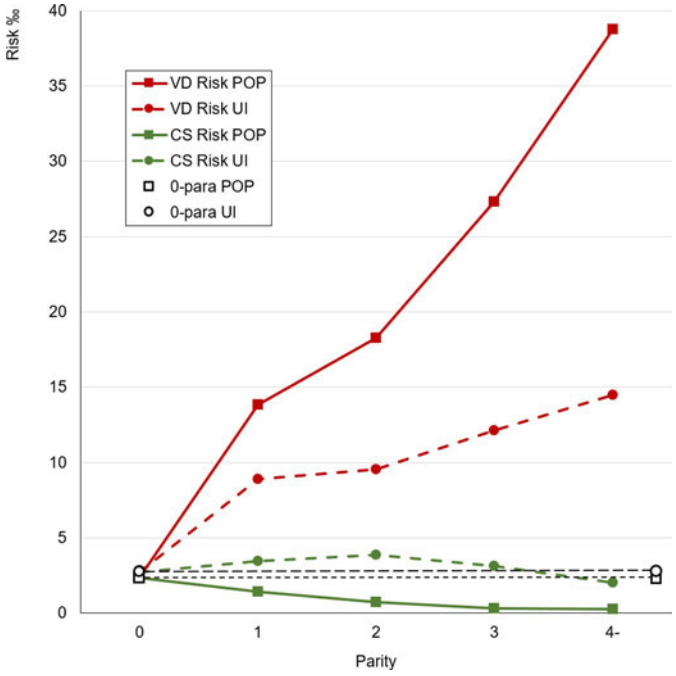
INTERPRETATION OF RESULTS

In women with one or more pregnancies delivered exclusively by C-sections, the risk of surgery for POP and SUI was negligible and on par with that in 0-para women. In contrast, the risk of surgery after VD increased consistently with the number of births. The first VD brought the largest risk increase for prolapse and incontinence surgery.

CONCLUDING MESSAGE

The result of the present study did not support the assumption that one or more pregnancies in themselves may cause long-term effects on the pelvic floor leading to POP and SUI surgery.

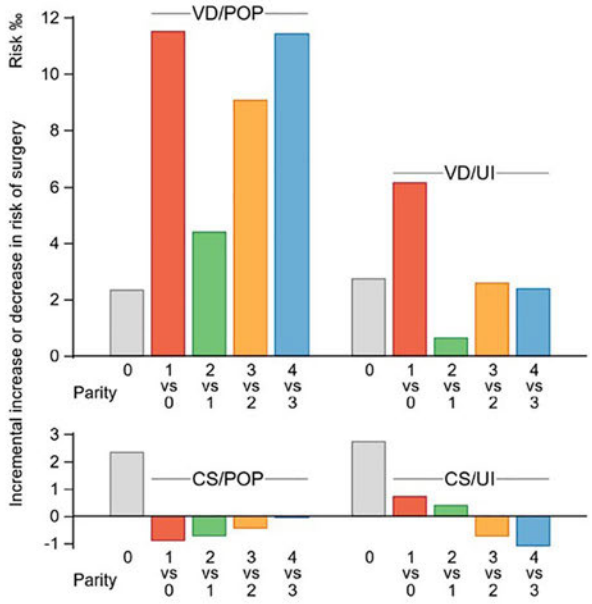
FIGURE 1



The cumulative absolute risk of surgery for POP and SUI

FIGURE 2

A



B

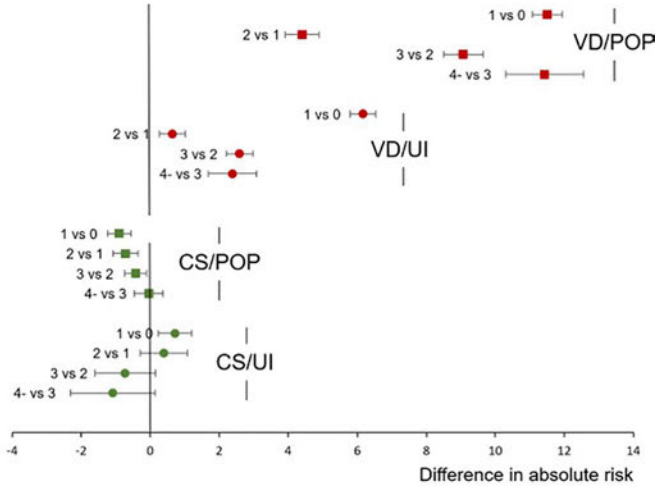


Figure 2A+B. The difference in absolute risk of surgery according to parity and mode of delivery

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MINIMAL INVASIVE ABDOMINAL SACRAL COLPOPEXY AND ABDOMINAL LATERAL SUSPENSION: A MULTICENTRIC PROSPECTIVE NON-INFERIORITY TRIAL

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HYPOTHESIS / AIMS OF STUDY
Abdominal Minimally Invasive Surgery (A-MIS), which is performed by minimally invasive approach such as laparoscopic, mini-laparoscopic and robotic has become widely used for advanced or multicompartmental prolapse treatment. Likewise, Abdominal Sacral Colpopexy (ASC) is considered the gold-standard for multicompartmental or advanced prolapse treatment. However, alternative surgical strategies, such as Abdominal Lateral Suspension (ALS) with mesh, have been developed in order to avoid the anatomical threats of suspension to the sacrum (1-2).

The aim of this study is to compare the gold-standard treatment for apical prolapse (ASC) with the recent surgical strategy (ALS) in term of objective and subjective apical cure rate. The primary outcomes were to determine the anatomic and symptomatic POP outcome, the secondary outcomes measures were to determine recurrence, reoperation rate, de novo POP and postoperative complications.

STUDY DESIGN, MATERIALS AND METHODS
This is a prospective multicenter non-inferiority trial on 360 patients with vaginal bulge and apical +/- anterior and posterior prolapse scheduled for abdominal approach who underwent ASC or ALS. The surgeries were performed in two Gynaecologic Centres, between April 2013 and January 2019.

The condition of non-inferiority for ALS surgery related to ASC surgery (indicated as a prolapse recurrence variation rate not exceeding 10%) was analyzed. The number of patients needed to analyze the non-inferiority condition was 300, with ALS/ASC ratio equal 2. The cohort of 300 patients obtained after adjustment for age and BMI, were divided in 100 subjected at ALS and 200 patients subjected at ASC; in addition, to calculate p- value of non-inferiority, confidence interval (CI) method was applied. Categorical data were described by absolute and relative frequency, continuous data by mean and standard deviation. Chi square test and t-test were applied to analyze categorical and continuous data, respectively. The values of $p < 0.05$ were considered significant. Statistical analysis was carried out by SPSS v.27 technology.

RESULTS
After 12 months follow-up the objective cure rate for apical defect was 92% for ALS and 94% for ASC (ALS recurrence 8% and ASC recurrence 6%; p-value of non-inferiority < 0.01). The recurrence prolapse rate in the anterior compartment for ALS and ASC were 16.1% and 19.4% respectively ($p = 0.652$), and in the posterior compartment were 50% and 14.5% respectively ($p = 0.019$). Overall, subjective cure rate in terms of absence of vaginal bulge was $> 90\%$ for both groups. Mesh complication rate were 0.7% and 1% for ALS and ASC. No patient had major postoperative complications in both groups, based on Clavien-Dindo scale.

INTERPRETATION OF RESULTS
The non-inferiority trial confirm that the new ALS strategy is not inferior to the gold standard ASC in terms of surgical treatment of apical POP.

CONCLUDING MESSAGE
A-MIS repair of apical prolapse with either ALS or ASC are safe, highly effective and durable.

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Funding I have had no collaboration with companies with commercial interests operating in the healthcare field and I did'n receive a grant **Clinical Trial** No **Subjects** Human **Ethics Committee** Comitato Etico Area Vasta Nord Ovest **Helsinki** Yes **Informed Consent** Yes

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1-YEAR OUTCOME AFTER BILATERAL UTEROSACRAL LIGAMENT REPLACEMENT - COMPARISON OF ABDOMINAL AND LAPAROSCOPIC SURGICAL TECHNIQUES IN TREATMENT OF PELVIC ORGAN PROLAPSE AND URINARY INCONTINENCE

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HYPOTHESIS / AIMS OF STUDY
Laxity of the anterior vaginal wall leads to the funnelling of the bladder neck and triggering inappropriate micturition reflexes and thus might lead to urinary incontinence. In the upright body position the anatomical support of the anterior vaginal wall (on which urethra and bladder base rest) is mainly ensured by the cervix / uterus, thus an intact apical suspension is mandatory.

Sacrocolpopexy (SCP) is the gold-standard for apical reconstruction. The technical performance of each SCP varies according to the surgeon´s discretion, and comparison of clinical outcomes may be hampered. Therefore, a comprehensible surgical technique for bilateral apical fixation with a minimum amount of synthetic material was developed. Evaluation of the clinical 1-year results after cervicosacropexy (either abdominal or laparoscopic) and its safety and efficacy are presented for the first time.

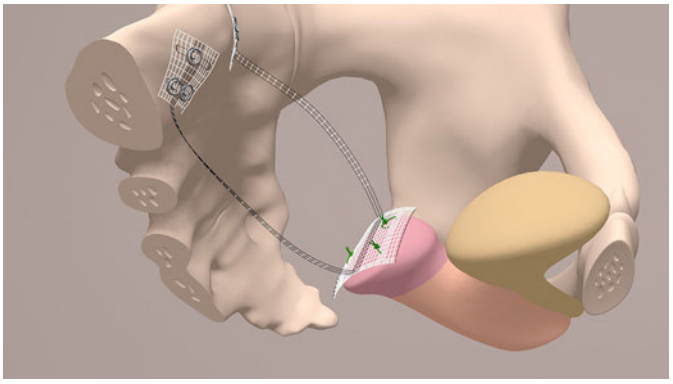
STUDY DESIGN, MATERIALS AND METHODS
Retrospective analysis in a tertiary center of women with POP-Q stages I-IV and urinary incontinence. All patients received a standardized bilateral uterosacral ligament (USL) replacement using polyvinylidene-fluoride tapes (PVDF) either open abdominal or laparoscopic cervicosacropexy. These PVDF tapes were identical in shape, that is 0.4 cm width and 8.8 cm length (Fig. 1). Clinical outcome was assessed at 12 months.

RESULTS
145 patients were evaluable, 75 patients were operated with the abdominal, 70 patients with the laparoscopic approach. No major complications occurred intraoperatively, and no mesh erosions were detected within 1-year postoperatively. There was no significant difference in clinical outcome one year after surgeries. Apical support (POP-Q stage 0) was restored in 100% of patients and urinary continence restored in 59% of patients (59% after laparotomy vs 62% after laparoscopy, respectively). After laparoscopy, patients stayed 3 days in mean compared to 5 days after laparotomy. Regarding the operating time, a laparotomy lasted in mean 120 minutes (89 - 168 minutes), whereas a laparoscopy lasted in mean 89 minutes (58 - 128 minutes).

INTERPRETATION OF RESULTS
In contrast to many other apical fixations, both USL were replaced using a clearly defined surgical technique (in term of type of material, size, shape of mesh, and positioning). This standardization ensured comparable and reproducible clinical outcomes, despite different surgical access paths.

CONCLUDING MESSAGE
This bilateral cervicosacropexy shows a very good anatomical result even one year after surgery, without any mesh complications. Beside the anatomical correction of the prolapse, the anterior vaginal wall (and its vesico-urethral junction) is emphasized and urinary continence could be restored. This surgical procedure is one alternative option in women with apical prolapse and urinary incontinence, especially since only a minimum of synthetic material is used.

FIGURE 1



Bilateral cervicosacropexy with replacement of both uterosacral ligaments for apical suspension.

Funding N/A **Clinical Trial** No **Subjects** Human **Ethics Committee** Ethical Committee of Medical Faculty University of Cologne, Germany **Helsinki** Yes **Informed Consent** Yes

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CONTENT VALIDITY OF QUALITY OF LIFE (QOL) INSTRUMENTS USED IN RANDOMISED CONTROLLED TRIALS (RCTS) EVALUATING SURGICAL INTERVENTIONS FOR PELVIC ORGAN PROLAPSE: A SYSTEMATIC REVIEW

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HYPOTHESIS / AIMS OF STUDY
Existing research quality on interventions for pelvic organ prolapse (POP), particularly surgical, is hampered by the lack of consensus regarding the outcomes that should be reported and how they should be measured. This renders research quality highly variable as studies have described many different outcomes leading to an inability to synthesise results and increasing research heterogeneity.

Currently there are no systematic reviews on content validity of QoL instruments in women with POP using standardised methodology. The objective of this systematic review was to evaluate QoL measurement instruments in POP for the consideration of inclusion in a core outcome and core outcome measure set (COS and COMS). Specifically, we aimed to evaluate content validity of widely used PROMs to measure QoL following surgical interventions for POP, using COSMIN standards.

STUDY DESIGN, MATERIALS AND METHODS
The design of this review was based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. A comprehensive literature search was conducted using EMBASE, MEDLINE, PsycINFO and PubMed, from their inception to December 2021. The search strategy consisted of 3 groups of search terms combined with the Boolean operator 'AND': 1) names of the PROMs 2) pelvic organ prolapse and 3) measurement properties. Our search terms were informed by previous systematic reviews published by a working group of CHORUS, an International Collaboration for Harmonising Outcomes, Research and Standards in Urogynaecology and Women's Health (https://i-chorus.org). These reviews evaluated reporting of outcomes and outcome measures used in anterior compartment, posterior compartment and apical vaginal prolapse RCTs. For the third group of search terms, a previously developed search filter that retrieved studies on the measurement properties was applied (1). This filter was adapted for all other databases. Snowballing and hand searches were also conducted using Google Scholar. Case reports, non-randomised and retrospective studies were excluded.

The titles and abstracts were screened individually against the inclusion criteria. Content validity studies were considered eligible for inclusion if they were full-text original articles, about women with POP and assessed the comprehensibility, comprehensiveness, and relevance of at least 1 of the PROMs. Any studies that focused on the development of any of the PROMs were also included. Cross-cultural adaptations were included if they performed a pilot study of the adapted questionnaire to evaluate comprehensibility. Full text articles were retrieved for abstracts that met the inclusion criteria or in cases where a decision could not be made based on title and abstract. Disagreements were resolved through consensus meetings among the researchers.

Using the COSMIN methodology for assessing content validity of PROMs, data extraction comprised of 3 stages (2). The first step evaluated the quality of PROM development, where the concept elicitation and cognitive interview study were assessed. Next, the quality of additional content validity studies on the PROM was assessed, where patients and professionals were asked about the relevance, comprehensiveness and comprehensibility of the PROM. These steps were rated using a 4-point scale: 'very good', 'adequate', 'doubtful' or 'inadequate'. The last step was evaluating the content validity of the PROM based on a summary of available evidence from the previous steps. Part of this included rating quality of evidence using a GRADE (Grading of Recommendations Assessment, Development and Evaluation) approach: 'high', 'moderate', 'low' or 'very low'.

RESULTS
After initially yielding 1476 results, 1308 records were removed following application of filters (human, full-text, English language) and deduplication. 168 records were screened via title and abstract against the inclusion criteria, of which 158 were excluded. 9 reports were assessed for eligibility by retrieving the full text, 4 of these were excluded for not concerning content validity. Following snowballing and hand-searching, 6 further studies were added. In total, 11 studies were included in this review (see Figure 1).

In total, 34 different QoL instruments from 117 RCTs were identified, of which 6 of the most commonly reported were included: ICIQ-VS, IIQ, P-QoL, PFDI, PFIQ and UDI. ePAQ-PF was also added following hand searches on Google Scholar.

Overall, PROM development was inadequate for all 7 instruments used to measure QoL in POP patients. While 7/7 PROMs involved patients in concept elicitation, only 3/7 PROMs included cognitive interviews with patients in their development (ePAQ-PF, ICIQ-VS, P-QoL). A total of 6 reports for 3/7 PROMs (PFDI, P-QoL, ICIQ-VS) assessing content validity were identified, demonstrating gaps in literature related to content validity studies. Quality of these studies was deemed doubtful to inadequate. The quality of evidence for all 7 PROMs included in this review was low to very low.

INTERPRETATION OF RESULTS
The results of this review illustrated gaps in evidence and quality of PROMs used in research and in the clinical management of POP. These PROMs should therefore be used with caution to interpret QoL.

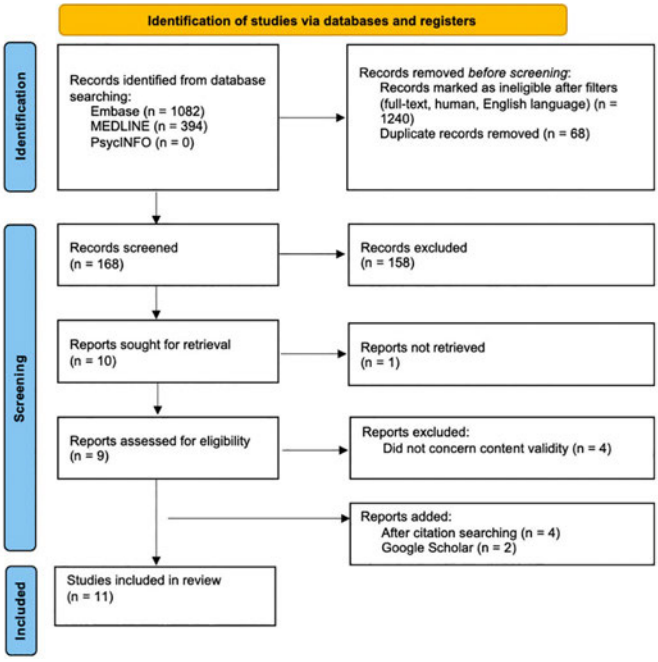
Patient involvement is vital especially in the concept elicitation stage of PROM development. This is done by undertaking focus groups/interviews to generate items that reflect concerns of patients. To develop a PROM specifically for POP, it is advisable to recruit patients from such a population, to ensure items of a PROM mirrors the patient experience and are relevant and comprehensive. Furthermore, cognitive interviews are fundamental in broadening patient involvement. Only 3/7 PROMs included cognitive interviews, thus it is not known whether patients experienced any challenges with the questionnaire or whether item modification was necessary in the remaining 4 PROMs. This means essential information may be missing or inaccurate.

While there are recommendations for assessing content validity during the development of new PROMs, this review supports previous literature highlighting poor reporting of qualitative research. As a minimum, PROM development should include a literature review, concept elicitation reviews or focus groups, data analysis, item generation and cognitive interviews.

Previous systematic reviews by CHORUS have highlighted the inconsistency and variations of outcome reporting in women with POP, as 34 different PROMs to measure QoL were identified. This study was carried out as part of a wider project to establish COS and COMS to reduce heterogeneity of outcome reporting in trials.

CONCLUDING MESSAGE
This review has shown gaps in quality of evidence around content validity of common QoL instruments used in women with POP (epAQ-PF, ICIQ-VS, IIQ, P-QoL, PFDI, PFIQ and UDI). There is an urgent need for adequate development and validation of PROMs. Researchers should consider using robust methodology. Content validity is the first measurement property to consider when selecting a PROM, and this study has illustrated that it is under investigated in patients with POP. These findings may contribute to the wider development of COS and COMS in POP to improve quality in research and clinical practice.

FIGURE 1



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RACIAL AND SOCIOECONOMIC DISPARITIES IN COST AND POST-OPERATIVE COMPLICATIONS FOLLOWING SACROCOLPOPEXY IN A NATIONAL INPATIENT DATABASE

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HYPOTHESIS / AIMS OF STUDY

Sacrocolpopexy provides the most durable surgical treatment for the management of apical pelvic organ prolapse. Previous literature suggests that minority races/ethnicities experience higher postoperative complications following surgical interventions for pelvic organ prolapse [1]. However, there is a paucity of literature examining disparities that may exist in cost and complications following sacrocolpopexy. We therefore sought to determine the association between socioeconomic factors, procedure charges, and postoperative complications among patients who underwent sacrocolpopexy. We hypothesized that, similar to previous studies exploring costs and complications after any surgery for pelvic organ prolapse [1], Black patients undergoing sacrocolpopexy would have an increased rate of complications and Hispanic patients would have lower associated procedure costs.

STUDY DESIGN, MATERIALS AND METHODS

This is a retrospective cohort study of the 2016-2017 National Inpatient Sample from the Healthcare Cost and Utilization Project, a database that was designed to produce national estimates of inpatient utilization, access, charges, quality, and outcomes [2]. We identified females >18 years of age with an ICD10 diagnosis code of apical prolapse who received open or laparoscopic/robotic sacrocolpopexy. Patients with a previous pelvic cancer diagnosis were excluded. We analyzed relationships between socioeconomic factors, procedure charges and postoperative complications in these patients. Multivariate logistic and linear regressions were used to identify variables associated with increased complications and costs, respectively.

RESULTS

We identified 4,440 women with a median age of 62 who underwent sacrocolpopexy between 2016-2017, of which 18.7% had complications. Hispanic patients had the highest median charge associated with surgical admission for sacrocolpopexy at $51,768 (IQR $35,379 to $79,405), followed by Other ($44,522; IQR $30,596 to $71,600), White ($43,471; IQR $29,733 to $66,476), and Black ($40,634; IQR $28,867 to $60,303) patients. Regression analysis revealed that protective factors against post-operative complications were Hispanic ethnicity (OR 0.76, 95% CI 0.59-0.99) and any concurrent hysterectomy (0.72, 0.61-0.85). Independent risk factors for post-operative complications were laparoscopic approach (3.78, 3.21-4.45) and a higher Charlson Comorbidity Index (Table 1). The most commonly observed post-operative complication was a revision or removal of graft procedure, of which Hispanic patients had the lowest rate (7.1%) and White patients had the highest rate (9.5%). Other complications, including post-operative hemorrhagic anemia and infections, were similar across races/ethnicities (Figure 1). Mesh-specific complications that did not involve a revision or removal procedure were low (<1%) across all ethnicity groups.

INTERPRETATION OF RESULTS

Hispanic patients observe significantly higher procedure charges and lower post-operative complications for sacrocolpopexy compared to other ethnicity groups. Significant predictors of post-operative complications among women undergoing sacrocolpopexy are laparoscopic approach and a higher Charlson Comorbidity Index. Paradoxically, concurrent hysterectomy served as a protective factor against post-operative complications. The most common postoperative complication experienced by all races/ethnicities was a revision or removal procedure related to the mesh implant, with Hispanics least likely to have this complication. Other mesh-specific complication rates were low regardless of race/ethnicity.

CONCLUDING MESSAGE

To our knowledge, this study is one of the first to examine racial and socioeconomic disparities in procedure charges and post-operative complications among patients undergoing sacrocolpopexy. Being of Hispanic ethnicity appeared to have a protective effect against post-operative complications, which may be partially driven by lower rates of revision or removal procedures in this population compared to other races/ethnicities. Studies with granular data on indications for revision/removal procedures are needed to confirm our findings and explore potential mechanisms underlying these variations.

FIGURE 1

Independent Variable	OR Complications (95% CI)	p-value
Race/ethnicity		
White	Referent	
Black	0.98 (0.71-1.35)	0.908
Hispanic	***0.76 (0.59-0.99)***	***0.043***
Other	0.79 (0.56-1.10)	0.154
Charlson Comorbidity Index^	***1.38 (1.28-1.48)***	***<0.001***
Geographic region		
Northeast	Referent	
Midwest	0.90 (0.69-1.16)	0.396
South	***0.74 (0.58-0.95)***	***0.017***
West	0.85 (0.66-1.09)	0.199
Sacrocolpopexy approach		
Open	Referent	
Laparoscopic	***3.78 (3.21-4.45)***	***<0.001***
Concurrent Hysterectomy		
None	Referent	
Any	***0.72 (0.61-0.85)***	***0.001***

^ Continuous Variable

Odds ratio (OR) and 95% confidence intervals (CI) represented for predictors of complications with statistical significance calculated at p<.05. Significant variables represented in bolded text.

Table 1. Multiple logistic regression evaluating patient demographic and hospital characteristics and their associations with post-operative complications following sacrocolpopexy.

FIGURE 2

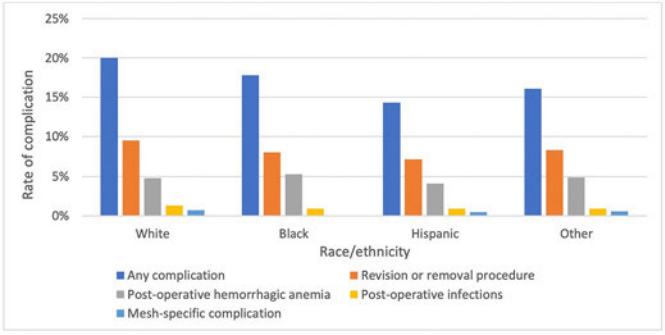

Figure 1. Rates of complication for each race/ethnicity following sacrocolpopexy.

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Funding None **Clinical Trial** No **Subjects** None

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DIFFERENTIAL INTERACTION BETWEEN VAGINAL FIBROBLASTS AND POLYPROPYLENE FROM PROLAPSE AND HEALTHY CONTROLS AND THE EFFECT OF MATERIAL'S SURFACE MODIFICATIONS.

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HYPOTHESIS / AIMS OF STUDY

Pelvic organ prolapse (POP) is a common and debilitating disorder that negatively affects the quality of life for many women. Its prevalence is as high as 30-50% in the general population, involves the descent of the pelvic organs and causes symptoms in almost 25% of patients. A high number of them require surgical treatment, where prosthetic materials, such as polypropylene, could be used through abdominal approach. Unfortunately, symptomatic recurrences and mesh-related complications can occur after their use. In part, this may be due to the fact that meshes are still far from being optimized for this application. More data are needed before a translationally specific design for POP surgical treatment can be achieved.

While substantial consideration is devoted to the design and validation of biomaterials, the nature of their interactions with the surrounding (compromised) biological microenvironment is commonly neglected. Whereas materials and devices are designed to modulate specific functions for a given application and tissue bed, the definition of material -tissue interactions have rarely considered differences in target tissue. Identifying key parameters in the in vivo microenvironment under healthy and disease conditions may be key to highlight the main biochemical signal transduction pathways involved in the biocompatibility complex. Here, we have tried to address contributions from both cell cues and biomaterials, with an emphasis on human (pathological) fibroblasts derived from patients with POP .

STUDY DESIGN, MATERIALS AND METHODS

Full thickness biopsies (>1 cm2) from the anterior vaginal wall were surgically excised from women suffering POP and healthy controls (n=5 both groups, based on information from previous studies) operated on for benign gynaecological pathology. Tissue collection was approved by the Clinical Ethics Committee and all participants signed a written informed consent. Biopsies were collected and immediately processed to isolate primary human vaginal fibroblasts by a double trypsin digestion. Experiments were carried out with fibroblast-derived cell lines within 3-8 passages and were repeated three times, using 3 technical replicates in each experiment.

Fibroblasts were characterised and compared on the basis of their proliferative index, cell migration rates, morphological features (automatic quantification of area, circularity, and aspect ratio), cytoskeleton protein expression (immunofluorescence staining of vimentin, F-actin, and vinculin), inflammatory and ECM gene expression, and functional aspects such as their ability to respond to microenvironmental cues (type I collagen as a scaffold and substrates of varying stiffness). Finally, two types of surface modifications were created on polypropylene scaffolds to improve cell adhesion and morphology compared to a standard / ordinary polypropylene: a) different surface roughness in the microscale (lower roughness: Ra= 1.62±0.14μm; higher roughness: Ra=4.16±1.38μm); and b) surface functionalization by covalent immobilization of an arginylglycylaspartic acid (RGD), the most common peptide motif responsible for cell adhesion in the extracellular matrix.

RESULTS

Pure fibroblast cell lines (vimentin+/cytokeratin-) were successfully obtained from all processed tissues. In vitro, fibroblasts from prolapsed tissues revealed lower proliferation rates than fibroblasts from non-prolapsed tissues, as well as a differentiated morphology (larger areas and more elongated shape) and higher cell migration rates. In contrast to healthy cells, actin stress fibres were evident in POP fibroblasts under the microscope, whereas vinculin (a marker of focal adhesions) showed no differences. The expression of genes coding for ECM proteins (FBN1, POSTN and BGN) and HTR2A (receptor for serotonin), all up-regulated in tissues from patients affected by POP (as we have previously observed), was also higher in POP fibroblasts. Conversely, no differences in the expression of inflammatory genes were detected. This distinct phenotype of POP vs healthy fibroblasts resulted in a reduced adaptability to changes in substrate stiffness in terms of cell adhesion and viability, particularly in contact with the softest substrates (< 8 KPa), in which a significant proportion of cells were not able to survive. Furthermore, POP fibroblasts cultured on polypropylene scaffolds also exhibited less adhesive properties and therefore impaired cell viability, compared to healthy fibroblasts. However, increasing polypropylene surface roughness and functionalization by covalently attaching an RGD peptide clearly improved POP fibroblast adhesion and survival.

INTERPRETATION OF RESULTS

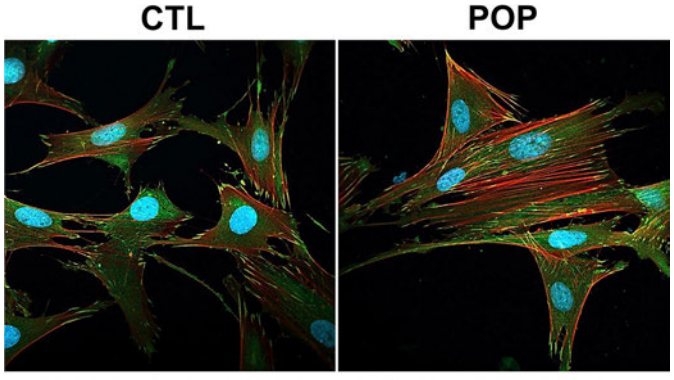
We have detected several phenotypical changes in fibroblasts derived from the vaginal wall of patients affected by prolapse, most of them related to their mechanical properties, such as the expression of cytoskeleton and extracellular matrix proteins. These alterations are possibly both cause and consequence of the overall phenotype of the prolapsed tissue, resulting in an impaired interaction with biomaterials and tissue repair. Our results reveal that the physico-chemical manipulation of a polypropylene surface certainly enhances cell adhesion and thus viability of POP fibroblasts.

CONCLUDING MESSAGE

Our contribution is based on the altered characteristics of the cells (fibroblasts) of the compromised POP host tissues, and the feasibility of surface modification of polypropylene devices (a polymer that is widely used in clinical practice).

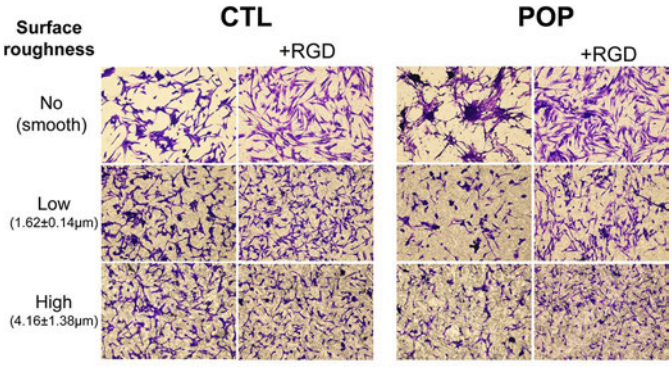
The results obtained can be potentially useful at least at two levels: a) the molecular mechanisms responsible for the maintenance of pelvic organ support structures are still poorly characterized; a better understanding of these mechanisms may help to identify women at risk and improve their prevention and treatment strategies; and, b) the response to the implantation of biomaterials can be improved by means of physicochemical modifications of the polymers used with an impact in the bioactivity zone. Overall, this can contribute to ameliorate the long-term treatment and repair of soft tissue defects.

FIGURE 1



Double labeling for F-actin and vinculin in fibroblasts isolated from healthy (CTL) and prolapsed (POP) anterior vaginal wall tissues. Fibroblasts were stained with anti-vinculin monoclonal antibody for focal adhesions (green) and TRITC-phalloidin for the actin cytoskeleton (red). Nuclei are shown in blue (DAPI).

FIGURE 2



Impact of polypropylene surface topography and functionalization on fibroblast morphology and adhesion. Fibroblasts from human healthy (CTL) and prolapsed (POP) anterior vaginal wall were cultured on unmodified (smooth), and modified (low and high roughness) polypropylene surfaces, with or wihout functionalization by an RGD-HBII covalent peptide.

Funding Proyectos de investigación en salud (Nº Expediente: PI17/01236). Instituto de Salud Carlos III. Ministerio de Economía, Industria y Competitividad. **Clinical Trial** No **Subjects** Human **Ethics Committee** Hospital Universitari Vall d'Hebron Clinical Research **Ethics Committee Helsinki** Yes **Informed Consent** Yes

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SESSION 8 - URODYNAMICS

Abstracts 133-144
14:35 - 16:05, Hall D
Chair: Prof Enrico Finazzi Agrò (Italy)

133 | www.ics.org/2022/abstract/133

CAN WE SPARE PRESSURE-FLOW STUDIES? UROFLOWMETRY PATTERN RECOGNITION USING COMPUTATIONAL PROCESSING: PRELIMINARY RESULTS.

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HYPOTHESIS / AIMS OF STUDY
Uroflowmetry is a noninvasive and relatively inexpensive test. Therefore, it is an indispensable, first-line screening test for most patients with suspected lower urinary tract dysfunction. It provides objective and quantitative information to understand both storage and voiding symptoms. The parameters classically analyzed are: maximum flow rate (Qmax), flow time, average flow rate, time to maximum urine flow, voided volume, and post-void residual urine volume. Although the shape of the flow curve may suggest specific types of abnormality, reliable information about the underlying dysfunction of the abnormal voiding cannot be derived from a flow curve alone.

Bladder outlet obstruction (BOO) due to Benign Prostate Hyperplasia is the most common condition causing male LUTS (MLUTS). However, not only BOO, but also detrusor underactivity (DU), is a common cause of MLUTS and has been reported to be present in 9-48% of men undergoing urodynamic evaluation for LUTS. Currently, only when flow signal is combined with intravesical and abdominal pressure recordings does it become possible, from the pressure-flow relationship, to analyze separately the contributions of detrusor contraction and bladder outlet function to the overall voiding pattern.

The aim of the present study is to create a classification algorithm capable of objectively distinguishing BOO and DU from uroflowmetry patterns in male patients. Accessible and correct identification of the underlying dysfunction might spare patients invasive pressure/flow tests and could contribute to the cost-effectiveness of the clinical diagnosis process.

STUDY DESIGN, MATERIALS AND METHODS
Study design and patient population

We performed a retrospective, observational, analytic and unicentric study. We included 124 male patients with voiding MLUTS subjected to urodynamic study, from 2012 to 2021. 62 consecutive patients with a urodynamic diagnosis of DU were selected as well as 62 patients with BOO. We excluded patients with undetermined results on the pressure/flow study (PFS), multiple urodynamic diagnosis, unavailable clinical data, or unacceptable uroflowmetry quality following the ICS standards. Urodynamic data was extracted from the institution's urodynamics database. Electronical medical records of included patients were reviewed.

This study was conducted in accordance with the ethical standards of the Declaration of Helsinki and was approved by the ethical committee of our institution.

Urodynamic examination

The diagnosis was established through PFS, which was performed in accordance with the ICS Good Urodynamics Practices protocol. Following ICS recommendations, Bladder contractility index (BCI = detrusor pressure at maximum flow (PdetQmax) + 5Qmax) and BOO index (BOOI = PdetQmax − 2 Qmax) were analyzed. DU was defined as BCI <100 and BOOI <40, whereas BOO was defined as BCI >100 and BOOI >40.

Free uroflowmetry was done the same day that PFS was performed. The free uroflowmetry signal was registered with a 10 observations per second ratio, and the patterns analyzed were up to 2-minutes long, resulting in up to 1200 flow measurement observations for every uroflowmetry chart. The precision of the measurements was 0,1ml/s. All the measurements were done with MMS equipment (Solar system®) and software (MMS v 8.17I, 2010).

Statistical analysis and algorithm creation

Uroflowmetry signal was normalized using spline and trace segmentation techniques. The signal was processed using FFT and Wavelets to extract the relevant characteristics. After signal processing, multiple classification algorithms have been tested: MLP, Logistic Regression, PLS, Random Forest and Support vector machine. Global and local approaches have been used. The evaluation and internal validation of the models have been performed using the Leaving one out (LOO) technique.

Demographic and urodynamic data are expressed as mean and standard deviation. Receiver operating characteristic (ROC) curve analysis was performed to identify optimal cutoff values. Statistical analyses were performed using R statistical software (version R 4.0.0; R Foundation for Statistical Computing).

RESULTS
Of the 124 men included in this study, 62 were assigned to the DU group and 62 to the BOO group. Clinical characteristics of the DU and BOO population are shown in figure 1. The age is comparable between groups. The presence of previous urological history was higher in the DU group. Urological history includes TURP, Radical prostatectomy and urethroplasty among other surgical procedures in the lower urinary tract. The prevalence of neurological pathology was higher in the DU group and diabetes was more prevalent in the BOO group. Prostate volume was higher for the BOO group.

Free uroflowmetry and PFS data are represented in table 1. Qmax and voiding efficiency were higher for the DU group. PdetQmax, BOOI and BCI were substantially higher for the BOO group.

The best performance for the study was obtained through a PLS classification algorithm. The application of this model to the sample using a LOO validation technique resulted in a ROC AUC of 0.8081. The sensitivity and the specificity for the UD group are 0,85 and 0,73, respectively. ROC curve is shown in Figure 1.

INTERPRETATION OF RESULTS
Despite the reasonable differences found between groups regarding Qmax and voiding efficiency, standard uroflowmetry parameters were comparable for both groups. Differences found in PFS results were expected, due to the prior classification of the patients based on such parameters.

Uroflowmetry is a noninvasive and relatively inexpensive test. In the last decade multiple attempts to find objective tools to analyze uroflowmetry outputs have been made. For distinguishing BOO and DU, Lee et al (1) created a parameter called DeltaQ, based on preexisting parameters (Qmax and Qave). Matsukawa et al (2) and Wada et al (3) postulated that sawtooth and interrupted waveform could be a predictor for DU. Although an interesting approach, depending on a certain pattern could restrict the applications of the analysis. The mentioned studies obtained AUC similar to the present study.

A machine-learning (ML) based algorithm was created and validated that can objectively differentiate between with BOO and DU. No specific pattern has been selected and all points on the flow curve have been considered. The probability of DU can be calculated by this algorithm, based on free uroflowmetry curve. This tool could help clinicians to decide whether to perform urodynamics and to reassure a surgical approach in case of a BOO result.

For this study, the AUC was obtained exclusively from the analysis of the flow signal. This could open the possibility of compiling data directly from the urodynamic devices on a much bigger scale. On the other hand, the incorporation of the clinical data to the algorithm could boost its perfor-

mance, although it could reduce its clinical practicality and limit the data management.

Our study has numerous limitations. We were not able to calculate the necessary due to the exploratory character of our study, and the sample size in the present study is low. In this direction, we would like to highlight that the aim of the present study was to show that free uroflowmetry patterns can be computationally analyzed instead of qualitatively assessed by urologists. We intend to pursue further research with larger sample sizes. Also, we divided patients into two groups, BOO and DU, regardless of the common coexistence of these two pathologies. Patients with USD and healthy patients were not included. Finally, it lacks external validation with a prospective population.

CONCLUDING MESSAGE

ML-based uroflowmetry pattern analysis may provide some help to distinguish between BOO and DU in MLUTS patients. Prospective and multicentric studies should be conducted to validate the results and maximize the algorithm training.

FIGURE 1

	Detrusor underactivity (n=62)		Bladder outlet obstruction (n=62)	
	μ	σ	μ	σ
Clinical data				
Age (years)	63.79	14.69	64.84	12.00
Urological history (%)	53.23	-	30.65	-
Neurological disease (%)	19.35	-	11.29	-
Diabetes Mellitus (%)	22.58	-	30.65	-
Ultrasound prostate volume (mL)	32.32	11.46	50.16	41.83
Free uroflowmetry				
Qmax (mL/s)	11.99	5.30	9.47	3.51
Voided volume (mL)	221.48	134.98	221.13	108.81
Flow time (s)	43.72	27.42	55.50	28.16
Post-void residual urine volume(mL)	75.16	96.86	87.71	133.16
Voiding efficiency (%)	79.10	21.86	71.60	18.95
Total bladder volume (mL)	296.65	174.76	308.84	191.67
Pressure/flow study				
Pdet Qmax (cm H_20)	29.27	13.41	93.06	24.05
BOOI (-)	14.76	15.03	74.13	26.56
BCI (-)	65.56	17.99	140.40	26.30

Table 1: Clinical and urodynamic data of DU and BOO patients

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FIGURE 2

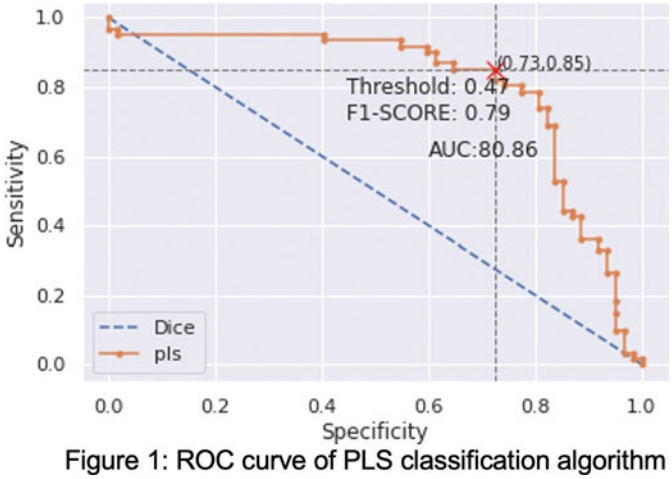

Figure 1: ROC curve of PLS classification algorithm

Figure 1: ROC curve of PLS classification algorithm

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Funding None **Clinical Trial** No **Subjects** Human **Ethics Committee** Instituto de investigación sanitaria La Fe **Helsinki** Yes **Informed Consent** Yes

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DIURNAL DIFFERENCE OF UROFLOW IN HEALTHY YOUNG MEN IN A CONTROLLED ENVIRONMENT ROOM

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HYPOTHESIS / AIMS OF STUDY

Elderly men sometimes complain that they have difficulty of urination during sleep period or first voiding of the day. The diurnal difference of maximal urine flow rate (Qmax) has been indicated in the elderly men with lower urinary tract symptoms (ref. 1), but little is known whether there is a difference or influence of daylight on Qmax in healthy young men. Here we show the diurnal difference of healthy young men in a controlled stable environment with varying daylight conditions.

STUDY DESIGN, MATERIALS AND METHODS

This study was conducted simultaneously with the experiments previously described (ref. 2). Twenty-one healthy young men (21 − 27 years old) were recruited from Kyoto university between November 2019 and February 2020. They participated in a 4-day study involving daytime (08:00-18:00 h) exposure in two light conditions, dim (< 50 lx) and bright (~ 2500 lx), in a random order (4-day study x2). Every urination was assessed by P-Flowdiary ® (Micronix Inc., Kyoto, Japan). Participants were allowed to urinate freely in the 2nd day of the experiment, while in the 3rd day they were directed to urinate at the fixed time of every 3 ~ 4 h. The Qmax at 04:00 h was compared with that at the closest amount of voided volume in the daytime between 11:00 h and 18:00 h (matched Day: mDay) because the Qmax is known to correlate with the voided volume. Identical meals (each 700 kcal, 60% from carbohydrates, 25% from fat, and 15% from protein; 3.8 g salt) were provided to participants at 08:00 h, 13:00 h, and 18:00 h. Participants consumed 25 ml/kg body weight per day of water every 2 h from 08:00 h to 24:00 h. Although they were not expected to follow a strict daily routine, to prevent extremes in activity, participants were not permitted to engage in strenuous physical exercise or to take a nap.

RESULTS

The mean age and BMI of the participants was 23.7 years old and 21.4, respectively. Three participants were excluded because of the missing data of Qmax for the experiment of free urination. The Qmax of after bed-11:00 h was significantly lower than those of 11:00-17:00 h, 17:00-23:00 h and before bed in the dim daylight experiment of free urination ($p < 0.05$ each, Dunnett's multiple comparison test, One-way ANOVA) and of 17:00-23:00 h in the bright daylight condition ($p < 0.01$, Dunnett's multiple comparison test, One-way ANOVA) (Fig. 1). The Qmax of before bed in the dim light daylight condition was significantly higher than that in the bright daylight condition ($p < 0.05$, Two-way repeated measures ANOVA followed by Sidak's multiple comparison test) (Fig. 1). Voided volume or average flow rate of them were not significantly different. As for fixed time urination, the Qmax at 04:00 h was significantly lower than that at mDay both under the dim daylight condition and the bright daylight condition ($p < 0.05$ and $p < 0.01$, respectively. Student's t-test) (Fig. 2).

INTERPRETATION OF RESULTS

Clear diurnal difference of Qmax existed in healthy young men under dim daylight conditions as well as bright daylight conditions. The bright daylight conditions significantly decreased the Qmax before bed compared with the dim daylight conditions, which may indicate that the bright daylight exposure can induce a phase shift advance in the diurnal variation of Qmax as like Na, Cl, UA excretion rhythm shift detected by Nakamoto et al (ref. 2). However, the mechanism of action of daylight exposure on Qmax before bed is unknown. It is supposed that this diurnal difference is derived from the involvement of diurnal difference of detrusor contraction, though pressure flow study is required to examine it.

CONCLUDING MESSAGE

Healthy young men had a clear diurnal difference of Qmax that decreased during sleep period and morning. The bright daylight exposure may induce a phase shift advance in Qmax before bed. Given these results of healthy young individuals, the diurnal difference of the Qmax is considered a physiological phenomenon that is instinctive in humans, i.e., circadian rhythm of our body.

FIGURE 1

Figure 1

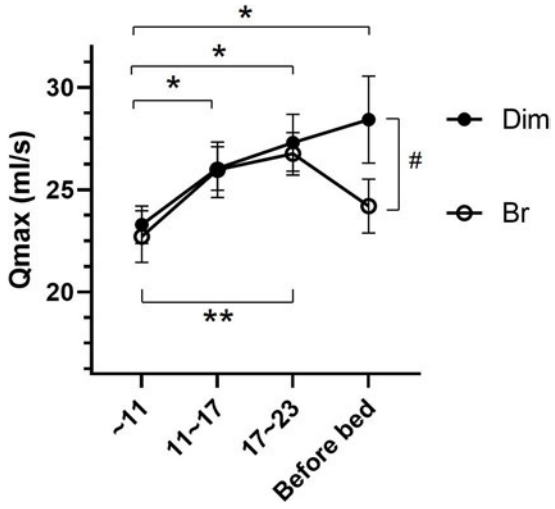

Figure 1. Diurnal differences of maximum flow rate (Qmax) in the free time urination of dim daylight condition (filled circle) and of bright daylight condition (white circle) (*p < 0.05, **p < 0.01 by Dunnett's multiple comparison test, One-way ANOVA; #p < 0.05

FIGURE 2

Figure 2

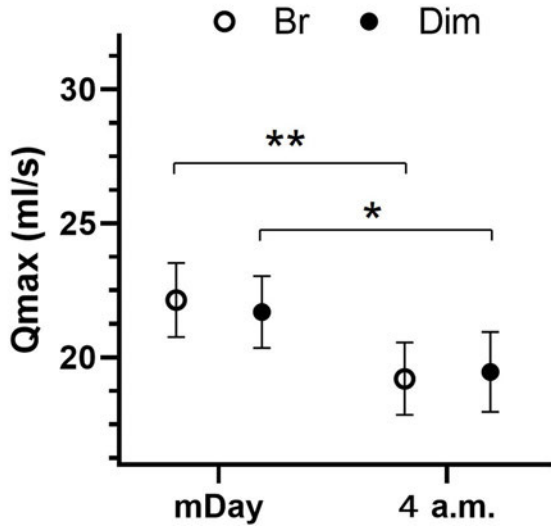

Figure 2. Diurnal differences of maximum flow rate (Qmax) in the fixed time urination of dim daylight condition and of bright daylight condition (*p < 0.05, **p < 0.01 by Student's t-test). mDay: matched Day, indicating the urination at the closest amount of

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Funding JSPS KAKENHI (Grant no. 17H04430 and 15H05682). **Clinical Trial** No **Subjects** Human **Ethics Committee Ethics Committee** of Kyoto University Graduate School **Helsinki** Yes **Informed Consent** Yes

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135 | www.ics.org/2022/abstract/135

TEST-RETEST VARIATION OF DETRUSOR VOIDING CONTRACTION WITH VARIATION OF BLADDER OUTFLOW RESISTANCE IN MEN WITH LUTS.

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HYPOTHESIS / AIMS OF STUDY

Detrusor contraction depends on outflow-resistance and a slowly (over many years) growing prostate demands an increase of detrusor contractility to maintain the ability to void. On the other hand, the uroflow-rate (urethral -flow controlling zone- distension) depends on detrusor voiding contraction strength. How differences in outflow resistance relate to differences in contraction in an individual is however remarkably little studied. One study reported test-retest differences of BOOI of plus or minus 14 of the BOOI (was 'AG index' at that time) and plus or minus 7 cmH2O for the outlet resistance quantifier URA, when a four -week interval was chosen. Variability of detrusor voiding contraction was however not included in this analysis and obvious differences of pressure zeroing procedures between patients and tests (as visible in the figures) were not considered.(1) Penile cuff pressure tests show a mean difference in maximum of isovolumetric contractions (as a measurement of contractility) of 4.0 ± 26 cm H2O in one study (PMID: 15371853) and -3.3 (32.0) cm H2O in another (PMID: 15371853). This testing does not directly account for the degree of outflow obstruction and, the correlation/association of maximum of isovolumic contraction with (maximum) of detrusor voiding contraction is not known. Furthermore, group mean values were reported but individual test-retest differences are more relevant. These studies nevertheless imply that short time differences in outflow resistance and voiding contraction are of relevance. The do however not clarify what contributes to the differences observed, and do not explain the balance between contraction and outflow resistance. (2) We present immediate and longer-term test-retest differences and how contraction varies with outflow resistance, both short time and longer time. We do this with the assumption that short time test-retest studies represent the variability of the combination of contraction and outflow obstruction, and the longer time may better represent if adaption of detrusor muscle to differences in outflow resistance occurs.

STUDY DESIGN, MATERIALS AND METHODS

273 men with LUTS without relevant concomitant abnormalities had ICS standard UDS with pressure flow study (PFS). ICS-standard UDS used fluid filled catheters, external pressure transducers, levelled to the symphysis pubis of the patient, saline fill with a rate of 10% of expected capacity per minute and voiding in private when the patient reports a strong sensation of bladder filling. 190 men (70%) had immediate test and retest, frequently sitting-standing, but also for other reasons. The other 83 men had longer term test-retest interval 1 month -10y for all possible reasons (e.g., long term continued pharmacological treatment, but also after surgical des-obstruction). The PFS parameters URA and BOOI as a measure of urethral resistance (outflow obstruction) and Wmax and BCI as quantifiers of detrusor voiding contraction (and detrusor underactivity) are used after correction of flow (peak-) artefacts.

The differences (dif.) between first and second PFS are calculated by subtracting the second measurement result from the first. (e.g., Wmax2 – Wmax1 = Wmaxdiff) these difference -values were plotted on X-Y graphs to show differences of (maximum of) voiding contraction versus differences in urethral resistance.

RESULTS

The figure shows (top row scatter-graphs) all URA differences with Wmax differences and (bottom row), the BOOI versus BCI differences, all with regression lines. Regression demonstrates that Wmax is 'more independent' of outflow resistance than BCI.

Correlation (all retests) of BOOIdif with URAdif is strong and significant (r.899, .000) and correlation of BCIdif with Wmax is weaker (r.493, .000). Correlation of URAdif with Wmax is absent (r.022, p723), correlation of BOOIdif with BCIdif is weak, however significant. (p.294, .000). Mean differences of long term and imtermediate (<5years) retests were not significantly different.

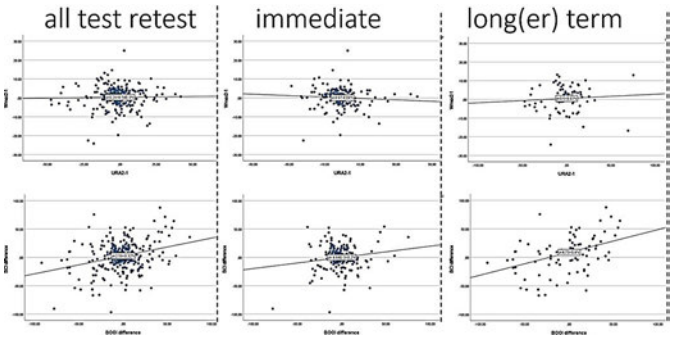
INTERPRETATION OF RESULTS

Analysis of both, regression and correlation shows that differences in outflow resistance have less influence on Wmax as a measure of contraction, than BCI. Wmax is not based on the same parameters as BOOI (and URA), while BCI is. Wmax appears more robust to grade contraction of the individual, because it is less sensitive to variations of BOO. Although Wmax (and BCI) have a tendency to increase with increasing grade of outflow obstruction the analysis of men with symptoms does not show evidence of compensation. It is not clear whether detrusor voiding contraction power/strength compensation occurs earlier in the development of pathophysiology (and or whether symptoms become bothersome when compensation is failing).

CONCLUDING MESSAGE

Test retest results of pressure flow studies with men learned that WFmax is, as a parameter to quantify detrusor voiding contraction (strength) less dependent on outflow obstruction than BCI.

FIGURE 1



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USABILITY AND INCIDENCE OF DETRUSOR OVERACTIVITY PATTERNS IN ONE YEAR OF URODYNAMIC STUDIES

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HYPOTHESIS / AIMS OF STUDY

Various patterns of detrusor overactivity (DO) have been described in literature[1, 2], and their clinical relevance have been discussed by the ICI-RS 2018.[3] This group stated that the patterns of DO need new definitions based on the stage of filling at which DO occurs, and on the shape and frequency content of an individual DO wave. Precise boundaries for these definitions have, however, not been included in the ICI-RS manuscript. To be clinically relevant, the patterns of DO should be reproducible and unambiguous. The goal of this study therefore is to assess the usability of the definitions of the patterns of DO mentioned by the ICI-RS 2018 and to explore the comprehensiveness required for future definitions. Furthermore, the incidence of these patterns in a historical cohort of urodynamic studies (UDS) are described.

STUDY DESIGN, MATERIALS AND METHODS

This retrospective study in a tertiary hospital included all ICS standard UDS (PMID: 27917521) performed in the year 2021 on patients with a minimum age of 18 years. Patients with augmentation cystoplasties were excluded. All UDS were performed using the Nexam Pro (MMS/Laborie, Portsmouth, NH) with a water-filled system and filling rate of 10% of the largest voided volume (bladder diary) per minute.

One investigator scored all DO patterns and categorized patient's clinical diagnosis to one of ten groups (Table 1). The following DO patterns were defined, either by the investigator or otherwise by their most recent definition in literature: 1: Absent: no DO contractions; 2: Phasic (cited): 'characteristic wave form and may or may not lead to urinary incontinence'[1]; 3: Terminal (cited): 'detrusor contraction occurring near or at the maximum of cystometric capacity, which cannot be suppressed, and results in incontinence or even reflex bladder emptying'[2]; 4: Compound (cited): 'phasic detrusor contraction with a subsequent increase in detrusor and base pressure with each subsequent contraction'[2]; 5: Sustained (cited): 'continuous detrusor contraction without returning to the detrusor resting pressure'[2]; 6: Other: patterns that do not meet the criteria listed above. Other types mentioned in literature are: a single contraction that is not terminal, or multiple sporadic contractions that are not phasic)[3]; 7: Undefinable: patterns that could not be properly measured e.g. due to a disturbed detrusor pressure trace. After-contraction[3] was not scored in this study.

In this study, two investigators achieved consensus on what constitutes the 'characteristic wave form' mentioned in the definition of phasic DO (2). Consensus was that the wave frequency in a phasic pattern does not have to be exactly constant (i.e. time intervals between waves may vary but an exact cut-off was not defined, a factor 2 variation was decided to be too large). A pattern can only be phasic after three waves due to the frequency constraint (e.g. two waves was scored as 'other'), and wave amplitude in a phasic pattern may vary (e.g. the amplitude of the final wave increases significantly and terminates the filling phase). Regarding the definition of terminal DO (3): if a patient reports strong desire during a contraction or cannot suppress the contraction it is practice in our hospital to give permission to void to prevent over-inhibition or incontinence. These cases were scored as 'Terminal DO' in this study. It was agreed that only one pattern of DO can exist per UDS.

First the absence of DO was extracted from the urodynamic diagnosis in written UDS reports in the hospital's patient management system. The UDS where DO was present were subsequently scored by examining the cystometry graphs at a time scale of 10 minutes per landscape A4 page and a pressure scale of 0 to 100cmH2O. The investigator scored high pressure DO (yes/no) if the detrusor pressure exceeded 40cmH2O at any point during DO. The investigator also scored UDS quality (good/average/poor), presence of hindering rectal activity on the abdominal pressure trace which obscured the pattern of DO (yes/no), concurrent loss of compliance (yes/no), decision certainty (yes/no) and recorded any considerations during decision making.

Results were analyzed using Excel 2016 (Microsoft, Redmond, WA) and presented using descriptive statistics.

RESULTS

In total 391 UDS of 380 patients were included after the exclusion of 11 UDS. DO was absent in 163 UDS (43% of total). DO pressure patterns were undefinable in 16 UDS due to hindering rectal activity (6) and/or poor measurement quality (12). The relative distribution of the remaining 212 patterns of DO was: 31% phasic, 31% terminal, 10% compound, 6% sustained, and 22% other. The incidence of ten clinical diagnosis categories in each pattern of DO are given in Table 1. DO pressures were high in 43% of phasic, 51% of terminal, 43% of compound, 69% of sustained and 31% of other patterns. Often a high pressure phasic pattern had a relatively large increase in amplitude for the last contraction, which then terminated the filling phase.

For UDS where DO was present, the investigator was unsure of the chosen pattern of DO in 97 cases. Besides hindering rectal activity (21) and suboptimal measurement quality (26), the definitions and agreed upon interpretations of DO patterns were sometimes still too ambiguous to apply to certain UDS. Most often the distinction between a phasic or other (i.e. multiple sporadic contractions) pattern was challenging to make because the wave frequency was not constant.

INTERPRETATION OF RESULTS

The most recent definitions of the ICI-RS 2018 patterns of DO are usable, but not unambiguous. Phrases like 'characteristic wave form' are open for interpretation, and therefore cause uncertainty during their application. The usability and reproducibility of these patterns of DO could be improved by objectifying their definitions. Characteristics of phasic wave forms should be described in terms of ranges of frequencies and amplitudes. Furthermore, we propose to include in the definition of terminal DO that the contraction terminates the filling phase, regardless of incontinence.

Application the current definitions in a historical UDS cohort showed some notable results. As expected based on figure 1 in ICI-RS 2018, most sustained patterns had a high pressure, but high pressures also occurred >40% in phasic, terminal and compound patterns meaning no pattern was inherently spared. The incidence of clinical diagnosis categories in each pattern of DO can help form hypotheses on their clinical relevance. Phasic and terminal patterns included UDS from all reported patient categories, with the phasic pattern containing relatively more neurogenic patients (notably spina bifida) and the terminal pattern containing relatively more male LUTS and post-prostate intervention incontinence. Furthermore, compound patterns only occurred in males or patients with neurogenic dysfunction and sustained patterns almost only occurred in patients with a neurogenic dysfunction.

CONCLUDING MESSAGE

Definitions of the ICI-RS 2018 patterns of DO were applied to one year of UDS in a tertiary hospital. These definitions were usable after doing some assumptions, but the usability and reproducibility of these patterns of DO could be improved by objectifying their definitions.

FIGURE 1

	Pattern of DO						
Patient category	**Absent n (% total)**	**Phasic n (% total)**	**Terminal n (% total)**	**Compound n (% total)**	**Sustained n (% total)**	**Other n (% total)**	**Total n**
Female incontinence	9 (6%)	7 (11%)	5 (8%)	0 (0%)	0 (0%)	1 (2%)	22
Female post incontinence surgery	7 (4%)	1 (2%)	1 (1%)	0 (0%)	0 (0%)	0 (0%)	9
Female frequency or urgency	9 (6%)	1 (2%)	2 (3%)	0 (0%)	0 (0%)	0 (0%)	12
Recurrent UTI or pain	18 (11%)	3 (4%)	3 (5%)	0 (0%)	0 (0%)	1 (2%)	25
Post-radical prostatectomy or post-TURP incontinence	17 (10%)	7 (11%)	15 (23%)	6 (29%)	1 (8%)	6 (13%)	52
Male LUTS	35 (21%)	15 (23%)	24 (37%)	7 (33%)	0 (0%)	17 (35%)	98
Female voiding dysfunction	7 (4%)	2 (3%)	0 (0%)	0 (0%)	0 (0%)	1 (2%)	10
Spina bifida	9 (6%)	12 (18%)	2 (3%)	1 (5%)	1 (8%)	4 (8%)	29
Other neurogenic dysfunction	38 (23%)	13 (20%)	11 (17%)	7 (33%)	10 (76%)	12 (25%)	91
Kidney disease or congenital anomalies	14 (9%)	4 (6%)	2 (3%)	0 (0%)	1 (8%)	6 (13%)	27
Total	163 (100%)	65 (100%)	65 (100%)	21 (100%)	13 (100%)	48 (100%)	375

The incidence of ten patient clinical diagnosis categories in each pattern of DO. UTI = Urinary tract infection; TURP = Transurethral resection of the prostate; LUTS = Lower urinary tract symptoms.

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INTERNATIONAL CONTINENCE SOCIETY DEFINITION OF DETRUSOR UNDERACTIVITY: AN ANALYSIS OF OBJECTIVE CLINICAL PARAMETERS OF FREE UROFLOWMETRY AND COMPARISON WITH THE LINPURR NOMOGRAM.

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HYPOTHESIS / AIMS OF STUDY
The International Continence Society (ICS) defines detrusor underactivity (DU) as “a contraction of reduced strength and/or duration, resulting in prolonged bladder emptying and/or a failure to achieve complete bladder emptying within a normal time span”. This definition is quantifiable by the non-invasive urodynamic parameters - voiding time (Vt), post-void residual (PVR) and voiding efficiency (void%). A well-established invasive method to grade detrusor voiding contraction is by the Schäfer pressure/flow nomogram (linearized passive urethral resistance relation), LinPURR. The goal of this study was to compare non-invasive parameters of DU with LinPURR contraction grading.

STUDY DESIGN, MATERIALS AND METHODS
Pressure-flow studies (PFS) and uroflowrates from men with lower urinary tract symptoms were included. Patients with volume $<$100mL, abnormal urinalysis, neurological or congenital disorders, pelvic or radical prostate surgery, or with urethral stricture were excluded. We determined Vt, PVR and void% of uroflowrate and related these parameters to dichotomised LinPURR contraction grading.

Thresholds of Vt $<$80 seconds, PVR $<$150 ml, and void% $>$80% were chosen.

RESULTS
327 PFS and uroflowrate studies were analysed. Void% had a sensitivity and specificity of 15-30% to predict urodynamic DU. Combining void% and Vt demonstrated a sensitivity of 6.7% and specificity of 59.5%; combining PVR and Vt a sensitivity of 6.9% and specificity of 64.5%.

INTERPRETATION OF RESULTS
When comparing noninvasive parameters void% was the most accurate single parameter to diagnose DU, performing better than a high PVR or a long Vt. Although 66.9% of patients with DU will be missed.

Adjusting the thresholds did result in higher sensitivity values, but lower specificity values.

The AUC values of void% as well as PVR and Vt were $<$0.62, suggesting that none of the parameters distinguished between normal contraction and DU well.

Uroflowrate is inevitably the result of contraction in combination with outflow resistance. This implies that for an accurate grading of contraction and a reliable diagnosis of DU, a PFS is mandatory. Nevertheless, void% and other uroflowrate parameters may be, or become, sensitive (and acceptably specific) parameters to evaluate the effect of therapy for an underactive bladder.

As there is no curative therapy for DU yet, the clinical implication for grading contraction is merely to differentiate between DU and BOO in patients with LUTS. When a therapy for DU will be developed, grading may be used to select proper candidates and to do proper proof of principle studies.

CONCLUDING MESSAGE
The noninvasive parameters, based on the ICS definition for DU, are not predictive for DU as single parameter or in combination. Void% is the most predictive parameter.

Funding None **Clinical Trial** No **Subjects** Human **Ethics not Req'd** It is a anonymous retrospective database study. **Helsinki** Yes **Informed Consent** No

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THREE DIMENSIONAL PROFILOMETRY-NEW METHOD OF GLOBAL ASSESSMENT OF THE URETHRAL PRESSURES

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HYPOTHESIS / AIMS OF STUDY
n use since the 1970s, urethral profilometry (UPP—Urethral Pressure Profile) is one of several measurements utilized as part of a full urodynamic diagnosis. It does, however, have a number of limitations as a test in everyday clinical practice. One of these disadvantages is its low reproducibility. This limitation results from the use of traditional catheters, which measure urethral pressure only from one direction of the urethral circumference. The urethra is not a symmetrical, thick tube. The pressure at different points of its circumference differ significantly which results from the urethra and pelvic floor anatomy and function. Consecutive measurements perofermed one by one , due to muscles reaction , do not allow to obtain precise , global pressures picture.

The presented study allows for the assessment of urethral pressure (Pura) along the entire length of the urethra. Pressure readings are taken at the same time in four directions radially every 90˚ with simultaneous measurement of the intra-bladder pressure (Pves). Dedicated software allows to obtain easy to interpretation three dimensional and mobile scan of urethral pressures. In pilot study reproducibility of the method is very high.

STUDY DESIGN, MATERIALS AND METHODS
The pilot study to present the method was performed in 2018. Second stage , with repeatibility assesment finished in 2021.

First , 25 women which presented in the clinic for the treatment of urinary incontinence or after previous pelvic floor repair surgery had the measurements performed to present the study technique. Afterwards group of 40 women with different LUTS had been randomised to two groups to asses the repeatibility of the method. First group had two measurements performed by one researcher to check the method repeatibility, and second group had the examination performed by two physicians to chek the intraoperator repeatibilty.

The examination was conducted according to the ICS standards.

Urethral pressure measurements: After micturition, a Foley catheter 12 or 14 Fr is used to empty the bladder of residual urine. Next, using the catheter, the bladder is filled with 200 mL of sterile water at room temperature or slightly warmer. In patients with reduced bladder capacity, the bladder is filled to the maximum volume, before it causes discomfort for the patient. After removal of the catheter, a cough test is performed to confirm the absence or presence of leakage of urine. While the patient is in a semi-sitting position, the catheter is inserted into the urethra to a depth guaranteeing that all the sensors are in the bladder. In order to confirm that the catheter has been accurately placed, a cough test is again performed. The auxiliary line on the catheter (indicating channel Pura1) should be directed ventrally. The catheter is then attached to a pulling mechanism, which is used to pull the catheter out. The speed of the catheter withdrawal in each case was 1 mm/s. The resting urethral profile is performed twice on each patient and the stress (dynamic) profile is performed once.

Special 5 channel catheter, quadruple capillary set and decicated software was used to perform the study.

RESULTS
Differences in pressure readings depending on the position of the catheter measurement channel in classic profilometry can be significant—even more than 50%. Depending on the location of the measurements taken regarding individual channels, differences in the functional length of the urethra were also found, with the P3 channel being the most variable indicator. We found that negative urethral pressures can be found along the whole lenght of the urethra, and as long as it is present in only one measuring channel patients can still be asymptomatic.

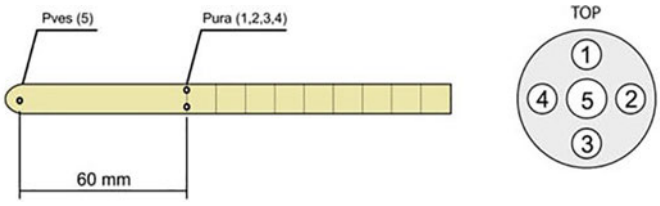
As for repeatibility - measurement deviations in pressure assessment less than 5 cmH20 [<5% of full measurement range] are accepted as resulting from the device settings and are clinically negligible. Similarily, for lenght measurements, deviations <5mm , for area measurment deviations less than 15 J/m2 and vector volume less than 50000 cmH2O2*mm ale due to the device settings and are clinically insignificant and negligible. In the table below (Table 1) standard deviations and percentage differences between measurements are presented. Depending on the parameter considered, from 67% to 100% of the records differed in less than 5%.

INTERPRETATION OF RESULTS
Three-dimensional profilometry likely results in the elimination of testing errors due to changes in the position of the catheter in the measurement channel. By using three-dimensional profilometry, the dimensional distribution of pressure in the urethra can also be comprehensively assessed during a stress test. Three-dimensional pressure distribution images can be obtained using dedicated software, and these images do not require complicated analysis.

It is assumed that the deviations of the measurements values up to 5% are within the measurement error and are negligible. Repeatibility of the functional examinations, such as urethral profilometry is influenced by many factors, among which are the patients movements, muscles tonus changes, patients relaxation or tensity. Taking all this factors into account, variability of the measurement values in presented study, which is generally less than 5% three dimensional profilometry can be considered as a method with good repeatability.What is more, the three dimensional recontructions of pressures distribution are comparable and compatible

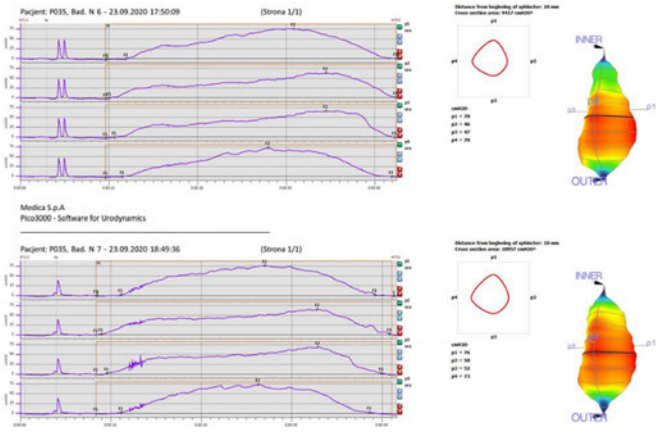
CONCLUDING MESSAGE
Three dimensional profilometry , as a method of intraurethral pressures assesment, requires technical difficulty, time, patient discomfort comparable with classical technique. At the same time allows to obtain much more data in a form easy for interpretation. What is more, the method seems to be repeatible and eas to learn.Three dimensional Urethral profilometry, as its classical eqivalent was invented, should stay rather a research tool, or a technique dedicated to a narrow group of patients with complex symptoms and pathologies, but is worth to be consideredas a usefurl clinical tool for complex diagnostics of the urethra.

FIGURE 1



5 channels catheter

FIGURE 2



Graphical interpretation of 3d urethral profile

Funding no **Clinical Trial** No **Subjects** None

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THE ROLE OF ELECTROMYOGRAPHY AND ITS ABNORMALITIES IN THE EVALUATION OF LOWER URINARY TRACT SYMPTOMS IN PATIENTS UNDERGOING URODYNAMICS.

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HYPOTHESIS / AIMS OF STUDY

There are limited studies on the role of electromyography and its abnormalities in males undergoing urodynamics for evaluation of lower urinary tract symptoms. Indeed, electromyographic abnormalities are poorly standardized. The aim of this study was to assess the role of electromyography and its abnormalities in the evaluation of lower urinary tract symptoms in males.

STUDY DESIGN, MATERIALS AND METHODS

Men undergoing urodynamics for evaluation of lower urinary tract symptoms (LUTS) from January 2021 to March 2022 are included in this study. This is an original retrospective cohort study. Preoperative evaluation included history, physical examination including focussed neurological examination, uroflowmetry (UFM), post-void residual urine (PVR), and International Prostate Symptom Score (IPSS). The primary objective was to determine the various urodynamic diagnosis of LUTS in patients with abnormal electromyography, and the secondary objective was to study the association of patients with abnormal EMG with preoperative factors. All urodynamic studies were analyzed and reviewed in a multidisciplinary team meetings to ensure accuracy of diagnosis.

Data are expressed as mean +/- standard deviation, and P-values were obtained using a two-tailed unpaired student t-test for pairwise parametric data comparisons. The Fisher Exact test compares categorical data given as a number (Percentage). Statistical significance was defined as a P value of less than 0.05. The statistical analysis tool SPSS (Statistical Package for the Social Sciences) v25 was used.

RESULTS

The study included 110 male patients. Abnormal EMG was found in 49 (44%) patients. The patients were further divided based on neurogenic cause or non-neurogenic cause. There were 15 (14%) patients with neurogenic abnormalities. Among neurogenic causes, three patients were found to have abnormal EMG. Type 1 Detrusor-sphincter dyssynergia (DSD) was found in two patients, and type 2 DSD was found in one patient. Among patients with non-neurogenic causes, 42 patients (38%) had abnormal EMG. These were further categorized into complete non-relaxation of the sphincter in 15 patients (13%), intermittently increasing in 17 patients (15%), Decrescendo pattern in three patients (2%), Crescendo pattern in two patients (2%), Crescendo-decrescendo pattern in one patient, Increased due to prolonged abdominal straining in seven patients (6%). The various urodynamic diagnosis in patients with abnormal EMG was Dysfunctional voiding combined with various other disorders like detrusor overactivity and detrusor underactivity. The seven patients having increased activity due to abdominal straining had a diagnosis of detrusor underactivity as these patients could not generate enough detrusor pressure.

INTERPRETATION OF RESULTS

EMG helped significantly change post urodynamics diagnosis in patients ($p = 0.00$). Figure 1 summarises the various urodynamic diagnosis obtained. Therefore, 38% of patients had their urodynamic diagnosis changed following EMG monitoring which could have been missed otherwise. The 6% of the patients having abnormal EMG due to abdominal straining can be easily identified by any expert urodynamic person.

CONCLUDING MESSAGE

For patients with LUTS or pelvic floor dysfunction, EMG is an essential criterion for diagnosing various urodynamic conditions. It might show the urethral sphincter's functional state. We should make every effort to obtain a high-quality EMG trace in order to establish an evidence-based diagnosis, rather than relying solely on the experience-based diagnosis.

FIGURE 1

Pre-UDS diagnosis * Post UDS diagnosis Crosstabulation

Count

		Post UDS diagnosis								
		BPE with OV	DESD	DO with DSD	DU with DSD	DV	DV with DU	Small capacity bladder with DV	Terminal DO with DV	Terminal DO with type 2 DSD	Total
Pre-UDS diagnosis	Functional obstruction	0	0	0	0	16	4	1	2	0	23
	Neurogenic bladder	0	1	1	1	0	0	0	0	1	4
	Overactive bladder	0	1	1	0	3	3	0	0	0	8
	Underactive bladder	0	0	0	0	2	0	0	0	0	2
	Underactive bladder/BOO	1	0	0	0	0	0	0	0	0	1
Total		1	2	2	1	21	7	1	2	1	38

Figure 1: Change in pre-post urodynamic diagnosis in patients:

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🏆 BEST IN CATEGORY PRIZE: MALE LOWER URINARY TRACT SYMPTOMS (LUTS) / VOIDING DYSFUNCTION

VISUAL ANALOGUE SCORE FOR URINARY SYMPTOMS – VASUS, VALIDATION OF A VISUAL SCALE FOR LOWER URINARY TRACT SYMPTOMS (LUTS) IN AN AFRICAN COUNTRY

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HYPOTHESIS / AIMS OF STUDY

Lower urinary tract symptoms (LUTS) are very prevalent in men and are widely dispersed across the globe. And its prevalence is often determined using the IPSS (International Prostate Symptom Score). In the evaluation of LUTS, there are difficulties associated with the quantification of something subjective as a symptom, increased by the difficulties already known in the use of IPSS in a low literacy setting. Validate a visual scale to assess LUTS, especially in developing countries, as an alternative to IPSS. VASUS consist of 5 questions, where Q1 and Q2 assess urinary stream quality, Q3 nocturia, Q4 incomplete emptying and Q5 QoL (figure 1).

STUDY DESIGN, MATERIALS AND METHODS

Between 2014 and 2017, we carried out a study in the male population over thirty years from São Tomé and Príncipe, a Portuguese speaking African Country. A stratified sample (age and district) of subjects completed IPSS, VASUS and a free flowmetry.

RESULTS

Eight hundred and twelve men born in São Tomé and Príncipe over 30 years of age (average age: 50.72, range: 30-95), distributed geographically (by district) and by age, completed the study protocol. Table 1 shows the main socio-demographic characteristics.

Positive correlations between IPSS and VASUS were found for all variables (p-value <0.0001), analyzed (Table 2). The Spearman correlation to the total result of the IPSS and VASUS was $r=0.547$ ($p<0.0001$) The highest value was found in the nocturia question (Q3) ($r=0.767$, $p<0.0001$).

VASUS and IPSS quality of life questions were positively correlated ($r=0.656$, $p<0.0001$). There was a strong association between this (VASUS Q5) and the total score in VASUS ($r=0.656$, $p<0.0001$).

In the evaluation of urodynamic variables, negative correlation for all variables was found, being stronger for VASUS than for IPSS (Table 1).

Comparison of Qmax (maximum flow) averages, in Q1 and Q2 of the VASUS ($F=55.31$; $p<0.0001$; $F=53.44$; $p<0.0001$) and Q5 of the IPSS ($F=29.55$; $p<0.0001$), between patients with mild symptoms and those with moderate to severe symptoms, showed strong statistical significance in both questionnaires.

INTERPRETATION OF RESULTS

With VASUS we created a visual scale that could be quickly and easily applied in a low literacy setting and that could be useful as a screening and also a monitoring tool.

When verifying the association of VASUS with the IPSS, namely when comparing questions with similar objectives such as nocturia (VASUS - Q3 and IPSS - Q7), the stream quality (VASUS - Q1 and Q2 and IPSS - Q5) or the quality of life (VASUS - Q5 and IPSS - Q8), we verified strong positive correlations. These results are in agreement with those verified for other visual scales.

CONCLUDING MESSAGE

To our knowledge, this is the first work to validate a visual scale for LUTS in a large-scale sample of individuals from the general male population without prior known LUTS-inducing urological disease. VASUS is a visual alternative to IPSS allowing evaluation of LUTS and having correlation with IPSS and flowmetry. Its use in developing countries with low levels of literacy will be an asset. The authors believe that widespread use of a scale such as VASUS in urology consultations is warranted, in order to increase daily practice objectification of LUTS.

FIGURE 1

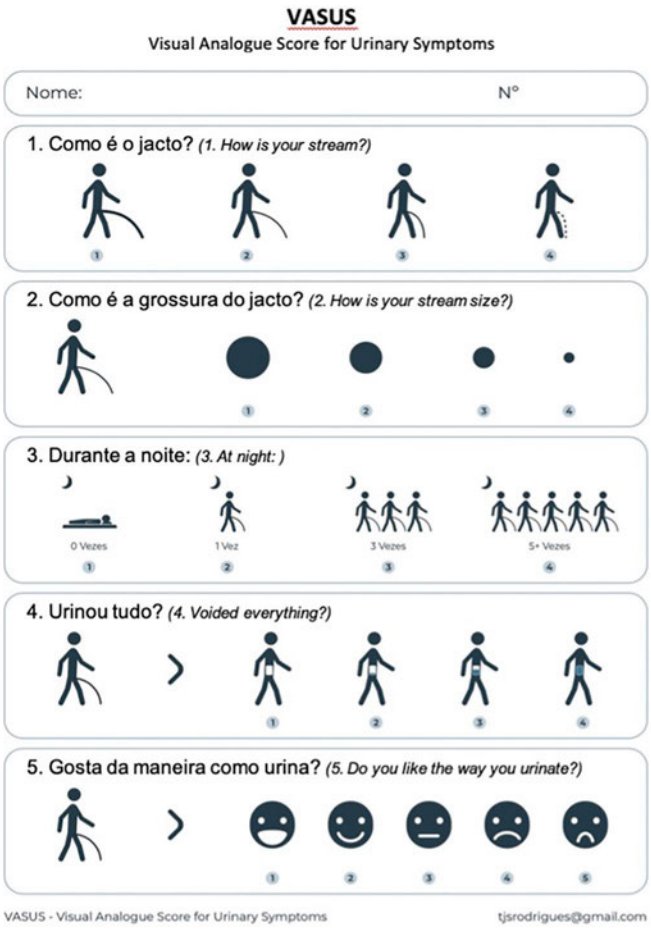

Figure 1 - Visual Analogue Score for Urinary Symptoms – VASUS

FIGURE 2

	Spearman's rank Correlation coefficient	p-value
Total VASUS vs Total IPSS	+0.505	<0.0001
VASUS Q3 vs IPSS Q7	+0.767	<0.0001
VASUS Q3 vs IPSS Q2 + Q4 + Q7	+0.683	<0.0001
VASUS Q1 vs IPSS Q5	+0.414	<0.0001
VASUS Q2 vs IPSS Q5	+0.411	<0.0001
VASUS Q1 + Q2 vs IPSS Q3 + Q5 + Q6	+0.399	<0.0001
VASUS Q1 + Q2 vs IPSS Q5	+0.439	<0.0001
VASUS Q4 vs IPSS Q1	+0.291	<0.0001
VASUS Q5 vs IPSS Q8	+0.656	<0.0001
Total VASUS vs. VASUS Q5	+0.425	<0.0001
Total IPSS vs IPSS Q8	+0.368	<0.0001
Total VASUS vs QMAX	-0.374	<0.0001
Total IPSS vs QMAX	-0.288	<0.0001
Total VASUS vs QAVE	-0.407	<0.0001
Total IPSS vs QAVE	-0.318	<0.0001
Weak stream: VASUS Q1 vs QMAX	-0.293	<0.0001
Weak stream: IPSS Q5 vs QMAX	-0.216	<0.0001

Table 1 - Association between VASUS, IPSS (total scores and subscores) and with urodynamic parameters.

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THE EFFECT OF USING A STANDARD ILLUSTRATED CONSENT FORM ON ANXIETY LEVELS IN THE URODYNAMIC INVESTIGATION: A PROSPECTIVE CLINICAL STUDY

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HYPOTHESIS / AIMS OF STUDY

Urodynamic studies are frequently used minimally invasive procedures for the investigation of lower urinary system functions Also, considering the risk of infection associated with these invasive tests, some studies have reported considerable anxiety during the procedure (1-3). The aim of this prospective randomized study was to measure anxiety associated with the urodynamic studies and to investigate the role of using a simple illustrated information sheet before the urodynamic study in reducing anxiety levels. In addition, we aimed to develop a new specific questionnaire as the Urodynamics Quality of Life-Anxiety Form (UQL-AF) in this study.

STUDY DESIGN, MATERIALS AND METHODS

A single-center prospective study, approved by the ethical committee, was performed at the urodynamics unit between the 1st of October, 2020 and the 1st of October, 2021. All subsequent patients between 18 and 80 years old who underwent urodynamic studies were included. Exclusion criteria involved a history of invasive procedures that can affect anxiety levels such as the previous history of urodynamic study, history of urethral catheterization, history of urological malignancy, previous surgery excluding circumcision, and history of gastrointestinal endoscopy. A regular consent form was signed by each patient who participated in this study before the urodynamic investigation. The patients were randomized into two groups by using a simple randomization method. The first group received a newly developed one-page illustrated information sheet attached to the regular consent form, while the second group took only the conventional consent form. All patients completed the "International Prostate Symptom Score" (IPSS) and "Marmara Overactive Bladder Questionnaire" (M-OBQ) forms. Both groups were also received the "Hospital Anxiety and Depression Scale" (HADS) to measure their anxiety levels before and 1 hour after the urodynamic study. In addition, the UQL-AF as a new original form was given to each patient in both groups. The results of these scales were compared.

RESULTS

A total of 122 appropriate patients were randomized into two groups. The mean age of the patients was 46.56 years. Of all patients, 54.9% were male and 45.1% were female. There was no statistical difference in quantitative and categorical variables between both groups. Also, no difference was seen between both groups in terms of systemic diseases, urodynamic indications, results of both IPSS and M-OBQ. Significant anxiety (HADS anxiety score ≥ 8) was detected in 50.9% of the patients before the urodynamic study in the whole group. Although the average HADS scores were not statistically significant in the baseline measurements before the procedure, they were lower in the first group that received illustrated sheet ($p = 0.756$ for HADS anxiety score, $p = 0.786$ for HADS depression score). Also, the number of patients with remarkable anxiety before the procedure was lower without statistical significance according to HADS values in the first group ($p = 0.717$). The proportion of patients with severe HADS anxiety and depression scores decreased significantly in both groups after 1 hour of the procedure (for HADS anxiety score, $p = 0.0001$ in group 1, $p = 0.001$ in group 2). The UQL–AF post-urodynamic study score was significantly lower in the first group that received the illustrated form ($p = 0.014$). A remarkable correlation was observed between HADS and UQL-AF scores.

INTERPRETATION OF RESULTS

In this study, urodynamic investigations were shown to cause significant anxiety in at least half of the patients by using the HADS. In the first group who received the illustrated information sheet, mean total HADS scores and the proportion of having notable anxiety (HADS anxiety score ≥ 8) were lower, although the difference was not statistically significant. However, a larger study may provide that using an illustrated sheet can significantly improve the degree of anxiety levels during urodynamics.

CONCLUDING MESSAGE

It was determined that UQL-AF, which we prepared specifically for the urodynamic investigation, was correlated with HADS. However, multicenter patient series are certainly needed for the validation of this new scale. When this is provided, UQL-AF may detect the patients with severe anxiety both before and after the urodynamic study and by applying a special anxiety-reducing approach to this group, both better results from the urodynamic investigation can be obtained and patient comfort can be increased.

FIGURE 1

		Received illustrated sheet		p value*	Not received illustrated sheet		p value*
		n	%		n	%	
HADS Anxiety (Score≥8)	Before UD	30	49,2%	0,000	32	52,4%	0,001
	After UD	20	32,8%		15	24,6%	
HADS Depression (Score≥8)	Before UD	27	44,3%	0,000	24	39,4%	0,000
	After UD	24	39,3%		21	34,4%	

**Yates Chi-Square Test*
(n: Number of people, %: Percentage rate, HADS: Hospital Anxiety and Depression Scale, UD: Urodynamic study)

Table 1. Comparison of the number of patients with "Hospital Anxiety and Depression Scale" (HADS) scores with borderline and abnormal results for the pre- and post-urodynamic periods in both randomization groups

FIGURE 2

	Received illustrated sheet						Not received illustrated sheet						p value*
	n	Min	Max	Avg	SD	IQR	n	Min	Max	Avg	SD	IQR	
UQL-AF before UD score	61	12	36	21,34	5,32	9	61	13	40	21,70	5,69	7	0,882
UQL-AF after UD score	61	16	52	31,64	8,79	13	61	21	65	35,64	8,56	12	**0,014**

** Mann-Whitney U Test*
(n: Number of people, Min: Minimum, Max: Maximum, Avg: Average, SD: Standard deviation, IQR: Interquartile range, UQL-AF: Urodynamics Quality of Life-Anxiety Form, UD: Urodynamic study)

Table 2. Urodynamics Quality of Life-Anxiety Form (UQL-AF) before and after the procedure for the largest, smallest, and mean values and the change of mean values according to the randomization groups

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FIRST STEPS TO UNDERSTANDING THE FREE AND INVASIVE MAXIMUM FLOW RATE DISCREPANCY

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HYPOTHESIS / AIMS OF STUDY

This study aims to compare the parameters of free and invasive uroflowmetry among female patients with different referral diagnoses in order to describe if the known difference between these two measurements varies in different clinical settings.

STUDY DESIGN, MATERIALS AND METHODS

This is a cross-sectional study. We reviewed Urodynamic studies performed from 2015 to 2021 in an academic hospital in Chile. Urodynamics were conducted following ICS good practices. Female adult patients with lower urinary tract symptoms were selected. Only patients who voided at least 150 ml in both free and invasive flowmetry were included. Patients with high-grade prolapse were excluded. Depending on the referral diagnosis and clinical suspicion patients were classified into 5 different groups (they could be part of more than one group): voiding dysfunction, mixed urinary incontinence, isolated stress urinary incontinence (SUI), isolated overactive bladder-urge incontinence (OAB) and prior anti-incontinence surgery. Each patient was asked to urinate with the same sensation they would do at home for a non-invasive uroflowmetry (measuring free maximum flow (fQMax). The cystometry was conducted using a 6 Fr double lumen catheter for bladder filling and measurement of intravesical pressure, and a rectal balloon catheter was installed to measure abdominal pressure. Warm saline solution was infused at a rate between 10-50 ml/min. Finally, a pressure-flow study (PFS) was carried out to evaluate invasive maximum flow (iQmax). Both Qmax measures were manually corrected. Comparison of both uroflowmetries (free and invasive) was conducted for the whole sample through Spearman's rank correlation coefficient and intraclass correlation coefficient (ICC).The difference between both Qmax (fQmax-iQmax = **Δ**Qmax) was calculated. Then, **Δ**Qmax was assessed among the different groups to see if there were any significant associations using U Mann-Whitney. Numbers are shown with median and interquartile range and were evaluated with non-parametric tests using IBM SPSS version 23.0 and two-tailed p-values <0.05 was considered as statistically significant.

RESULTS

891 urodynamic studies from female patients were reviewed and 407 patients met the inclusion criteria forming the analysis group. Overall, patients' mean age was 53.9 + -12 years, other socio demographic information is shown in table 1. Our population had a referral diagnosis of: voiding dysfunction (VD) (6.6%), mixed urinary incontinence (MUI) (61.7%), stress urinary incontinence (SUI) (24.6%), overactive bladder (OAB) (7.4%) and prior anti-incontinence surgery (13.3%). They had a median of 2 vaginal deliveries (IQR 3). 12.8% complained of vaginal bulge. They used a median of 3 pads/day (IQR 3) and their daily and nightly micturitions were 7(IQR 5) and 1 (IQR 2), respectively.

Free Qmax was higher (30 ml/sec) and correlated poorly (r: 0271, $p<0.001$) with the iQmax (17 ml/sec). The F-Test to assess reliability of the two measurement tools showed there was a systematic error when measuring Qmax ($p<0.001$). Intraclass correlation coefficient (ICC) showed that only 14.8% of the variability among the measurement tools corresponded to a random error, in other words most variability was explained by systematic error.

The comparison between both fQMax and iQmax is shown in Table 2. The whole group had a median of 12 ml/sec difference between both micturitions. This contrast behaved differently among the groups, showing that voiding dysfunction patients had a much lighter difference (only 5 ml/sec), whereas patients with SUI showed a deeper difference with 17 ml/sec.

INTERPRETATION OF RESULTS

There is a bad correlation between free and invasive Qmax(1,2) and the systematic error shown by these two tools makes them not interchangeable. Theories proposed to explain this big gap includes that a catheter may provoke: a) diminution of the cross-sectional area of the urethra; b) a poor urethral-pelvic floor relaxation; and c) a urethra-bladder reflex leading to a poor detrusor contraction(1-3). Our results let us hypothesize that different urethras react variably to instrumentalization. Low resistance bladder outlets like in SUI patients seem to be more affected by the presence of the catheter, while patients with a presumed impaired urethral relaxation, like in voiding dysfunction, seem to be affected to a lesser extent.

CONCLUDING MESSAGE

Maximum flow rate in free and invasive measurement are not interchangeable, the latter is around 12 ml/sec lesser than the former. The presence of a urethral catheter importantly affects the measurement of urine maximum flow rate. This phenomenon varies among different kinds of patients.

FIGURE 1

Table 1: Clinical and demographic characteristics

Characteristic	
Patient	407 (100%)
Age (yr)	53 (15)
Diabetes	11.5%
Arterial Hypertension	28.3%
Pelvic Organ Prolapse	42 (10.3%)
Clinical group	
Voiding dysfunction	27 (6.6%)
Isolated Overactive Bladder-Urge incontinence	30 (7.4%)
Isolated Stress Urinary Incontinence	100 (24.6%)
Mixed Urinary Incontinence	251 (61.7%)
Incontinence Surgery	54 (13.3%)
Urodynamics	
Uroflowmetry Vol (ml)	313 (211)
Uroflowmetry Q_{max} (ml/s)	30 (16)
Uroflowmetry PVR (%)	24.8 (29)
Pressure-Flow Vol (ml)	426 (223)
Pressure-Flow Q_{max} (ml/s)	17 (13)
Pressure-Flow PVR (%)	7,8 (20)
ΔQ_{max} (ml/s)	12 (16)
Δ PVR (%)	10.9 (28.4)

Values are presented as percentage or medians and interquartile ranges.
Vol: Volume; Qmax: Maximum flow rate; PVR: Post-void residual. ΔQ_{max}: Maximum flow rate difference between groups.

FIGURE 2

Table 2: Comparison of Free and Invasive flowmetry between patients in different clinical groups according to the referral diagnosis/clinical suspicion.

	UF Q_{max} ml/sec	PF Q_{max} ml/sec	ΔQ_{max} ml/sec	p-value
Total 407	30 (16)	17 (13)	12 (16)	
Voiding Dysfunction (n= 27)	21 (13)	16 (13)	5 (18)	**0.004**
Isolated SUI (n=100)	34 (17)	15 (10)	17 (20)	**0.002**
Isolated OAB (n=30)	23.5 (25)	16 (13)	12 (21)	0.609
Anti-incontinence Surgery (n=54)	25 (15)	15 (12)	9 (17)	0.069
MUI (n=251)	30 (16)	18 (13)	11 (16)	0.142

Values are presented as medians and interquartile ranges.
UF: Uroflowmetry; FP: Pressure Flow; Vol: Volume; Qmax: Maximum flow rate; PVR: Post-void residual. ΔQmax: Maximum flow rate difference between groups.

Table 2: Comparison of Free and Invasive flowmetry between patients in different clinical groups according to the referral diagnosis/clinical suspicion.

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STATISTICAL PROCESS CONTROL AS A TOOL FOR THE ANALYSIS OF QUALITY CONTROL IN URODYNAMIC STUDY

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HYPOTHESIS / AIMS OF STUDY

To analyze the quality control in urodynamic study by using proportion control chart of statistical process control.

STUDY DESIGN, MATERIALS AND METHODS

15 urodynamic study (UDS) traces conducted at the Urodynamic center of our hospital were randomly selected from each month of 2020, with a total of 180 samples been included according to the including criteria. Statistical process control (SPC), a tool provided visualization to the problem of process management [1], was applied to analyze the incidence of all artifacts, which including non-standard zero setting, did not do the cough test, did not record all the UDS measurements, catheter displacement, and baseline drift. According to the study data and Shewart chart selecting criteria, we chose the proportion control chart (p-chart) with 3 standard deviations (3-sigma) control limits for further analysis. We calculated the Center line (CL), Lower Control Limit (LCL), which equal to CL-3-sigma, Upper Control Limit (UCL), which equal to CL + 3-sigma, of all artifacts incidence in UDS process. Then we did the stabilization process to get controlled quality control in UDS process.

RESULTS

We calculated the proportion of the incidence of all kinds of artifacts in each month, through p-chart calculation formula, we got the value of CL, UCL, and LCL in one year (Table 1). We set the value of LCL to zero when LCL had a negative value, since the proportion cannot be negative. The Zone A, B, C were divided in the p-chart according to 3-sigma limit rule. The Zone A is between the 2-sigma and the 3-sigma limit, the zone B is between the 2-sigma and 1-sigma limit, and the zone C is between the 1-sigma and the center line [2]. (Figure 1. a).

INTERPRETATION OF RESULTS

Our results showed that 8 data points were within the zone C, 11 data points were within the zone B, but an outlier was found in October (0.87) in the p-chart for all artifacts, which exceeded the UCL (0.69). This might be a result of special cause variation. After the value in October was removed, the p-chart showed a significant improvement in quality control as evidenced by all data points were within the zone A (Figure 1. b).

CONCLUDING MESSAGE

By using the p-chart, we found the total artifacts occurrence showed an outlier point above the UCL in October, which might indicate an abnormal quality control in October. Then we did further investigation, we found that in October 2020, our urodynamic center had accepted some candidates from other hospitals, for these candidates, they might have a lack of practical experience and knowledge of UDS. This indicated that attending recognized training would increase the ability to perform urodynamic examination [3]. SPC approach plays an important role in the evaluation of UDS process and guides us to find the cause of the bad behavior in process management, and it could be served as a predictive model to predict the future performance of UDS process. Any point outside of the control limits indicates something unusual (a special cause). A point below the LCL represents an opportunity to see if something positive happened to the process. However, further analysis with larger sample is still needed.

FIGURE 1

Table 1. Basic description of the incidence of all artifacts in the UDS process in 2020

Month	Number of cases	Number of artifacts	Proportion	UCL	LCL	CL
1		5	0.33			
2		6	0.4			
3	n=180	3	0.2			
4		3	0.2			
5	Male: 98	2	0.13			
6	Female: 82	4	0.27	0.69	0	0.33
7		6	0.4			
8	NBD: 42	4	0.27			
9	NNBD: 138	4	0.27			
10		13	0.87			
11		4	0.27			
12		5	0.33			

NBD: neurogenic bladder dysfunction; NNBD: non-neurogenic bladder dysfunction

UCL: Upper control limit; CL: Center line; LCL: Lower control limit

Table 1. Basic description of the incidence of all artifacts in the UDS process in 2020. NBD: neurogenic bladder dysfunction; NNBD: non-neurogenic bladder dysfunction UCL: Upper control limit; CL: Center line; LCL: Lower control limit

FIGURE 2

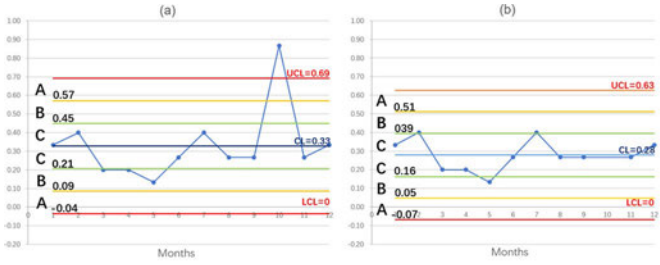

Figure 1. (a) p-chart for all artifacts. (b) p-chart for all artifacts after stabilization

UCL: Upper control limit; CL: Center line; LCL: Lower control limit

The zone A is between the 2-sigma and the 3-sigma limit, the zone B is between the 2-sigma and 1-sigma limit, and the zone C is between the 1-sigma and the center line.

Figure 1. (a) p-chart for all artifacts. (b) p-chart for all artifacts after stabilization. The zone A is between the 2-sigma and the 3-sigma limit, the B is between the 2-sigma and 1-sigma limit, and the C is between the 1-sigma and the center line

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COMPARISON OF SIMULTANEOUS WATER AND AIR PRESSURE MEASUREMENTS DURING THE VOIDING PHASE OF INVASIVE URODYNAMICS IN MEN

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HYPOTHESIS / AIMS OF STUDY

This study aimed to compare pressure measurements made simultaneously via air and water during urodynamic studies (UDS), by repurposing the air-charged catheter (ACC) filling channel to measure pressure as a water-filled catheter. To assess variability due to the use of two different channels, the same comparison was made in a control group where dual water pressure measurements were made in water filled catheters (WFC). The diagnostic implications of any pressure measurement differences were also assessed. We believe this to be the first study comparing pressures measured via both air and water simultaneously in one catheter that is independent from the manufacturer of T-DOC ACCs.

STUDY DESIGN, MATERIALS AND METHODS

Male patients, over the age of 16, with lower urinary tract symptoms who had been referred for urodynamic investigation were recruited prospectively in a single centre. Patients were split into two groups: one group using ACCs (comparing air and water pressure measurements), and the other group using WFCs (comparing dual water pressure measurements). All urodynamic tests were performed by the first author and according to ICS Good Urodynamic Practice (GUP) guidelines [1].

In both groups the filling channel of the catheters was repurposed to measure pressure via water (the water reference pressure) during the voiding phase. The filling channel of the bladder catheter was connected to a three-way tap to enable switching between the saline pump for filling and the transducer for pressure measurement during voiding. This meant dual pressures in the bladder were only measured during voiding. Dual pressures in the rectum were measured throughout both filling and voiding.

The water-filled rectal catheter had an open fingercot covering the measurement and filling ports to prevent faecal blocking and adhere to ICS GUP guidelines [1]. This was not possible for the rectal catheter in the ACC group due to potential interference with the measurement balloon. It was acknowledged that this could affect the water reference pressure measurement in the rectum. Therefore, in order to try and prevent faecal blocking, the ACC filling channel was flushed prior to voiding. Additionally, all abdominal pressure traces were screened by two independent assessors for validity in order to exclude those with poor pressure response indicative of blockage. This exercise was blinded with regards to intra-vesical and detrusor pressure, and to group allocation, to try and minimise bias.

In each catheter, the measurement channel pressure (air or water) was compared with the filling channel water reference pressure at maximum flow using paired- sample t-tests, correlation (Spearman's rank analysis), and Bland-Altman analyses. The root mean square difference (RMSD) between the measurement channel and filling channel was calculated for intra-abdominal (Pabd), intra-vesical (Pves), and detrusor (Pdet) pressures throughout detrusor contraction. Differences in diagnoses between the paired pressure measurements were assessed by plotting the detrusor pressure at maximum flow (PdetQmax) for each patient on a LINPURR/ICS nomogram.

RESULTS

Seventy-five patients were recruited to the study. Fifteen patients were excluded, leaving sixty studies for analysis (30 patients in the ACC group, and 30 patients in the WFC group). Patients were excluded for the following reasons: unable to void (5), unable to catheterise (4), water-filled rectal catheter not covered by finger cot in error (2), excluded following Pabd validity assessment (2), tap not turned to measure pressure via water prior to voiding in error (1), bladder catheter expelled (1).

All paired pressure measurements at maximum flow were strongly correlated (rho = > 0.97) apart from air and water in ACCs measuring Pabd (rho = 0.79). The mean difference (measuring channel minus filling channel water reference pressure) of the Pabd measurement in ACCs was 5.7 cmH2O with a standard deviation of 7.8 cmH2O ($p = 0.0003$), compared to 0.6 cmH2O with a standard deviation of 2.3 cmH2O ($p = 0.1$) in WFCs. The mean difference of the Pves measurement in ACCs was -1.6 cmH2O with a standard deviation of 4.8 cmH2O ($p = 0.09$), compared to 1.3 cmH2O with a standard deviation of 2.0 cmH2O ($p = 0.002$) in WFCs.

Figure 1 displays example urodynamic traces during the voiding phase with the smallest and largest Pdet RMSD in each group. In the ACC group, the mean RMSD between the measuring (air) and filling (water) channels during the voiding detrusor contraction for Pabd, Pves and Pdet was 7.4, 4.8 and 9.3 cmH2O respectively. In the WFC group this was 2.0, 1.3 and 2.7 cmH2O.

Figure 2 shows PdetQmax plotted against Qmax for each patient on overlaid ICS and LINPURR nomograms. Two measurements are plotted for each patient, one using PdetQmax from the measuring channel pressure and the other using PdetQmax from the filling channel pressure. There are 10 diagnoses that cross one obstruction boundary between the paired air and water pressure measurements in ACCs, and six that cross a bladder contractility boundary. This compares to only two patients crossing an obstruction boundary between the paired water and water pressure measurements in WFCs, and one patient crossing a contractility boundary.

INTERPRETATION OF RESULTS

The main finding of this study was the significantly higher Pabd measured via air compared to water in the rectum. This could be attributed to a difference between the heights of the ACC tip and the external WFC transducer. If the ACC tip is lower than the transducer, which is feasible since the distal rectum tilts backwards, the pressure measured via air will be higher. Studies comparing ACCs and WFCs in females using separate ACCs and WFCs made similar findings [2] [3]. However, this does not address the large range of pressure differences measured in ACCs which was approximately ± 20 cmH2O.

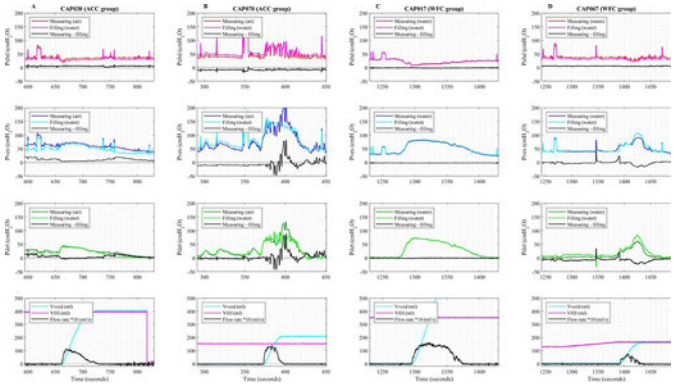
The standard deviation of the intravesical pressure difference was also much larger in ACCs compared to WFCs. The observed differences, which ranged between approximately ± 10 cmH2O may result from height differences between the WFC external transducer and ACC tip. In most cases a higher Pves was measured via water than air, which may reflect a tendency of the more rigid T-DOC ACC to point upwards in the bladder, above the external transducer.

Figure 2 illustrates the diagnostic implications of using air instead of water to measure pressures during UDS. There are 10 diagnoses that cross an obstruction boundary in the ACC group, and six that cross a bladder contractility boundary. These differences in diagnoses mean that ACCs and WFCs cannot be used interchangeably because of the effects the different technology could have on diagnosis, and therefore the clinical management of patients. Consideration should be given to whether revision of normal values and nomograms for use with ACCs would allow the technology to be used more reliably in male patients undergoing UDS.

CONCLUDING MESSAGE

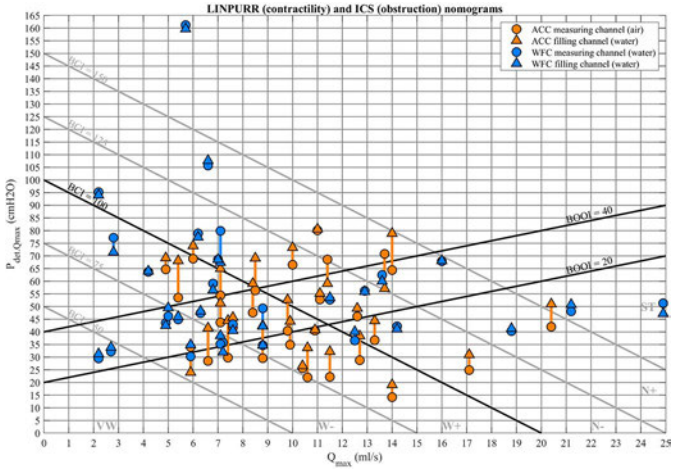
ACCs cannot be used interchangeably with WFCs for UDS in male patients due to the impact of pressure differences on urodynamic diagnoses. The largest contribution to this effect is differences between air and water measurement of Pabd. Small diagnostic differences were also observed with dual water pressure measurements in water-filled catheters.

FIGURE 1



Voiding phase urodynamic traces showing the best and worst Pdet agreement during detrusor contraction in each group.

FIGURE 2



PdetQmax plotted against Qmax for each patient on the ICS and LINPURR nomograms.

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Funding None **Clinical Trial** No **Subjects** Human **Ethics Committee** Health and Social Care Research **Ethics Committee** B **Helsinki** Yes **Informed Consent** Yes

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SESSION 9 - FEMALE LOWER URINARY TRACT SYMPTOMS

Abstracts 145-156
14:35 - 16:05, Hall K
Chair: Dr Anna Rosamilia (Australia)

145 | www.ics.org/2022/abstract/145

INCREASED LEVELS OF URINE METABOLITES FOUND IN A FEMALE AGING POPULATION WITH OVERACTIVE BLADDER SYNDROME

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HYPOTHESIS / AIMS OF STUDY

Urine storage and release by the bladder are controlled by the peripheral and central nervous systems. [1] Neurotrophins are a class of growth factors that were originally found in the nervous system where they promote growth and survival of neurons [2]. Nerve ending activity is regulated by neurotrophins, among other brain-derived neurotrophic factor (BDNF). The latter is essential in neuroregeneration and its dysregulation contributes to pathologies of the urinary tract. [3] BDNF has been proposed to be a marker for overactive bladder syndrome (OAB). The aim of this study is to examine the levels of proBDNF, BDNF and associated proteins in the urine of a female aging population. We hypothesized that urinary proBDNF/BDNF ratio is unbalanced in aging women with OAB compared to control subjects from the same age group.

STUDY DESIGN, MATERIALS AND METHODS

In this cohort study, we analyzed urine samples from control and OAB patients to compare the relative amounts of BDNF and proBDNF, along with the proteases involved in the maturation and degradation of BDNF. Urine and blood samples from 20 controls and 20 OAB female patients between the ages of 50 to 80 years were obtained with validated questionnaires. ProBDNF and BDNF were measured using specific ELISA kits (Biosensis). MicroRNAs involved in the control of proBDNF synthesis were measured by RT-qPCR after polyadenylation. Activity of matrix metallopeptidase-9 (MMP-9) was measured using an enzymatic kit. Sortilin and Cortisol were also measured using specific ELISA kits. Results were adjusted with creatinine levels. Data were further adjusted for age, renal function and insulin resistance.

RESULTS

BDNF/creatinine levels were not different in the urine of controls versus OAB patients. ProBDNF/creatinine measures were lower in the OAB population. The ratio BDNF/proBDNF was therefore higher (0.051 ± 0.0078 vs 0.135 ± 0.027) in the OAB population ($P < 0.005$). (Figure 1) MicroRNAs known to control the translation of proBDNF mRNA by binding its 3'UTR sequence, namely MiR-26b-5p, Mir-26-1a-5p, MiR-10a-5p and MiR-103a-3p were not expressed differently between control and OAB patients. Other miRNAs, MiR-15b-5p, MiR-142-3p and MiR-103a-3p that control proBDNF expression through downstream or upstream pathways were not affected as well. On the other hand, enzymatic activity of MMP-9, one of the main enzyme converting proBDNF to BDNF was higher in the OAB group. The microRNA MiR-491-5p, that negatively controls MMP-9 expression was in accordance potently decreased in the OAB group. There was no statistical significance between the levels of sortilin or cortisol measurements found in the urine of controls when compared to OAB patients ($P > 0.005$).

INTERPRETATION OF RESULTS

These results suggest that the ratio BDNF/proBDNF might be a better indicator, or potential biomarker of OAB, than BDNF alone. The decrease in proBDNF levels could be the result of the enhanced activity of MMP-9 activity rather than transcription or translation control, highlighting the role or proteases in a bladder pathology such as OAB.

CONCLUDING MESSAGE

OAB related to aging can be clinically correlated to the BDNF proteolysis imbalance, rendering it as a potential biomarker and therapeutic target. Albeit, concomitant age-related factors, such as polypharmacy and presence of chronic disease, may contribute to the relationship between BDNF and aging-related OAB phenotype.

FIGURE 1

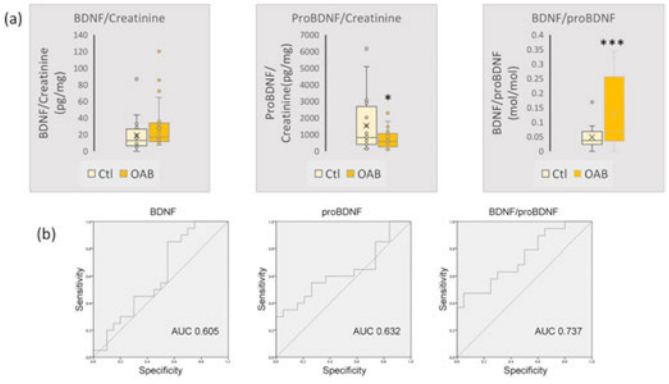

Figure 1. (a) Levels of BDNF/ Creatinine (left), proBDNF/ Creatinine (medium) and BDNF/proBDNF ratio in urine samples (control n=20, OAB n=20). **(b)** ROC curves analysis of BDNF, proBDNF and ratio. Curves were plotted for the specificity and sensitivity of BNDF/creatinine, proBDNF/creatinine and ratio BDNF/proBDNF. Area under curve (AUC) is indicated on each graph. Ratio BDNF/proBDNF displayed the higher AUC. Student t-test (*P<0.05, ***P<0.005).

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Funding Canadian Urology Association, Quebec NetwMedical-Biomedical Research **Ethics Committee** (REC) of the Integrated Health and Social Services University Network for West-Central Montreal (IRB: 2016-328, 15-022ork on aging **Clinical Trial** No **Subjects** Human **Ethics Committee** Medical-Biomedical Research **Ethics Committee** (REC) of the Integrated Health and Social Services University Network for West-Central Montreal (IRB: 2016-328, 15-022) **Helsinki** Yes **Informed Consent** Yes

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A MULTIDISCIPLINARY APPROACH TO MANAGING PATIENTS WITH RECURRENT URINARY TRACT INFECTIONS – INITIAL EXPERIENCE FROM OUR COMPLEX UTI CLINIC

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HYPOTHESIS / AIMS OF STUDY
Urinary tract infections (UTIs) are the most common outpatient infections that are referred to the urologist and it represent a substantial financial burden on the health care system.

According to ICS, Urinary Tract Infection is defined as the finding of microbiological evidence of significant bacteriuria and pyuria usually accompanied by symptoms such as increased bladder sensation, urgency, frequency, dysuria, urgency urinary incontinence, and/or pain in the lower urinary tract (1).

In April 2021, we established a multidisciplinary complex UTI clinic in collaboration with specialist nurses and microbiologists with an aim of improving these patients' symptoms and quality of life (QoL) with a holistic approach.

STUDY DESIGN, MATERIALS AND METHODS
A prospectively maintained database of all 83 patients {(median age 54 years (16-85 year) and (M: F of 1:13)} who were referred to our clinic, within a one-year period were reviewed. Patients' demographics, significant co-morbidities, number of infections per year, urine culture result (causative bacterial organism and antibiotic sensitivities), investigations performed, and treatment outcome were recorded. Pre-treatment QoL and post-treatment PGI-I (Patient global impression of improvement) Scale were measured. All clinics were supported by specialist nurses and microbiologists and a complex UTI multidisciplinary team meeting was arranged on monthly basis.

RESULTS
Outcomes are detailed in table 1.

A total number of 83 patients were referred to our complex UTI clinic either by General Practitioners (GP) or by fellow Urologist, our record showed a distribution of male: 6 (7.3%) and female: 77 (92.7%) Age distribution showed a minimum age of 17 years and a maximum age of 85years. The mean age was 52.42 with a median of 54 years. Escherichia Coli (51.8%) was identified as the most common causative organism and this is consistent to the findings in other studies. Subgroup of our patients was further investigated with USS renal tract, CT Urogram, and cystoscopy to rule out underlying pathology. Abnormal renal USS, CTU, and cystoscopy were reported in 8.3%, 9.5%, and 8.3% respectively including diagnosis of bladder (1) and renal cancer (2).

All patients received verbal and written information on general cystitis prevention measures. 13 (15.6%) patients did not respond to oral treatment and hence received intravesical treatment. Pre-treatment 50% of patients report a significant impact on their QoL. Over 80% of patients had good improvement on the PGI-I scale after the treatment

INTERPRETATION OF RESULTS
In our complex UTI clinic, most of our patients were females and they account for 92.7% of patients. Significant comorbidities were noted in 29 patients (36%) and these co-morbidities were significantly linked to the recurrent UTIs in these patients. On evaluation of urine samples obtained, Escherichia coli was the commonest organism isolated and Nitrofurantoin was the most sensitive antibiotic. Patients seen in our clinic were discussed in the complex UTI clinic MDT and the appropriate treatment plan was agreed and this was discussed with the patient either via a face to face or a telephone clinic appointment. All our patients were educated on general cystitis preventive measures. Other treatment used were low dose prophylactic antibiotics based on urine culture and sensitivity result, methenamine hippurate and estrogen cream for women with atrophic vaginitis. Patients who didn't improve on these initial treatments either received glucose aminoglycans (GAG) replacement therapy or intravesical Gentamicin based on MDT recommendation.

Overall, significant improvement in symptoms and quality of life was observed for the patients managed at complex UTI clinic using a multidisciplinary approach which involved urologist, specialist nurses and microbiologist.

CONCLUDING MESSAGE
Urinary tract infections are undoubtedly one of the commonest bacterial infection affecting humans, causing a huge financial burden the health care system and the tremendous mental and social effects it has on these patients hence a negative impact on their quality of life (QoL).

The main stay of treatment over the years has been the use of antibiotics and this has been challenged by the rising cases of antibiotics resistance by these organisms. Our initial experience has shown that UTI can be successfully managed with a systematic and multidisciplinary approach that can not only resolve infection but can also significantly improve patients' QoL.

FIGURE 1

Table 1:

Patient Demographic	Total number of patients (N): 83 Gender: Male n: 6 (7.3%); Female n: 77 (92.7%) Age distribution Mean: 52.42 Median: 54 Minimum age:17 Maximum age: 85 (SD: 19.4) Significant comorbidities: 29 (36%) Post-menopausal females: 37 (44.5%)
Mode of referral	GP:44 (53%) Specialist: 39 (47%)
Frequency of UTI	<3 episodes in 12months: 7 (8%) > 3 episode in 12 months: 76 (92%)
Presentation[1]	Frequency: 80 (96%) Urgency: 68(82%) Nocturia: 3(3.6%) Dysuria: 18 (21.6%) Haematuria: 6 (7.2%) Abdominal pain: 12 (14.3%) Flank pain: 4 (4.8%)
Hospital admission with UTI	Yes: 4 (4.8%) No: 79 (95.2%)
Causative organism[2]	Escherichia Coli: 43 (51.8%) Klebsiella : (10) 12.2% E. fecalis: 5 (6%) Pseudomonas: 4 (4.8%) Others (including mixed growth): 13.4% Culture negative: 9 (10.8%)
Antibiotic sensitivities[2]	Nitrofurantoin:93% Cefalexin: 86% Trimethoprim:78% Co.Amoxiclav : 71% Amoxicillin: 38%
Investigation[3]	Abnormal findings Flexible cystoscopy: 7 (8.4%) Renal USS:7 (8.4%) CT Urogram: 8 (9.6%)
Treatment received before referral	Cystitis preventive measures: 11 (13.1%) Antibiotics: 83 (100%) Methanamine hippurate n: 5 (6%) Cranberry Juice n: 3 (3.6%) D Mannose n: 4(4.8%)
Treatment given at UTI clinic[4]	Cystitis preventive measure: 83 (100%) Low dose Antibiotics: 50 (60%) Methenamine hippurate: 31 (37%) Vaginal estrogen cream: 23 (28%) CISC: 13(15.5%) Intravesical gentamicin: 7 (8.4%) Intravesical GAG replacement therapy: 6 (7.2%)
Treatment response	UTI resolved at completion of treatment Yes: 48 (57.8%) Ongoing treatment: 35(42.2%)[5]
Pre- treatment impact on quality of life (QoL)	Significant: 42 (50.6%) Moderate: 12 (14.5%) Minimal: 29 (34.9%)
Patient global impression of improvement (PGI-I)	PGI-I 5 (Good improvement): 70 (84.3%) PGI-I 4 (Some improvement): 11 (13.3%) PGI-I 3 (No improvement): 2 (2.4%)

[1] Most patients had more than one symptom at presentation
[2]Some patients had more than one organism on urine culture result.
[3] Post -menopausal women had flexible cystoscopy and imaging done while young patients had investigations done if indicated e.g. Flank pain, haematuria, suprapubic pain or persistent UTI
[4]Patients had a combination of more than one treatment.
[5] This includes patient awaiting intravesical instillations

Table illustrating the demographics and outcome of patients in our complex UTI clinic

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COMPARISON OF POSTPARTUM POSTVOID VOLUMES AFTER VAGINAL DELIVERY AND CAESAREAN SECTION: A PROSPECTIVE PILOT-STUDY

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HYPOTHESIS / AIMS OF STUDY
Postvoid residual volumes (PVRV) in the postpartum period are poorly studied and a cut-off value to diagnose postpartum urinary retention (PPUR) is not well-defined. Most studies and guidelines use a PVRV of 150 ml to diagnose PPUR. [1] Asymptomatic patients are classified as “covert” PPUR, and those with symptoms of incomplete voiding as “overt” PPUR. One recent study has shown that mean PVRV after vaginal delivery might be higher than the cut-off of 150 ml. [2] To this date, no study has compared the distributions of PVRV after vaginal delivery with PVRV after cesarean section.

This study aims to investigate the distribution of PVRV in postpartum women and to compare PVRV after vaginal delivery and cesarean section.

STUDY DESIGN, MATERIALS AND METHODS
This was a prospective observational study in a tertiary academic hospital about postvoid residual volumes after delivery. Inclusion criteria: age ≥ 18 years of age at date of delivery, delivery at the study site, and written informed consent. Exclusion criteria: lack of consent and “overt” PPUR.

All measurements were done in the first 24 hours after delivery or the removal of an indwelling catheters. Measurements were performed by bladder scan and/or transabdominal ultrasound in the 15 minutes after micturition. Those with PVRV ≥ 150 ml but normal micturition quantities (at least 200 ml), serial ultrasound scans were proposed during the hospital stay.

Women were asked to answer the section about bladder function of the adapted version of the German pelvic floor questionnaire to evaluate bladder symptoms in the four weeks prior to delivery. [3]

Descriptive statistics were performed using contingency tables with absolute and relative distribution for categorial variable with mean and standard deviation or median and interquartile ranges for continuous variables. Secondary endpoints were analyzed using Chi-Square-test/Fisher-exact-test (categorial variables) and Mann-Whitney U-test/Kruskal-Wallis-test (continuous variables).

Four arbitrary cut-offs to investigate risk factors were chosen prior to analysis: 150 ml (cut-off for PPUR), 250 ml (cut-off in a recent study [2]), the 75th percentile and the 95th percentile of PVRV. Risk factors were calculated using univariate and multivariate regression analysis. Associations between potential predictors and outcome are reported as odds ratios with 95% confidence intervals.

RESULTS
A total of 105 patients were included in the study with 57 in the vaginal delivery-group and 48 in the cesarean section group. Seven women (7%) in the vaginal delivery group developed overt PPUR and were therefore not included in the final analysis. No differences for age, BMI and parity were found between the groups.

Mean postpartum postvoid residual volume was 153 ml, and no differences between both groups were found (173 vs 133 ml; $p = 0.15$). The 75th percentile was 211 ml and the 95th percentile 464 ml, respectively. In total, 39% of women (39/98) had PVRV ≥ 150 ml and 21% (21/98) even ≥ 250 ml. In women with vaginal delivery 44% (22/50) had PVRV > 150 ml, and in women with cesarean section 35% (17/48) had PVRV ≥ 150 ml ($p = 0.39$). (see fig. 1)

Incomplete voiding was significantly associated with PVRV above the four cut-offs ($p = 0.008$ for PVRV ≥ 150ml, and $p < 0.001$ for PVRV ≥ 250ml, ≥75th percentile, and ≥ 95th percentile, resp.). Nevertheless, 25% of all women with complaints of incomplete voiding had PVRV ≤ 150 ml. The other 75% had mean micturition volumes of 474 ml, showing no difference to women without voiding difficulties. In the follow-up of the 39 women with PVRV ≥ 150 ml, 15 women were available for control scans, with 40% having PVRV below 150 ml at the second or third scan. No patient had symptomatic urinary retention at hospital discharge and no complications due to increased PVRV were found.

In multivariate analysis, no risk factors for any of the PVRV cut-offs could be identified.

58% of all participants answered the German pelvic floor questionnaire. Women with a reduced quality of life and those who suffered from bladder symptoms prior to delivery had significantly higher scores (3.2 vs 1.3; $p < 0.001$ and 3.0 vs 1.0; $p < 0.001$, resp.). No association was found between these two groups and increased PVRV or feeling of incomplete voiding after delivery. Prior to delivery, 23% of respondents complained of incomplete voiding, with only three of these (23%) having a persistence of symptoms after delivery ($p = 0.09$) with only one having presented a PVRV ≥ 150 ml. No association was found between women who presented subjective incomplete voiding prior to delivery and increased PVRV or subjective incomplete voiding after delivery, respectively.

INTERPRETATION OF RESULTS
In this study, first postpartum postvoid residual volumes did not seem to differ between the two types of delivery. Nevertheless, after vaginal delivery, almost half of the women had PVRV ≥ 150 ml. Even after cesarean section, more than a third had PVRV ≥ 150 ml. While incomplete voiding is associated with increased PVRV, most women had still high micturition volumes. Additionally, most women normalize their PVRV before hospital discharge without the need for any intervention. Still, 7% of all women had overt PPUR with an impossibility to void and had to be excluded from the study.

Like another study group, we found mean postpartum PVRV to be ≥ 150 ml. [2] In our study, we also investigated women after cesarean section. Based on the results of the two studies, it might be advisable to re-evaluate the current cut-off for covert PPUR. Evidently, our study does not show an absence of long term problems, but we showed that most women with increased PVRV normalize their PVRV during the following days, and this makes long term consequences rather unlikely.

No risk factors were identified but this could be due to the number of participants in each group. Although incomplete voiding is not infrequent before delivery, we found no association with voiding difficulties in the postpartum period. Incomplete voiding was well associated with PVRV ≥ 150 ml or more and might be sufficient to identify patients at risk of increased PVRV.

CONCLUDING MESSAGE
The current cut-off value of 150 ml to define postpartum urinary retention is lower than the mean postvoid residual volume in this study. This is the second study that shows mean postpartum PVRV ≥ 150 ml. [2] To avoid unnecessary treatments in postpartum women, a higher cut-off value than 150 ml to diagnose PPUR seems advisable. Most women’s PVRV return to normal before hospital discharge without any intervention.

FIGURE 1

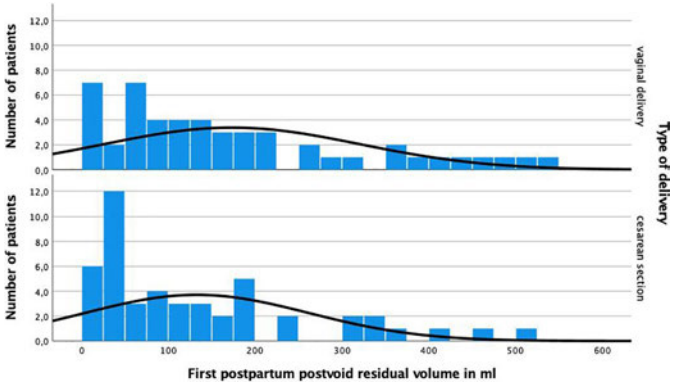

Fig. 1: Postvoid residual volume in women with vaginal delivery (top) and cesarean section (bottom).

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IT IS LIKELY THAT TWO PARAMETERS, WITH DIFFERENT AIMS, ARE NEEDED TO DETERMINE DETRUSOR VOIDING CONTRACTION STRENGTH IN FEMALE PATIENTS.

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HYPOTHESIS / AIMS OF STUDY
Many adult women have lower urinary tract (LUT) symptoms and dysfunction. Their incidence of bladder outflow obstruction (BOO) is however low. Underactive detrusor voiding contraction (DVC) is equally relevant in both sexes. Deterioration of the detrusor muscle contractile quality and quantity plays a role regarding to LUTS and advancing age.

An objective and graded diagnosis of the pathophysiology of (detrusor) voiding dysfunction and of underactive DVC can be useful when ineffective voiding (reduced voiding percentage (Void%) (PVR)) or prolonged voiding is present. This will become especially relevant when a specific treatment for DU is available. A second aim to quantify DVC in women however, is prediction of ability to void effectively after a (potentially somewhat) obstructing intervention for urinary incontinence. Based on current evidence it is undetermined whether one or more of the known parameters are suitable for both aims.

The quantification of detrusor contraction force in men is, based on the currently known physiology of micturition, neither overly complex nor very controversial. In women on the other hand, the micturition usually has a higher flowrate, which means a much faster detrusor muscle contraction shortening speed. Determining the detrusor force at such a high shortening speed is less straightforward and clinical cutoffs are more difficult to obtain.

Standard parameters for DVC force based on pressure flow studies (PFS) are Watts-factor (WF), and BCI, which are especially satisfactory for analysis of men. WFmax and BCI do not give significantly different results per patient in men, especially not if there is some bladder outflow obstruction. These parameters seem however less applicable and are less validated in women. Several clinical studies find a moderate association with symptoms and or ineffective micturition when using the standard parameters e.g., diagnosing DU. Some research suggests an adjustment to the BCI for women from BCI = pdetQmax + 5Qmax to PIP(1) = pdetQmax + Qmax (or DECO when PIP/100 is used) to obtain a better association with stop flow testing. (1,2)

We tested in a large database which of the PFS –analysis parameters was best associated with ineffective voiding; with high PVR and low Void%, and whether or not the alternative BCI, PIP(1) is a better quantifier of detrusor voiding dysfunction in women.

STUDY DESIGN, MATERIALS AND METHODS
We analyzed 1332 PFS of women with signs and symptoms of LUTD without relevant neurologic abnormalities and excluded 221 measurements of women that voided <100mL or >800mL and or had a PVR of >500mL with the PFS. Indication for UDS has been SUI-syndrome(8%) urgency/ OAB syndrome(28%) (bladder/pelvic pain/recurrent UTI(31%) voiding symptoms(9%) Mixed/unspecific UI(20%) enuresis/pre-kidney transplant/ other(4%).

1111 women had a mean age of 50,2y (16-91) and voided 363mL (101-782mL) with PVR 41mL (0-492mL). Mean Qmax was 19,9mL/s (2,5-71,7mL/s) with a mean PdetQmax of 26,3cmH2O (-9,1-92,5). PVR result was very skewed with a median of 0mL; 729 (66%) had void% 100.

RESULTS
27 (2,4%) women had BOO and 393 (35,4%) had DU when BCI<100 is used. PVR correlated very weakly negative with age: pearson R .182 (p.000), negative with contraction; BCI: R -.318 (.000), WFmax R -.232 (.000) and weakly positive with BOOI: R .234 (.000) and URA R .210 (.000).

Figure 1 shows PFS results (PdetQmax/Qmax) of all patients in the PFS-plot: The patients with a voiding efficacy <80% are marked♦ and present mainly in the (left lower) low flow -low pressure (=DU) area. The majority of the patients in this area had effective voiding (66,1%). BOO(I >40) is rare (right side area) and especially patients with BOO and DU had (8/11) PVR.

Women with ineffective voiding were older (55,5y vs 47,8y p.000) voided less; (279mL vs 381mL p.000) and had lower Qmax (13,6 vs 21,4mL/s p.000).

The ROC Curve analysis (fig 2.1) shows that Wmax, Qmax and BCI (left upper corner) are superior to predict effective micturition and outflow resistance parameters have a slightly less (and negative) predicting value towards PVR.

Adapting BCI to PIP(1) (second (ROC 2.2) (dotted line) has a negative effect on predictive value for PVR. (Adapting BCI to PdetQmax + 10Qmax equals the original BCI). The effectivity of voiding of women is predominantly affected by contraction (emptying) velocity (Qmax).

INTERPRETATION OF RESULTS
Detrusor voiding contraction of women happens at higher velocity than men. Contraction velocity (flowrate) is more relevant than force (pressure) in women when compared to men.

The parameters WF, Qmax and BCI show an acceptable association with ineffective voiding in women and can be used for the diagnosis and grading of detrusor underactivity. BOO is rare in women but parameters that quantify BOO (BOOI and URA) but also associate with ineffective voiding, and are useful to exclude DU as a cause of PVR and ineffective voiding in women.

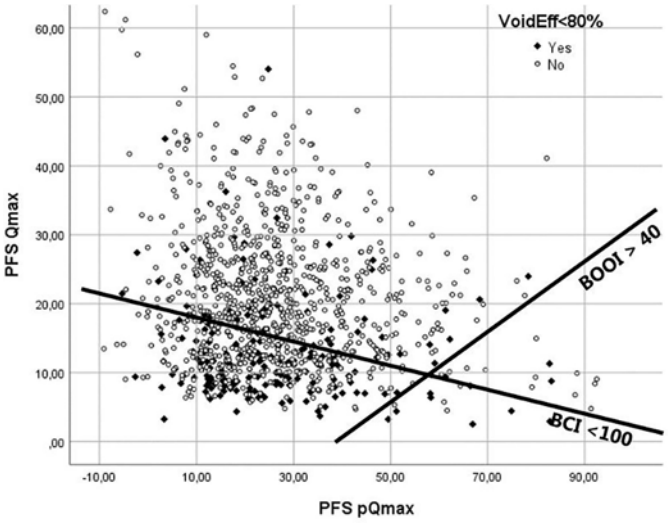
If BCI is adapted to PIP(1) and, the sum of pressure and flow thus includes less weight to the flow -value, its validity to associate with ineffective voiding reduces. If PIP(1) associates better with maximum of isovolumic contraction (stop flow -test) then PIP(1) may be a parameter that is superior in the ability to predict voiding after anti -incontinence surgery. This should be prospectively tested.

CONCLUDING MESSAGE
A large study analyzing PFS results, demonstrates that the contraction parameters Qmax, WFmax and BCI associate with ineffective voiding in women. Age and outflow obstruction are negatively associated. These contraction parameters are useful to diagnose and grade detrusor underactivity.

PIP(1) is an adaption of BCI and associates less with ineffective voiding than BCI. PIP(1) however, may be more useful (than BCI) to predict the ability to void after anti incontinence surgery but this should be prospectively tested.

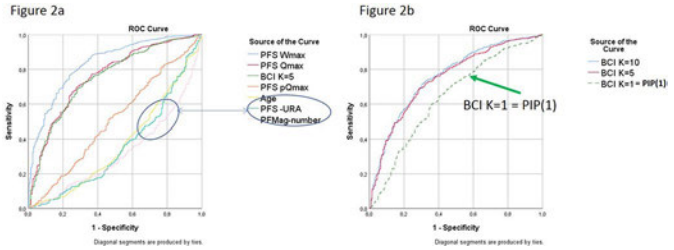
Analysis of a very large set of voidings of women, with the full range of symptoms of dysfunction, has learned the relevance and validity of the diverse pressure flow study parameters. On theoretical clinical epidemiological grounds BCI and PIP(1) may have different clinical diagnostic relevance, related to the two aims of assessing detrusor voiding contraction strength in women.

FIGURE 1



PFS results (PdetQmax/Qmax plot) of all patients included. Black diamonds indicate voided% <80.

FIGURE 2



ROC Curve analysis: 2a Standard PFS parameters and 2b Standard BCI and adapted BCI (and PIP(1)); both graphs: versus prediction of ineffective voiding

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BOTULINUM TOXIN INJECTIONS INTO THE URETHRAL SPHINCTER IN WOMEN WITH CHRONIC URINARY RETENTION DUE TO FOWLER'S SYNDROME: A TWO YEAR STUDY DURING THE COVID PANDEMIC

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HYPOTHESIS / AIMS OF STUDY
Chronic urinary retention in young women is uncommon and Fowler's Syndrome typically presents as painless urinary retention, characterised by a primary disorder of urethral sphincter relaxation typically associated with an elevated urethral pressure profile and abnormal findings in urethral sphincter EMG. Sacral neuromodulation is effective in treating urinary retention in nearly 70% of women with Fowler's syndrome, however this treatment may not be feasible for all patients because of concomitant medical co-morbidities, patient choice, or in health care settings with limited financial resources. A recent clinical trial demonstrated that EMG guided transperineal injections of botulinum toxin into the external urethral sphincter was an effective and safe outpatient-based alternative for managing urinary retention [1].

The aim of this study was to prospectively evaluate the delivery of botulinum toxin treatment for managing urinary retention in women with Fowler's syndrome in a real-world setting during the COVID pandemic and to evaluate efficacy, safety and side-effect profiles.

STUDY DESIGN, MATERIALS AND METHODS
A service offering botulinum toxin injections into the urethral sphincter for managing urinary retention in women with Fowler's syndrome was set up in 2011. Due to the COVID pandemic, several services were closed in 2020 however the sphincter botulinum toxin clinic was prioritised and, exceptionally, kept open so that women could continue to receive this treatment to avoid going into urinary retention and falling back on catheterisation. Women meeting the criteria for Fowler's Syndrome, (abnormal concentric needle EMG of the striated urethral sphincter and/or abnormally elevated urethral pressure profile) were offered this treatment in case they were not suitable for sacral neuromodulation. OnabotulinumtoxinA was injected into the external urethral sphincter as an outpatient procedure. 1 mL 2% lidocaine was injected on either side of the external urethral meatus initially, then 100 U onabotulinumtoxinA dissolved in 2 mL saline was injected into the striated urethral sphincter transperineally.

Women were followed up after 4 weeks through a telephone consultation, and they contacted the department for repeat injections when the effects began to diminish, after an embargo period of 12 weeks.

Efficacy and side effects were assessed at baseline and 4 weeks after the injection using a standard battery of questions and questionnaires (International Prostate Symptom Score (IPSS) and Patient Perception of Intensity of Urgency score).

RESULTS
Women who were not required to shield and were deemed to be at low risk for developing COVID-related complications were seen in designated parts of the hospital where adequate precautions could be taken signed off by the Trust Infection Control Team ("green" COVID pathway). During this period, 17 women diagnosed with Fowler's Syndrome (mean age 35.0 ± 12.4 years) received 100U botulinum toxin injected EMG-guided into the external urethral sphincter as an out-patient procedure between 1st January 2020 and 31st December 2021. 14 (87.5%) women were dependent on intermittent self-catheterisation (ISC) and 2 (12.5%) had voiding difficulties but were not ISC dependent. 48 injections were administered and 12 women (71%) reported improvements in urinary symptoms across 37/48 injections (77% of injections). 9 women (53%) received >1 injection [median 4 injections/patient, median interval 3.5 months].

The improvements observed by women who responded to the injections (n = 37 injections in 12 women) are summarised in Figure 1.

Amongst women requiring to recommence intermittent self-catheterisation, the mean time to requiring ISC was 2.95 ± 0.41 months [median 3 months].

Side effects reported were relatively mild:

- transient stress incontinence (n = 3), resolving within 2 weeks
- short-lasting pain and bleeding (n = 3), resolving within 24 hours
- Increased pre-existing urinary urgency incontinence (n = 2)

Compared between baseline and 4 weeks post-injection, there was an improvement in mean International Prostate Symptom Score (IPSS) score from 20.5 to 12.83 and improvement in Patient Perception of Intensity of Urgency score from 0.87 to 2.03 ($p < 0.05$) (n = 6).

INTERPRETATION OF RESULTS
The results of this audit suggest that it has been feasible to continue offering sphincter botulinum toxin injections for the management of chronic urinary retention due to Fowler's Syndrome during the pandemic. None of the women had developed COVID when evaluated at 4 weeks after injection. Treatment effects could be accurately assessed over the phone at four weeks, however questionnaire data was not easy to collect.

71% of women reported benefit to treatment, with a duration of effect that was expected for striated muscles (median 3 months). The results suggest that the most common improvement was a reduction in ISC requirement, and 32% of respondents became free of catheterisation. Other benefits in those who continued to catheterise included a greater ease and reduced pain with catheterisation. Perception of bladder fullness was also found to improve as well. Side effects associated with botulinum toxin were uncommon, and stress urinary incontinence was reported by only a small number of patients and occurred transiently. The outcomes in this real-world support the findings from an earlier clinical trial in women with Fowler's Syndrome [1] and in adults with dysfunctional voiding [2].

CONCLUDING MESSAGE
The results of this study suggests that transperineal EMG-guided minimally-invasive urethral sphincter botulinum toxin injections administered during the COVID pandemic significantly improved urinary symptoms amongst women with urinary retention due to Fowler's syndrome and was well tolerated.

FIGURE 1

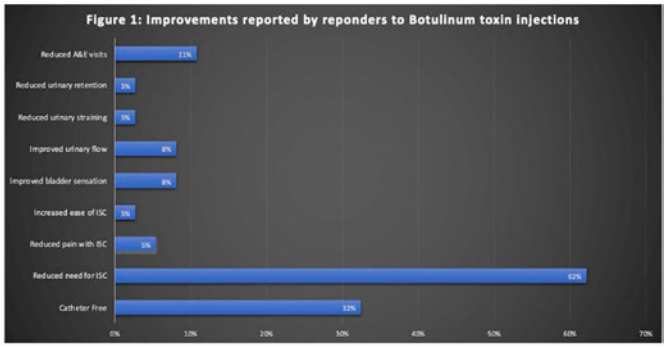

Figure 1: Improvements reported by reponders to Botulinum toxin injections

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Funding None **Clinical Trial** No **Subjects** Human **Ethics not Req'd** Approval from the Queen Square Clinical Audit Committee and Trust Clinical Effectiveness and Safety Group and assessments were conducted as part of routine clinical management. **Helsinki** Yes **Informed Consent** Yes

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SELF-REPORTED URINARY INCONTINENCE DURING COVID-19 INFECTION AND AFTER RECOVERY: A PRELIMINARY REPORT WITH BRAZILIAN SURVIVORS

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HYPOTHESIS / AIMS OF STUDY
Several studies investigate the physical, psychological and social impact of COVID-19 infection in people who survived the disease. Among the physical sequelae, the musculoskeletal and joint systems are frequently affected, and muscle weakness is one of the most common symptoms. However, there is still no current evidence regarding the pelvic floor muscles function in COVID-19 survivors and it is not known the impact of the personal history of COVID-19 on urinary complaints.

Previous studies already reported the worsening of urinary incontinence (UI) among women in lockdown[1]. One hypothesis for this finding is the symptomatology of individuals affected by COVID-19, since the most common clinical manifestation among those infected is coughing. Besides, coughing and dyspnea are symptoms that are commonly reported after recovery by patients that had mild disease. Furthermore, the manifestation of these symptoms repeatedly can trigger pelvic floor muscle fatigue. In addition, COVID-19 virus seems to use the angiotensin-converting enzyme 2 (ACE2) as a host cell receptor, receptors that have a high expression in the small intestine and medium expression in the bladder. This factor could lead to a negative impact of the disease in the digestive and urinary systems.

Therefore, in this preliminary report, we aimed to specifically analyze the occurrence of UI before, during and after COVID-19 infection, and to report the prevalence of UI in the last three months in women and men who survived the disease.

STUDY DESIGN, MATERIALS AND METHODS
This is a cross-sectional study conducted in Brazil between December 2021 and March 2022. The inclusion criteria were Brazilian participants residing in national territory, aged 18 or more, with a personal history of COVID-19 and UI complains that could be reported before, during or after the disease, and that were recovery until three months. Those who did not fill completely the instruments used for the evaluation were excluded from this study. The data collection was performed using a semi-structured questionnaire available on Google Forms platform. The first part of this questionnaire contained questions related to sociodemographic information (i.e., age, marital status, level of education) and one question related to the personal infection by COVID-19, in which participants should answer when the last infection occurred. Sequentially, participants should answer one semi-structured question related to UI during COVID-19 infection, where they should report if they were incontinent before the COVID-19 infection or if they started to present the urinary symptom during or after the infection. Then, the current urinary symptoms were analyzed by the International Consultation on Incontinence Questionnaire - Short Form (ICIQ-SF) by identifying women who reported a urinary loss in the past four weeks in any of the following situations: before reaching the toilet, while sneezing or coughing, while sleeping or dressing and/or lost without any reason. The data analysis was performed using the SPSS software, version 21.0 (SPSS Inc., Chicago, IL, EUA), and are presented in frequency and percentage.

RESULTS
A total of 566 participants were included in the present study. The majority of participants were women, married and with more than 11 years of study (Table 1). One-hundred and sixteen (20.5%) participants were incontinent before COVID-19 infection, while 140 (24.7 %) and 98 (17.3%) individuals associated the start of UI while they were infected and after they were recovered from COVID-19, respectively (Table 2). From the all sample, 212 participants (27.5%) were continent before, during and after recovery.

A higher percentage of participants that reported UI before, during or after COVID-19 infection were classified as current incontinent, according to the qualitative UI questions from ICIQ-SF (Table 2). From the continent participants before, during and after infection participants, 84 reported current UI.

INTERPRETATION OF RESULTS
The findings of the present study showed that a higher percentage of participants with UI before, during or after recovery of COVID-19 infection are still incontinent. These results highlight to health professionals, especially those who work in the urogynecology area, that survivors from COVID-19 may require assistance to treat urinary symptoms.

There are some possible justifications for these findings. The first one is related to the general weakness of the musculoskeletal system that could impact directly the pelvic floor muscles function. This factor could lead to urinary leak during stress situations. However, if the patient reported other impairments related to weakness, as balance dysfunctions or immobility, the individual could face some difficult to reach the bathroom during a desire to urinate, what could lead to urgency UI.

Furthermore, the sympathology of COVID-19, more specifically coughing, could contribute to UI complains, as the repetition of this symptom could cause fatigue of pelvic floor muscles and also repetitive microtrauma to this area. In addition, considering the synergism between the abdominal muscles and pelvic floor muscles, the implications and symptoms related to the respiratory system could also be associate with the UI: for example, some difficult to activate the diaphragm and to recruit synchronously the pelvic floor muscles during breathing and also during stress activities could lead to UI. Finally, patients infected by COVID-19 reported higher indices of anxiety and this symptom can be classify as a risk factor for symptoms of urgency UI[2].

Future studies should investigate the association between some variables that could possibly be related to UI symptoms that started during COVID-19 infection. In addition, factors related to the gravity of the COVID-19 should be include in future models, to analyze the association between the severity of the disease and current UI symptoms.

CONCLUDING MESSAGE
A higher percentage of survivors reported before, during or after COVID-19 infection are still incontinent. Health professionals should be aware of the continence status of individuals recovery from COVID-19.

FIGURE 1

Table 1. Characteristics of the sample (n=566).

Variables	n (%)
Age#	42.0±9.3
Gender	
Female	551 (97.3)
Masculine	15 (2.7)
Marital status	
With conjugal life	392 (69.3)
Without conjugal life	174 (30.7)
Years of study	
Until 8	32 (5.7)
Between 9 and 11	58 (10.2)
More than 11	476 (84.1)
Last infection by COVID-19	
Less than 1 month	297 (52.5)
Between 1-3 months	269 (47.5)

mean and standard deviation

Table 1. Characteristics of the sample (n = 566).

FIGURE 2

Table 2. Frequency and percentage of UI symptoms before, during and after COVID-19 infection; and presence of current UI (n=354).

Assessment of UI before, during or after recovery COVID-19 contamination n (%)		Current UI reported on the last month* n (%)
UI before contamination	116 (20.5)	109 (93.9)
UI during contamination	140 (24.7)	123 (87.8)
UI after recovery	98 (17.3)	85 (86.7)

UI=urinary incontinence

*% was calculated according the frequency and percentage reported by women during infection

Table 2. Frequency and percentage of UI symptoms before, during and after COVID-19 infection; and presence of current UI.

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IMPACT OF PELVIC FLOOR MUSCLE TRAINING ALONE AND ASSOCIATED WITH GAMETHERAPY ON QUALITY OF LIFE DOMAINS

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1. UFRN

HYPOTHESIS / AIMS OF STUDY

The quality of life (QoL) of women with urinary incontinence (UI) is affected in different proportions, depending on the type and severity of symptoms. UI can cause serious medical, social, psychological and economic implications (1). It is expected that conservative and surgical interventions can improve the QoL of patients with UI. Pelvic floor muscle training (PFMT) is recognized as a conservative treatment, presenting level 1 and degree of evidence A for the treatment of stress urinary incontinence (SUI) and mixed urinary incontinence (MUI) (2). Currently, gametherapy is a new therapeutic approach that has been used associated with PFMT. This modality can add to the treatment as a motivational and amused factor (3). However, there are still few publications about this new modality for UI treatments. Therefore, the aim of this study was to compare QoL in women with MUI before and after two conservative interventions: PFMT isolated and associated with gametherapy.

STUDY DESIGN, MATERIALS AND METHODS

Randomized, blinded clinical trial study was performed. 32 women with MUI were divided equally into two groups: PFMT (pelvic floor muscle training group – n = 16) and GG + PFMT (gametherapy + pelvic floor muscle training group – n = 16). The study included women aged between 45 and 70 years, who did not have an intact hymen, did not perform PFMT, did not use hormone replacement therapy (HRT) for at least three months and did not have a diagnosis of diabetes, neurological disorders or a previous history of epilepsy. The research was carried out in four stages: (1) Evaluation 1 (baseline): the evaluation form was used including sociodemographic information, life habits, urogynecological, obstetric and sexual history. Pelvic floor function was assessed using the modified Oxford scale and manometry. The quality of life was measured by the World Health Organization Quality of Life – bref (WHOQOL-bref) questionnaire. The questionnaire has 26 questions, two about general QoL and the other 24 divided into four domains: physical, psychological, social relationships and environment. (2) Intervention: The training was performed twice a week for eight consecutive weeks, during 40 minutes per session. all interventions were performed individually in both groups. PFMT consisted of three modalities: breathing exercises, abdominal exercises and pelvic mobility exercises. Each exercise was performed associated with the contraction of the pelvic floor muscle (PFM). There were progressions throughout the training in each modality. Gametherapy used a video game by Nintendo® brand, Wii®, with Wii Balance Board® that it is responsible for the interface between the machine and participant. Wii Fit Plus® games from the balance segment were used: Lotus Focus and Peguin Slide and from the aerobic segment: Step Basic and Hula Hoop. Each game was performed associated with the contraction of the PFM. All volunteers received educational content on the location and function of the PFM, types of UI, bladder and bowel functioning, as well as guidance on risk factors. (3) Evaluation 2: It was performed after 8 sessions; (4) Evaluation 3: It was performed after 16 sessions. The evaluator was blinded. This project was approved by the Ethics Committee in Research and registered on the Brazilian Registry of Clinical Trials – ReBEC virtual platform. For sample size calculation, the g*power software (Universität Düsseldorf: Psychologie) was used. Means and standard deviation of the World Health Organization Quality of Life – bref (WHOQOL-bref) of 13 patients with MUI were used, with a sample size proposed with a confidence level of 95% and power of 80%. Data normality distributions were evaluated using the Kolmogorov-Smirnov test. Data were presented as mean and standard deviation for quantitative data, while categorical variables were described in absolute and relative frequency. An ANOVA test with repeated measures was used for the time factor (evaluations 1, 2 and 3) and for the group factor (PFMT and GG + PFMT), followed by a Bonferroni post hoc. The level of statistical significance adopted was $p < 0.05$. Analyzes were performed using SPSS® version 22.0 software.

RESULTS

The mean age of the sample was 50.12 ± 8.62 in PFMT and 54.43 ± 9.96 in GG + PFMT, most had more than eight years of schooling, had children, did not have regular menstrual cycles, were sexually active, were overweight and sedentary. There was a difference between the times (evaluation 1, 2 and 3) for the Whoqol question 2 ($p = 0.024$). The time x group comparison, there was a difference in the psychological domain ($p = 0.001$). There was a difference between groups in the domains: psychological ($p = 0.007$); social relationships ($p = 0.008$); and environment ($p = 0.006$). Comparing the groups individually by time, there was a difference for the psychological domain between the groups at baseline ($p = 0.0001$) and evaluation 2 ($p = 0.03$); for the domain social relationships occurred at baseline ($p = 0.003$) and for the domain environment was at baseline ($p = 0.0001$) and evaluation 3 ($p = 0.011$).

INTERPRETATION OF RESULTS

It is possible to find several questionnaires to evaluate the quality of life, some of them specific for urinary incontinence, others for lower urinary tract symptoms and others generic as WHOQOL.

It is observed to improve the QoL of women with UI, which is an important determinant of their physical, mental, and social functioning. The literature shows that PFMT is an effective non-surgical treatment for UI in women. The duration of PFMT should not be shorter than 6 weeks and it is advised to perform supervised PFMT. PFMT can be used isolated or combined with other therapy for the treatment of UI in women as gametherapy (4). Possibly, our findings resulted in an improvement in QoL considering that the intervention protocol followed the previously proven scientific findings on the effectiveness of the PFMT.

According to Dumoulin et al. (2014), women treated with any type of training for PFMs are more likely to report cure or improvement of symptoms, have fewer episodes of urinary leakage per day and less urine leakage based on the 1h pad-test. These findings have a positive impact on quality of life and justify our data.

Both intervention showed good acceptance, with no no dropout, easy applicability and has been shown to reduce the urinary symptoms. The gametherapy is similar to the PFMT intervention in terms of clinical improvement and QoL. Thus, it can be said that this technique can bring good results in clinical practice in urogynecology, in populations similar to that of this study.

Our data also showed significant differences in three WHOQL domains. However, comparison with other studies becomes difficult due to the different types of questionnaires to assess UI and QoL. Thus, it is essential that future clinical trials use valid measures for QoL (5).

CONCLUDING MESSAGE

Statistically significant differences were found between the results in the two groups, in the psychological, social relationship and environment domains. Thus, both interventions proved to be effective in improving the quality of life of women with MUI.

FIGURE 1

Table 1. Comparison of quality of life between time and group.

	EVALUATION 1			EVALUATION 2			EVALUATION 3		
VARIABLES/ DOMAINS	GG+PFMTG	PFMTG	p value	GG+PFMTG	PFMTG	p value	GG+PFMTG	PFMTG	p value
WHOQOL Q1	3.81 ± 0.83	3.4 ± 0.50	0.086	3.75 ± 0.85	3.56 ± 0.81	0.28	3.81 ± 0.54	3.75 ± 0.42	0.20
WHOQOL Q2	3.06 ± 0.99	2.8 ± 0.94	0.45	3.56 ± 0.62	3.12 ± 1.02	0.07	3.5 ± 0.63	3.62 ± 0.80	0.343
PHYSICIST	3.67 ± 0.78	3.25 ± 0.64	0.08	3.81 ± 1.55	3.47 ± 0.65	0.45	3.58 ± 0.54	3.37 ± 1.02	0.57
PSYCHOLOGICAL	3.91 ± 0.39	3.10 ± 0.50	0.0001*	3.09 ± 0.51	3.46 ± 0.57	0.03*	3.65 ± 0.50	3.42 ± 0.81	0.35
SOCIAL RELATIONSHIPS	3.80 ± 0.42	3.21 ± 0.58	0.003*	3.75 ± 0.62	3.33 ± 0.60	0.074	3.74 ± 0.70	3.47 ± 0.67	0.06
ENVIRONMENT	3.38 ± 0.49	2.77 ± 0.32	0.0001*	3.38 ± 1.13	2.94 ± 0.49	0.11	3.29 ± 0.47	3.24 ± 0.79	0.011*

Note: Q1: question 1. Q2: question 2. GG+PFMT : gametherapy + pelvic floor muscle training group. PFMTG - pelvic floor muscle training group. * statistically significant values (p<0.05)

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Funding CAPES **Clinical Trial** Yes **Registration Number** U1111-1179-5886 **RCT** Yes **Subjects** Human **Ethics Committee** Committee on Ethics and Research of the Federal University of Rio Grande do Norte **Helsinki** Yes **Informed Consent** Yes

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RELAXIN-2 DURING PREGNANCY ACCORDING TO GLYCEMIA AND CONTINENCE STATUS

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HYPOTHESIS / AIMS OF STUDY

Relaxin is an insulin-like hormone that has physiological targets in organs that are important for insulin action (e.g., the pancreas, the liver and muscle).[1] It is widely known in clinical practice and academic field that higher levels of relaxin are a risk factor for pelvic dysfunction (PD) such as urinary incontinence (UI).[2] Although this mechanistic explanation is reasonable, clinical research on relaxin concentration dosage and UI assessment is limited and inconclusive, thus, its impact on PFM function is not yet known. The primary aim is to investigate relaxin concentration between GDM and non-GDM during pregnancy according to UI status.

STUDY DESIGN, MATERIALS AND METHODS

This was a cross-sectional study approved by the Institutional Ethical Committee (Protocol Number CAAE 82225617.0.0000.5411). All subjects met the following inclusion criteria: pregnant women period between 24 to 40 weeks of gestation; singleton pregnancy; 18–40 years of age; had not received PFM training or any musculoskeletal PFM treatment before or during pregnancy. The participants were allocated in GDM group if they presented fasting glycemic levels ≥92 mg/dL or 1 hour ≥180 mg/dL or 2 hours ≥153 mg/dL. In addition, participants who had lower levels composed the Non-GDM group. To compose the subgroups according to urinary incontinence status, ICIQ-SF and ISI questionnaires were applied on the same day as relaxin dosage.[3] So, we composed 4 different groups: non-gestational diabetes mellitus continent group (non-GDM-C), non-gestational diabetes mellitus incontinent group (non-GDM-PSUI), gestational diabetes mellitus continent group (GDM-C) and gestational diabetes mellitus incontinent group (GDM-PSUI). The sample size calculation was performed a priori using G*Power. Considering that any other previous research performed the measurement proposed by this study, we considered to the calculations a one-way analysis of variance test, power of 0.80, probability of error α 0.05, effect size of 0.25. According to the study design, it was considered for the calculation four groups (non-GDM-C, non-GDM-PSUI, GDM-C and GDM-PSUI); the estimated sample size required was 180 participants (45 in each group).

RESULTS

282 participants were successfully included in this study, of these, 186 were Non-GDM and were divided according to continence status, 81 were continent and 105 with PSUI; 96 were GDM which divided into 46 continent and 50 with PSUI. The baseline characteristics of 282 participants are summarized on (Table 1). The age of GDM-PSUI was similar to other groups, the pre-gestational BMI was higher compared to the Non-GDM-C and the gestational BMI was higher compared to the Non-GDM-C and GDM-C. The OGTT (fasting; 1 hour and 2 hours), as expected, were different between the Non-GDM and GDM group. The groups were matched for gestational age, maternal weight gain, ethnicity, and previous C-section. The prevalence of PSUI was statistically similar (p = 0.485) between the non-GDM (56.5%) and GDM (52.1%) groups. When relaxin-2 concentrations were compared between the non-GDM and GDM groups, excluding the stratification by continence status, the analysis showed similar levels 510.5 (58.7-2563.1) and 437.9 (76.3-3369.7) pg/mL (p = 0.216). Tests comparing groups by continence status showed a significant difference (p = <0.001). The GDM-PSUI showed lower relaxin levels than the GDM-C (p = 0.027) and Non-GDM-C (p = 0.001) groups. In addition, the Non-GDM-PSUI group had lower relaxin levels compared to the Non-GDM-C group (p = 0.023) (figure 1).

INTERPRETATION OF RESULTS

Our findings showed that the relaxin-2 concentration was associated to the presence of PSUI on GDM and non-GDM groups. Contradicting the literature, the relaxin-2 levels of pregnant with PSUI were lower comparing to pregnant continent. Our main aim was quantifying the relaxin-2 concentrations in the presence to GDM and incontinence, there is no data available considering BMI and maternal age influencing relaxin-2 concentration, but it is important to consider that our groups diverged regarding maternal age and pre-gestational and gestational BMI. These differences should be addressed to the group composition, since in general maternal age and higher BMI are the risk factors of GDM and should be enrolled on the incontinence pathophysiology. DeLancey and Petros highlight the importance of the functional balance between connective tissues and PFM for the continence process. According to hormonal theory, estrogen, progesterone and relaxin-2 are the three most common hormones associated with UI . Relaxin is recognized as an anti-fibrotic hormone. The relaxin's action facilitates collagen degradation as it promotes changes in its concentration and remodels the matrix metalloproteinases, gelatinases, collagenases, alpha smooth muscle, in addition to decreasing the gene expression of collagen I and III, and inter-collagen fibril interactions leading to increased collagen fibril sliding and ligament length. Although in clinical practice and even in academic field the concept of higher levels of relaxin leads to pelvic dysfunction, in particular, UI, articles correlating it with the dosage of relaxin concentrations are scarce, have poor methodological quality and small sample, thus, findings are of limited value to allow this statement. In our study, we found that pregnant women with PSUI in both the GDM and non-GDM groups, presented lower levels of relaxin in comparison to continent groups, contradicting the higher levels hypothesis. No studies were found comparing non-GDM and GDM groups regarding or not continence status.

CONCLUDING MESSAGE

Contrasting physiological action on extracellular matrix underlying the subjects of this article, while diabetes leads to a fibrosis process, relaxin, on the other hand leads to anti-fibrotic process. Further studies are needed to investigate the influence over time and determine the strength of the connection between lower levels of relaxin on PFM impairment and fibrosis in GDM population, especially in GDM-PSUI.

FIGURE 1

Table 1. Baseline characteristics of study participants according to glycaemic and continence status.

	Non-GDM-C (n= 81)	Non-GDM-PSUI (n=105)	GDM-C (n= 46)	GDM-PSUI (n=50)	*p* value
Age (years)	26 (18-38)	24 (18-39)[a]	29 (18-41)[a]	26 (18-41)	0.022
Gestational age	28 (24-38)	28 (24-38)	29.5 (24-38)	31.5 (24-38)	0.086
Pre-pregnancy BMI	23.6 (16.8-42.5)[a]	26.3 (16,8-44,4)	26.2 (18.7-35.9)	28.7 (18.5-48.4)[a]	0.000
BMI gestational	27.5 (18.7-44.3)[a]	29.2 (18.7-49.3)	28.2 (20.4-38.9)[b]	33.9 (21.6-49.5)[ab]	0.001
Weight gain (kg)	7.5 (-1.0-29.0)	7 (-21.0-27)	7.4 (-26-18.8)	7.2 (-32-17)	0.792
OGTT-75g fasting (mg/dL)	74 (50-90)	73 (58-87)	86.5 (64-124)	93 (73-119)	0.000
OGTT-75g 1 hour (mg/dL)	108 (62-167)	112 (42-166)	145 (82-220)	151.5 (88-235)	0.000
OGTT-75g 2 hours (mg/dL)	97 (51-151)	97 (49-143)	131 (72-205)	144.5 (72-217)	0.000
Caucasian	65 (80.2%)	83 (79%)	32 (69.6%)	37 (74%)	0.491
Prior cesarean delivery	9 (11.1%)	27 (25.7%)	9 (19.6%)	12 (24.0%)	0.086

n: sample; BMI: body mass index; kg: kilograms; OGTT-75g: oral glucose tolerance test of 75 grams; [a,b]equal letters represent post-hoc differences; Kruskal-Wallis test, followed by Dunn's multiple comparisons and chi-square test. Non-GDM-C: non-Gestational diabetes mellitus continent group; Non-GDM-PSUI: non-Gestational diabetes mellitus incontinent group; GDM-C: Gestational diabetes mellitus continent group; GDM-PSUI: Gestational diabetes mellitus incontinent group; p < 0.05 significant difference between the four groups.

Table 1. Relaxin-2 concentration according to glycemic and incontinence status.

FIGURE 2

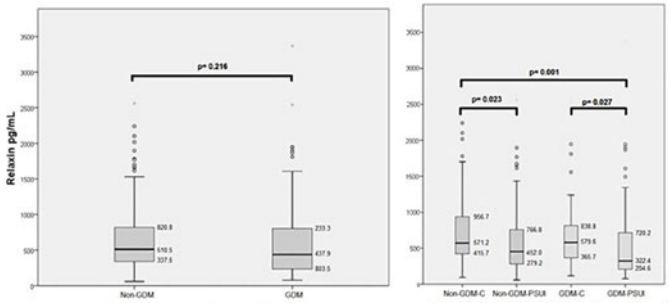

Figure 1. Relaxin-2 concentration according to glycemic and incontinence status.

Figure 1. Relaxin-2 concentration according to glycemic and continence status.

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ASSOCIATION BETWEEN PELVIC ORGAN MOBILITY EVALUATED BY DYNAMIC MAGNETIC RESONANCE IMAGING AND OVERACTIVE BLADDER AND/OR VOIDING DYSFUNCTION

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HYPOTHESIS / AIMS OF STUDY

One of etiologies of overactive bladder (OAB) in patients with pelvic organ prolapse (POP) has been considered bladder outlet obstruction. In this study, we measured variables on pelvic organ mobility (POM) evaluated by dynamic magnetic resonance imaging (dMRI) and exploratively investigated the association between those and the presence or absence of OAB and/or voiding dysfunction (VD).

STUDY DESIGN, MATERIALS AND METHODS

We included 118 patients with a mean age of 60.3 years who had POP of stage II or less at rest and stage III or more when straining during dMRI. The presence or absence of OAB was diagnosed with overactive bladder symptom score, while the presence or absence of VD was determined by voiding International Prostate Symptom Score (vIPSS) ≥ 5 (vIPSS5), maximum flow rate (Qmax) < 15 mL/s (Qmax15), and post-void residual urine volume (PVR) ≥ 50 mL (PVR50) [1, 2]. We divided the patients into four groups: group 1 (G1), patients with OAB and VD; group 2 (G2), those with OAB only; group 3 (G3), those with VD only; group 4 (G4), those without OAB and VD. The variables on POM were measured by dMRI at rest and during straining, including the bladder neck, the most dependent position of the bladder after straining, uterine cervix (C), and anorectal angle (AR), imaginary cardinal (iCL) as well as uterosacral (iUSL) ligaments, H as well as M-lines, the anterior vaginal wall length (AVWL), posterior urethrovesical angle (PUVA), and angle of the urethral inclination (AUI). Data are presented as mean (SD), and $p < 0.05$ was considered statistically significant with ANOVA followed by Tukey-Kramer's test.

RESULTS

1. Demographics of the patients (Table 1)

About half of the patients had neither OAB nor VD determined by above criteria, and there was no significant difference in POP stage with POP-quantification system among the groups. Twenty-nine and 89 patients complained of pelvic pressure and vaginal bulge, respectively. Only three patients had diabetes. Kappa coefficient for grouping based on vIPSS5, Qmax15, and PVR50 was 0.3876 for vIPSS5 vs Qmax15, 0.4420 for vIPSS vs PVR50, and 0.4414 for Qmax15 vs PVR50.

2. OAB and VD determined by vIPSS5 (Table 2)

G1 showed significantly more uterine cervical hypermobility and greater strain on iCL and iUSL than G4. G2 had significantly higher body mass index (BMI) and greater strain on iCL and iUSL than G4. G3 had significantly and tended to have smaller strain on iUSL than G1 and G2, respectively.

3. OAB and VD determined by Qmax15 (Table 2)

G1 had significantly higher BMI and greater strain on iCL strain than G4. G2 had significantly more parity, more cervical hypermobility, a greater degree of pelvic floor ptosis at rest, and greater strain on iCL and iUSL thanG4. G3 were significantly older, had significantly less longitudinal movement in AR during straining, and greater strain on AVW than G4.

4. OAB and VD determined by PVR50 (table 2)

G2 had significantly more cervical hypermobility and greater strain on iCL and iUSL than G4, and tended to have more cervical hypermobility than G3. Moreover, G2 had a significantly greater degree of pelvic floor ptosis at rest and greater strain on iCL and iUSL than G3. G3 had significantly fewer parity than G2 or G4.

INTERPRETATION OF RESULTS

In terms of LUTS, weakness of CL and USL was potentially associated with OAB as well as the combination of OAB and VD, while cervical hypermobility was potentially associated with OAB and VD. On the other hand, those variables on POM were associated with OAB alone when VD was determined by objective measures, namely, decreased Qmax and increased PVR. In addition, in patients with VD determined by PVR50, weakness of CL and USL was significantly different between OAB and VD. Patients with OAB had more impaired pelvic floor represented by AR in VD determined by Qmax15 and PVR50. Furthermore, hyperextension of AVW was associated with lower Qmax. Not performing pressure flow study was main limitation of this study.

CONCLUDING MESSAGE

Cervical hypermobility and weakness of CL and USL might be associated with both OAB and voiding symptoms. Pelvic floor impairment might be also involved in OAB. On the other hand, the measured variables on POM associated with VD determined by Qmax and PVR were not clearly identified. The respective mechanisms for VD, as determined by symptoms, uroflow, and residual urine, might be different in patients with POP.

FIGURE 1

Table 1. Demographics of patients

	G1	G2	G3	G4	p ANOVA	p Tukey-Kramer
OAB and vIPSS5						
n	19	16	23	60		
Age	63.6 (10.36)	62.3 (11.28)	60.9 (8.29)	58.4 (11.65)	0.2428	
Body mass index	23.9 (2.26)	24.6 (3.17)	23.1 (2.96)	22.0 (2.94)	0.0058	G2 vs G4, 0.0121
Parity	2.4 (0.60)	2.1 (0.96)	1.9 (1.06)	2.0 (0.74)	0.2341	
POP stage, I/II/III/IV	0/3/15/1	0/5/11/0	1/5/17/0	3/19/37/1	0.7086	
OAB and Qmax15						
n	9	26	22	58		
Age	62.9 (7.08)	63.0 (11.76)	65.0 (8.63)	57.2 (10.56)	0.0096	G3 vs G4, 0.0178
Body mass index	25.3 (2.49)	23.9 (2.71)	27.8 (3.51)	22.3 (2.68)	0.0105	G1 vs G4, 0.0227
Parity	2.1 (0.60)	2.3 (0.84)	2.2 (0.87)	1.8 (0.76)	0.0314	G2 vs G4, 0.0428
POP stage, I/II/III/IV	0/2/7/0	0/6/19/1	1/6/15/0	3/17/37/1	0.9307	
OAB and PVR50						
n	9	26	17	63		
Age	67.1 (8.58)	61.6 (11.07)	59.6 (11.71)	59.3 (10.38)	0.2031	
Body mass index	24.6 (2.47)	24.1 (2.79)	22.7 (3.13)	22.4 (2.89)	0.0221	NS
Parity	2.2 (0.44)	2.3 (0.87)	1.5 (0.87)	2.0 (0.75)	0.0107	G2 vs G3, 0.0075 G3 vs G4, 0.0393
POP stage, I/II/III/IV	0/2/6/1	0/6/20/0	1/3/12/1	3/20/40/0	0.2502	

Mean (SD); G1, patients with overactive bladder (OAB) and voiding dysfunction (VD); G2, patients with OAB alone; G3, patients with VD alone; G4 patients without OAB and VD.
NS, not-significant; POP, pelvic organ prolapse; PVR50, post-void residual urine ≥50 mL; Qmax15, maximum flow rate ≤ 15 mL/s; vIPSS5, voiding International Prostate Symptom Score ≥5

Table 1

FIGURE 2

Table 2. Variables on pelvic organ mobility by groups of patients

	G1	G2	G3	G4	p ANOVA	p Tukey-Kramer
OAB and vIPSS5						
n	19	16	23	60		
C-Ry	0.5 (10.30)	3.5 (10.24)	7.4 (10.37)	8.02 (9.38)	0.0225	G1 vs G4, 0.0230
C-Sx	25.6 (15.99)	37.2 (20.54)	33.3 (14.01)	39.8 (16.68)	0.0137	G1 vs G4, 0.0088
C-Sy	-29.7 (17.70)	-30.7 (26.20)	-22.6 (12.36)	-18.6 (13.99)	0.0153	NS (G1 vs G4, 0.0569 G2 vs G4, 0.0509)
C-xx	-19.4 (13.07)	-15.3 (11.87)	-10.53 (11.20)	-10.1 (11.63)	0.0182	G1 vs G4, 0.0181 (G1 vs G3, 0.0782)
AR-Ry	-19.4 (8.76)	-20.4 (9.99)	-12.5 (9.36)	-13.5 (10.23)	0.0111	NS (G2 vs G3, 0.0691 G2 vs G4 0.0659)
iCL-S	125.4 (18.09)	118.6 (28.80)	113.2 (17.78)	106.8 (21.76)	0.0088	G1 vs G4, 0.0079
iCL-ε	1.4 (0.25)	1.4 (0.21)	1.3 (0.15)	1.3 (0.17)	0.0025	G1 vs G4, 0.0124 G2 vsG 4, 0.0257
iUSL-S	93.8 (19.55)	88.1(25.58)	83.5 (14.95)	76.5 (21.53)	0.0099	G1 vs G4, 0.0104
iUSL-ε	1.4 (0.24)	1.4 (0.32)	1.2 (0.22)	1.2 (0.21)	0.0008	G1 vs G4, 0.0049 G1 vs G3, 0.0312 G2 vs G4; 0.0226 (G2 vs G3 0.0819)
OAB and Qmax15						
n	9	26	22	58		
C-Ry	3.2 (10.74)	1.4 (10.22)	5.9 (7.85)	8.3 (10.29)	0.0288	G2 vs G4, 0.0202
C-Sy	-30.0 (26.75)	-30.2 (20.22)	-24.5 (13.22)	-18.4 (13.50)	0.0127	G2 vs G3, 0.0158
C-xx	-17.9 (13.12)	-17.4 (12.57)	-14.2 (10.99)	-8.9 (11.54)	0.0083	G2 vs G4, 0.0144
AR-Ry	-19.8 (8.52)	-19.9 (9.61)	-16.0 (8.42)	-12.6 (10.45)	0.0087	G2 vs G4, 0.0106
AR-yy	-16.3 (9.50)	-20.1 (9.67)	-17.1 (10.71)	-24.3 (11.76)	0.0229	G3 vs G4, 0.0452
AR-D	17.9 (8.62)	21.3 (9.68)	19.1 (9.23)	25.3 (11.61)	0.0448	NS (G3 vs G4, 0.0954)
iCL-S	131.4 (21.78)	119.1 (23.59)	115.4 (20.19)	106.9 (20.95)	0.0046	G1 vs G4, 0.0098 (G2 vs G4, 0.0796)
iCLε	1.4 (0.28)	1.4 (0.22)	1.3 (0.15)	1.3 (0.17)	0.0017	G2 vs G4, 0.0016 (G2 vs G3, 0.0864)
iUSL-S	94.3 (19.05)	90.1 (23.62)	85.0 (20.19)	76.6 (20.02)	0.0129	G2 vs G4, 0.0367 (G1 vs G4, 0.0887)
iUSL-ε	1.4 (0.31)	1.4 (0.27)	1.2 (0.19)	1.2 (0.22)	0.0007	G2 vs G4, 0.0011 (G1 vs G4, 0.0502)
AVW-ε	1.2 (1.06)	1.0 (0.99)	1.7 (1.29)	1.0 (0.89)	0.0450	G3 vs G4, 0.0285
OAB and PVR50						
n	9	26	17	63		
C-Ry	1.7 (12.50)	1.9 (9.61)	8.7 (9.72)	7.3 (9.75)	0.0435	NS (G2 vs G4, 0.0969)
C-Sy	-30.9 (21.79)	-29.9 (22.03)	-17.4 (11.53)	-20.8 (14.13)	0.0266	NS (G2 vs G3, 0.0812 G2 vs G4, 0.0940)
C-xx	-14.5 (5.27)	-18.6 (14.13)	-9.0 (8.23)	-10.7 (12.35)	0.0220	G2 vs G4, 0.0262 (G2 vs G3, 0.0523)
AR-Ry	-18.8 (10.59)	-20.2 (9.89)	-10.3 (12.24)	-14.4 (9.23)	0.0069	G2 vs G3, 0.0081 (G2 vs G4, 0.0536)
iCL-S	122.0 (13.39)	123.1 (26.25)	101.2 (13.87)	111.4 (22.10)	0.0096	G2 vs G3, 0.0084 (G2 vs G4, 0.0994)
iCL-ε	1.4 (0.14)	1.4 (0.26)	1.3 (0.18)	1.3 (0.16)	0.0021	G2 vs G3, 0.0394 G2 vs G4, 0.0028
iUSL-S	85.5 (14.72)	93.2 (24.37)	76.0 (17.95)	79.7 (20.94)	0.0261	G2 vs G3, 0.0489 G2 vs G4, 0.0349
iUSL-ε	1.4 (0.16)	1.4 (0.31)	1.1 (0.14)	1.2 (0.23)	0.0008	G2 vs G3, 0.0047 G2 vs G4; 0.0038

Mean (SD); parentheses showing p <0.01; G1, patients with overactive bladder (OAB) and voiding dysfunction (VD); G2, patients with OAB alone; G3, patients with VD alone; G4 patients without OAB and VD.
AR, anorectal angle; AVW, anterior vaginal wall; C, uterine cervix; D, distance in diagonal direction; ε, strain; iCL, imaginary cardinal ligament; iUSL, imaginary uterosacral ligament; NS, not-significant; POP, pelvic organ prolapse; R, at rest; PVR50, post-void residual urine ≥50 mL; Qmax15, maximum flow rate <15 mL/s; S, during straining; vIPSS5, voiding International Prostate Symptom Score ≥5; x and y, x and y-coordinates; xx and yy, distance in x- and y-directions.

Table 2

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CORRELATION OF PELVIC FLOOR MYOFASCIAL TRIGGER POINTS AND PELVIC FLOOR SYMPTOMS IN WOMEN VISITING THE UROGYNECOLOGICAL OUTPATIENT CLINIC: A CROSS-SECTIONAL STUDY

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HYPOTHESIS / AIMS OF STUDY

Chronic pelvic pain affects a significant number of women, with a prevalence, which is described to be between 5,7% and 26,6% worldwide. Although the etiology of chronic pelvic pain is mostly multifactorial. One source of pain seems to be the presence of myofascial trigger points, which, however, are often overlooked or ignored. There is evidence, that women with pelvic floor symptoms often experience pain and have positive trigger points upon pelvic floor examination. However, the correlation of these findings has not yet been systematically examined and sufficiently understood.

The aim of this study is to examine the correlation between myofascial trigger points and pelvic floor symptoms using a standardized pelvic floor examination method and a validated pelvic floor questionnaire.

STUDY DESIGN, MATERIALS AND METHODS

The study was performed in the outpatient urogynecological department of our clinic. Study participants underwent a standardized physical examination assessing myofascial trigger points in different muscle groups including pubococcygeous, iliococcygesous, obturator as well as at the bladder base. In addition, pelvic floor muscle tone was assessed. Participants also filled out the standardized German version of the Australian pelvic floor questionnaire, which consists of a total of 43 questions regarding bladder-, bowel- and sexual function as well as prolapse symptoms. The questionnaire provides a scoring system for each category (0-10) as well as a total score (0-40). Demographic data was retrieved from the patients' medical records. Statistical analysis was performed using the Mann-Whitney-U test and chi-squared or exact Fisher's test. All evaluations were done using the statistical software R.

RESULTS

A total of 110 women were included in the study. Mean age was 55.9 (SD ± 17) years. Pelvic floor muscle tone was assessed as normal in 71 (64.5%) and high in 39 (35.5%) of the participants. The mean score of the pelvic floor questionnaire was 8.23 (SD ± 3.94). The overall questionnaire score showed a significant correlation with pain at all muscle groups (except bladder base). All four domain scores (bladder, bowel, prolapse and sexual function) were significantly correlated with painful trigger points in different muscle groups. Age was not significantly correlated with pain or pelvic floor symptoms, except from sexual function, where the correlation was negative ($p < 0.001$). A significant correlation could also be found between high pelvic floor muscle tone and the overall questionnaire score ($p < 0.001$) as well as the bladder function score ($p < 0.001$) and various pain scores of the different groups. Table 1 shows an overview of the most important findings.

INTERPRETATION OF RESULTS

The existence of myofascial pelvic floor trigger points seems to be reflective of pelvic floor symptoms, as assessed with a standardized pelvic floor questionnaire.

CONCLUDING MESSAGE

Further research in order to examine and understand the mechanism of this correlation may help in the diagnosis and also offer more effective therapeutic options.

FIGURE 1

	Questionnaire domain scores				
	Bladder	Bowel	Prolapse	Sexual	Overall Score
Myofascial pain location					
- Pubococcygeous R	0.031	0.004	0.004	<0.001	<0.001
- Pubococcygeous L	0.085	0.173	0.601	<0.001	<0.001
- Iliococcygeous R	0.236	0.281	0.046	0.215	0.013
- Iliococcygeous L	0.187	0.505	0.082	0.111	0.032
- Obturatorius R	0.035	0.102	0.072	<0.001	<0.001
- Obturatorius L	0.039	0.086	0.019	<0.001	<0.001
- Bladder	0.401	0.227	0.276	0.058	0.090
High tone pelvic floor	<0.001	0.001	0.016	0.002	<0.001

P values of the correlations between myofascial pain locations and questionnaire scores (Spearmann's rank correlation, p values correspond to Mann-Whitney-U tests and chi-squared or exact Fisher test when the expected frequency is less than 5)

Funding No conflict of interest, no funding. **Clinical Trial** Yes **Public Registry** No **RCT** No **Subjects** Human **Ethics Committee** Ethikkommission Nordwest- und Zentralschweiz (EKNZ) **Helsinki** Yes **Informed Consent** Yes

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POST-OPERATIVE OUTCOMES AND URODYNAMIC FINDINGS AFTER CONTINENCE MESH REMOVAL

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HYPOTHESIS / AIMS OF STUDY
The use of mesh in urogynaecology has created much controversy in the last years.

The real prevalence of mesh complications is still largely debated due to different definitions used, variable length of followup considered amongst studies, great variability of clinical manifestations, as well as underreporting. What is now clear, is that the rate of mesh-related complications is higher in patients who have had multiple meshes inserted and that the most frequently reported complications include mesh extrusion and pain.

Similarly, data regarding outcomes following mesh removal can vary greatly in different studies and depending on symptoms considered; furthermore mesh removal itself may have risks which need to be discussed with patients, including: persistent or recurrent incontinence, urethral strictures, persistent pain or de novo pain, urethral injury, urethrovaginal fistula.

Our study aims to analyze urodynamics findings and patients reported outcomes after removal of a mid-urethral sling for different indications.

STUDY DESIGN, MATERIALS AND METHODS
Ours was a retrospective analysis, we included in the study all the women who were referred to the Female Pelvic medicine and Reconstructive Surgery Division of University College London Hospital and underwent vaginal removal of a mid-urethral sling (TVT, TVT-O, TOT) between January 2014 and January 2020.

Data regarding patients demographics, past surgical history, post operative patients' reported symptoms and results of video-urodynamics investigations performed 4 months after surgery were recorded on the patients' electronic records, collected and analyzed retrospectively.

R program was used for statistical analyses of the data.

RESULTS
A total of 204 patients were included in the study. Population characteristics are summarized in table 1: 61.8% of the women included had a TVT, 20.1% a TVT-O and 21.6% a TOT mesh inserted. Notably 7 patients had 2 different continence meshes inserted while no patient had more than 2 slings.

Post operative outcomes are summarized in table 2: 8%, 80.5%, 2.9% of the women included reported voiding dysfunction, stress urinary incontinence (SUI) and overactive bladder (OAB) symptoms respectively, after mesh removal. No patients reported worsening pain after surgery and 10.1% suffered from prolapse symptoms.

Video-urodynamics investigations proved the presence of pure SUI, pure DO and mixed urinary incontinence in 67.3%, 6.8%, 14.3% of patients respectively; only one patient had urodynamically diagnosed voiding dysfunction while 2 women were found to have a urethral stricture and 10 (9.8%) a significant cystocoele.

INTERPRETATION OF RESULTS
Our data shows that recurrence of SUI is the single most frequent complication after continence mesh removal, both in terms of patients' reported symptoms and urodynamic findings. Women seldom reported OAB symptoms (2.9%), while the prevalence of DO seems to be higher when investigated; on the other hand, 8% of the patients reported some form of difficulties passing urine while only 1 patient (0.7%) had voiding dysfunction confirmed at urodynamics. Finally, in our subset, no patients reported a worsening of their pain following continence mesh removal.

CONCLUDING MESSAGE
The occurrence of some kind of bladder dysfunction after continence mesh removal is extremely frequent, women should be counseled pre-operatively about risks of surgery. Furthermore, after continence mesh removal, patients should be properly investigated through urodynamics studies as the underlying bladder problems may be more complex than suggested by patients' symptoms only.

FIGURE 1
Table 1 - Population's characteristics

Age at mesh insertion (yrs)	54 (30-81)	Median (range)
Age at clinical evaluation (yrs)	58 (35-86)	Median (range)
BMI (Kg/m2)		
<25	34 (16.6%)	n (%)
25-29.9	79 (38.7%)	n (%)
30	61 (44.6%)	n (%)
Mesh type		
TVT	126 (61.8)	n (%)
TVT-O	41 (20.1)	n (%)
TOT	44 (21.6)	n (%)
2 meshes	7 (3.4)	n (%)
3 meshes	0 (0.0)	n (%)
Previous surgeries		
Hysterectomy	55 (27.1)	n (%)
Prolapse	40 (19.7)	n (%)
Continenence	15 (7.4)	n (%)
Previous mesh-complication surgery		
Partial Removal	49 (24.1)	n (%)
Erosion	1 (0.5)	n (%)

Table 1

FIGURE 2

Table 2 - Post Operative findings

PostOp Pain	N (%)
Improved	185 (94.4)
Unchanged	11 (5.6)
Worse	0 (0.0)
PostOp Voiding Dysfunction	
No	184 (92.0)
Yes	16 (8.0)
PostOP SUI	
No	39 (19.5)
Yes	161 (80.5)
PostOp Prolapse	
No	179 (89.9)
Yes	20 (10.1)
PostOp OAB	
No	198 (97.1)
Yes	6 (2.9)
PostOp Urodyanmics	
Normal	16 (10.9)
SUI	99 (67.3)
OAB	10 (6.8)
Mixed	21 (14.3)
Voiding Dysfunction	1 (0.7)
Cystocele	20 (9.8)
Urethral stricture	2 (1.0)

Table 2

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ROBOT-ASSISTED VESICO-VAGINAL FISTULA REPAIR: COMPARISON OF THE EXTRAVESICAL AND TRANSVESICAL TECHNIQUES

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HYPOTHESIS / AIMS OF STUDY

Robotic vesico-vaginal fistula repair (R-VVF) was described in 2004 with the aim to minimize the morbidity of the abdominal VVF repair. Almost two decades later, the literature on r-VVF remains scant. The objective of this study was to assess the outcomes of R-VVF and to compare the transvesical and extravesical techniques.

STUDY DESIGN, MATERIALS AND METHODS

The charts of all female patients who underwent a R-VVF from March 2007 to December 2021 at four academic institutions were reviewed retrospectively. All surgeons involved had already a robust robotic surgery experience at the beginning experience (>50 cases) but limited experience with VVF repair. All abdominal VVF repair over the study period were performed using a robotic approach. All centers used a vaginal approach in case of easily accessible vaginal fistulous orifice. The decision to use a vaginal or an abdominal approach was not standardized across centers and left at the surgeons' discretion. The patients' characteristics, the surgical technique details (iflap interposition vs. not, transvesical versus extravesical approach, excision of fistulous tract vs not) and peri-operative outcomes were recorded. The success of VVF-R was defined as the absence of clinical recurrence. The outcomes of the extravesical vs transvesical techniques were compared.

RESULTS

Twenty-two patients were included over the study period. the median age was 43 years (IQR 38-50). The causes of VVF-R were either post-surgical (77.3%), post-obstetrical (18.2%) or post-trauma (4.5%). Fistulas were supratrigonal and trigonal in 18 and 4 cases respectively. The fistulous tract was systematically excised and an interposition flap was used all but two cases (90.9%%). The transvesical and extravesical techniques were used in 13 and 9 cases respectively. The patient andfistula's characteristics are presented in table 1. There were more supratrigonal fistula in the extravesical group (100% vs. 69.2%; p = 0.11). One intraoperative complication occurred in the extravesical group: an ureteral injury which was immediately sutured (11.1% vs. 0%;p = 0.41). The operative time tended to be shorter in the extravesical group (179 vs. 229 minutes;p = 0.13). There were only three postoperative complications, all minor: one gross hematuria in the extravesical group (Clavien grade 1), one hematoma requiring blood transfusion and one pyelonephritis in the transvesical group (both Clavien grade 2) (11.1% vs. 15.4%; p = 0.99). The length f hospital stay did not differ significantly between the to groups (5.1 vs. 4.1 dys; p = 0.56). None of the patients had vesico-vaginal fistula recurrence after a median follow-up of 14 months (IQR 3-21).

INTERPRETATION OF RESULTS

The present series, one of the largest R-VVF reported to date, is consistent with the few series already published with a 100% cure rate and excellent perioperative outcomes. Systematic excision of the fistulous tract and the high rate of flap interposition may explain the high success rate. The transvesical and extravesical approach yielded similar outcomes but the transvesical approach may allow to treat more complex fistulas (e.g. infratrigonal)

CONCLUDING MESSAGE

Robotic vesicovaginal fistula repair is feasible with a very high success rate and a low perioperative morbidity. The transvesical and extravesical techniques seem to yield similar outcomes but the transvesical technique may allow to treat more complex cases.

FIGURE 1

Table 1 : patients and fistula's characteristics

	Whole cohort (N=22)	Transvesical technique (N=13)	Extravesical technique (N=9)	p-value
Median age (years)	43 (38-50)	44 (38-49)	43 (36-54)	0.67
Mean BMI (kg/m²)	26.7 (±8.2)	26.3 (±7.5)	27.3 (±9.7)	0.86
ASA Score				
1	10 (45.5%)	4 (30.8%)	6 (66.7%)	0.24
2	2 (40.9%)	7 (53.8%)	2 (22.2%)	
3	3 (13.6%)	2 (15.4%)	1 (11.1%)	
Vesicovaginal fistula cause				
Post surgical	17 (77.3%)	11 (84.6%)	6 (66.7%)	0.24
Post-obstetrical	4 (18.2%)	1 (7.7%)	3 (33.3%)	
Post trauma	1 (4.5%)	1 (7.7%)	0 (0%)	
History of radiation therapy	0 (0%)	0 (0%)	0 (0%)	NA
History of previous attempt of surgical repair	5 (22.7%)	4 (30.8%)	1 (11.1%)	0.36
Fistula location				
Supratrigonal	18 (81.8%)	9 (69.2%)	9 (100%)	0.11
Trigonal	4 (18.2%)	4 (30.8%)	0 (0%)	
Fistulous orifice size				
< 1 cm	11 (50%)	5 (38.5%)	6 (66.7%)	0.39
≥ 1 cm	11 (50%)	8 (61.5%)	3 (33.3%)	

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SESSION 10 - GERIATRICS/GERONTOLOGY

Abstracts 157-168
14:35 - 16:05, Hall G
Chair: Prof Adrian Stuart Wagg (Canada)

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THE MANAGEMENT OF URINARY INCONTINENCE IN NURSING HOMES: FINDINGS FROM A SCOPING REVIEW

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HYPOTHESIS / AIMS OF STUDY
To identify the effects of interventions for the management of urinary incontinence in nursing homes

STUDY DESIGN, MATERIALS AND METHODS
A scoping review with methods adapted from the Joanna Briggs Institute Methodology for JBI Scoping Reviews (2015). Electronic databases (MEDLINE, EMBASE, PsychINFO, CINAHL, JBI Evidence-Based Practice Database, and The Cochrane Database of Systematic Reviews) were searched from 2010 to September 2021. Search results were supplemented by scanning the references of relevant reviews. Three reviewers independently screened the titles and abstracts of all identified sources, while five reviewers completed a full-text review of the remaining material and abstracted data from the relevant studies.

RESULTS
A total of 3,885 records were located through the database search and one additional study was found through citations. After exclusions and screening of 370 full-text articles, 30 publications about interventions in this setting were included in the final analysis: 7 systematic reviews, 15 randomised-controlled trials, and 8 quasi-experimental studies.

Interventions evaluated included: toileting assistance programs, physical activity and functional training, drug therapies, technology-based interventions, staff education/training, and multi-component interventions for the management of urinary incontinence in nursing homes. Two randomised controlled trials and one quasi-experimental study demonstrated support for prompted voiding. Despite strong association between functional status and incontinence in nursing home residents, evidence for interventions to reduce rates of urinary incontinence through exercise programs was limited and inconsistent. Evidence for anticholinergics in this population was also inconsistent, with concerns expressed about an increased risk of adverse effects (i.e. dry mouth, constipation, hip fractures and decline in cognitive performance). Two studies offered evidence for use of technology-based interventions, namely (i) a telemonitoring system to detect the onset of wetness episodes and transcutaneous posterior tibial nerve stimulation.

Eleven studies evaluated interventions to improve staff knowledge, attitudes or practice, including 7 randomised controlled trials and 4 quasi-experimental studies. As outcomes differed between studies, the effects of education/training were unable to be pooled. Education/training was delivered either directly or indirectly. In general, where nursing home staff received direct education/training, there were improvements in continence outcomes such as reductions in urinary leakage, improvements in residents' quality of life, staff knowledge and attitudes, and increased staff compliance with assessments, toileting and documentation. In studies where training was indirect, evidence was inconsistent.

Multi-component interventions such as physical activity combined with prompted voiding and increases in food and fluid intake facilitated by one or more specialist healthcare professional produced improvements in urinary incontinence in nursing home residents.

INTERPRETATION OF RESULTS
Further research should focus on multi-component interventions that aim to maintain or improve nursing home residents' functional status and reduce their care dependence. Improvements in staff knowledge, attitudes and continence care practices in nursing homes are possible, particularly when led by specialist healthcare professionals. Direct forms of education for nursing home staff about urinary incontinence and its management appear more effective than passive learning approaches. The use of anticholinergics for urinary incontinence in frail older adults should be approached cautiously due to adverse effects.

CONCLUDING MESSAGE
Urinary incontinence continues to be a pervasive problem in nursing homes. This scoping review suggests a bundled approach to care seems to offer most benefit, i.e. where efforts are made to increase residents' activity level, nutritional status, hydration and opportunity to use the toilet. This should also be combined with direct forms of education for staff to ensure compliance.

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BEST IN CATEGORY PRIZE: GERIATRICS / GERONTOLOGY

THE IMPACT OF PREVALENT OVERACTIVE BLADDER ANTICHOLINERGIC USE ON COGNITIVE CHANGE IN ADULTS WITH NORMAL COGNITION, MILD COGNITIVE IMPAIRMENT, OR DEMENTIA

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HYPOTHESIS / AIMS OF STUDY

Overactive bladder (OAB) is a common condition in both the general population and in those with cognitive dysfunction. It is defined as urinary urgency, usually with frequency and urgency, and may or may not include urgency incontinence. These symptoms are significant as they can lead to falls and fractures, skin breakdown, institutionalization and impair quality of life. There is a large body of research suggesting that OAB anticholinergic medications may lead to cognitive dysfunction, and an increased risk of dementia; however there is a need for more studies in those with pre-existing cognitive dysfunction, and studies with longer follow-up periods.(1) In addition, the APOE-e4 allele is a genetic risk factor for Alzheimer's, and may lead to increased sensitivity to anticholinergic-mediated cognitive decline(2); to our knowledge it hasn't been evaluated in the context of OAB anticholinergics. Our objective was to use routinely collected data from the National Alzheimer's Coordinating Centers (NACC) to see if the use of OAB anticholinergics was associated with an increased risk of cognitive decline, and to examine if APOE-e4 carrier status interacts with any observed cognitive decline with OAB anticholinergic use.

STUDY DESIGN, MATERIALS AND METHODS

This is a retrospective, propensity-score matched cohort study using prospective collected data from the NACC. The NACC started collecting prospective data from approximately 40 specialized Alzheimer's research centers in the United Sates in 2005. Participants may volunteer to be included in the NACC dataset, or they may be offered enrollment by participating clinicians. We identified all participants who were enrolled between September 1 2005 and January 1 2020. We excluded people if: they did not have at least one follow-up visit, their medication list was not available, they were already on an OAB anticholinergic medication at enrollment, they had a cognitive condition other than normal cognition, mild cognitive impairment, or dementia, they were missing genetic testing results for APOE-e4 allele status, or if there was >4 years between their first and second visit.

Our primary exposure was defined as new reported use of an OAB anticholinergic medication (oxybutynin, tolterodine, solifenacin, trospium, darifenacin or fesoterodine) at a subsequent NACC visit. Medication use was determined by having the patient bring all medication bottles to the appointment, and these were reviewed by study staff. We considered APOE-e3/e4 or APOE-e4/e4 status as being positive for the APOE-e4 allele. Our co-primary outcomes were the clinical dementia rating (CDR, $0=$no dementia, $4=$severe cognitive impairment) and the mini-mental state examination (MMSE, which measures orientation, attention, memory, language and visual-spatial skills and is scored from 0-30; a lower score represents increased cognitive impairment). Secondary outcomes included the Boston naming test, Wechsler Adult Intelligence Scale-revised (WAIS-R), and the trail making test part B. Outcomes were compared between the baseline visit and the next follow-up visit.

We created a propensity score using 38 variables available in the NACC dataset that were relevant to cognition such as age, gender, language, years of education, marital status, vision and hearing impairment, and the prevalent use of several medications. Patients who were newly taking an OAB anticholinergic medication were matched 1:1 with participants who were not newly taking an OAB anticholinergic medication using the propensity score, data era (pre/post 2015), total number of NACC visits, and based on their cognitive status (normal, mild cognitive impairment, or dementia). Comparisons between primary and secondary outcomes were carried out using t-tests; a conditional logistic regression model (odds ratio, OR) was used to determine if OAB anticholinergic medication exposure predicted a clinically important cognitive decline based on our primary endpoints (≥ 1 point increase on the CDR, or a ≥ 3 point decrease on the MMSE). Means and standard deviation (SD) are reported. Statistical analysis was carried out using SAS 9.4, and a two-sided $p<0.05$ was considered significant. This analysis was exempt from ethics review.

RESULTS

Our initial cohort consisted of 44,713 people, and after exclusions we were left with 18,835 people. We were able to successfully match 782 of the possible 792 participants who newly started an OAB anticholinergic to 782 participants who did not start an OAB anticholinergic. After matching, all measured baseline characteristics were similar (selected ones are shown in table 1). Among the new OAB anticholinergic users, the most common OAB anticholinergic medications were oxybutynin (299/782, 38%), tolterodine (178/782, 23%), and solifenacin (163/782, 21%).

The mean time between the primary visit and follow-up visit was 445 (SD 153) days. There was no significant difference in the change in the primary or secondary outcomes between the unexposed and exposed participants (table 2). The proportion of participants who had a clinically significant change in the CDR score and MMSE score was similar among unexposed and exposed participants (8.1% versus 10.1%, and 20.7% versus 21.9% respectively). In the conditional logistic regression model, there was no significant increased risk of important cognitive decline among OAB anticholinergic users (MMSE decrease ≥ 3 points, OR 1.06, 95%CI 0.79-1.43, $p=0.70$ and CDR increase ≥ 1 point, OR 1.38, 95%CI 0.93-2.05, $p=0.11$). There was no significant interaction between APOE-e4 carriers and clinically important cognitive decline measured with either the CDR ($p=0.38$) or MMSE ($p=0.95$). Results were similar within each cognitive group (normal, mild cognitive impairment, dementia). There was an increased risk of a clinically important change in CDR among users of oxybutynin or tolterodine (OR 1.65, 95%CI 0.98-2.77) that was close to statistical significance ($p=0.06$); this was not seen in users of the other anticholinergics (OR 1.05, 95%CI 0.56-1.97, p-0.87).

INTERPRETATION OF RESULTS

We did not find that the prevalent use of OAB anticholinergic medications was associated with a clinically important change in overall cognitive status, or with a change in three tests of cognitive function. Additionally, APOE-e4 allele carrier status did not have a significant interaction with OAB anticholinergic medication and cognitive decline. This study provides a level of reassurance that the risk of significant cognitive dysfunction in a population with baseline cognitive dysfunction is not impacted by OAB anticholinergic medications, particularly when looking at newer OAB anticholinergic medications (solifenacin, trospium, darifenacin or fesoterodine). The previous literature on longer-term effects (6-12 months) of OAB anticholinergic medications on cognition has been conflicting (with studies both suggesting or refuting a significant effect on cognition), limited by methodologic flaws, and generally not conducted in those with variable levels of baseline cognitive function.(1)

Strengths of our study include the use of valid and sensitive measures of cognitive function, the use of a change threshold to define clinically important cognitive decline (which considers the minimally important differences of the CDR and MMSE), and the creation of matched groups using a propensity score. Limitations of our research include the lack of data on the duration of use of the OAB anticholinergic medications, and the fact that some people may have used OAB anticholinergic medications in between visits and discontinued them before there follow-up (and therefore counted as a non-user).

CONCLUDING MESSAGE

In a population with mixed normal and cognitive impairment, we did not find that there was a significant difference in the proportion of people that developed cognitive impairment when comparing new anticholinergic OAB medication users to propensity score-matched nonusers.

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FIGURE 1

Variable	Value	OAB AC users n = 782	Non-OAB AC users n = 782	p-value
General characteristics				
Age at initial visit	Mean (SD)	74.1 ± 9.0	74.7 ± 8.4	0.196
Sex	Male	302 (38.6%)	303 (38.7%)	0.959
Cognitive status at UDS visit	Normal cognition	393 (50.3%)	393 (50.3%)	1.000
	Mild cognitive impairment	173 (22.1%)	173 (22.1%)	
	Dementia	216 (27.6%)	216 (27.6%)	
Year of education	<12	45 (5.8%)	51 (6.5%)	0.496
	12 to 13	200 (25.6%)	200 (25.6%)	
	14 to 16	251 (32.1%)	263 (33.6%)	
	17+	286 (36.6%)	266 (34.0%)	
Visual impairment		234 (29.9%)	256 (32.7%)	0.484
Hearing impairment		582 (74.4%)	572 (73.1%)	0.751
Living situation	Lives alone	202 (25.8%)	209 (26.7%)	0.445
	Lives with spouse or partner	506 (64.7%)	492 (62.9%)	
	Lives with relative or friend	60 (7.7%)	56 (7.2%)	
	Other	14 (1.8%)	25 (3.2%)	
Medication use				
Antihypertensives		433 (55.4%)	444 (56.8%)	0.575
Antiadrenergic agent		84 (10.7%)	82 (10.5%)	0.870
Calcium channel blocking agent		129 (16.5%)	141 (18.0%)	0.422
Diuretic		100 (12.8%)	120 (15.3%)	0.146
Lipid lowering medication		356 (45.5%)	358 (45.8%)	0.919
Anticoagulant or antiplatelet agent		272 (34.8%)	277 (35.4%)	0.791
Antidepressant		224 (28.6%)	233 (29.8%)	0.617
Antipsychotic agent		16 (2.0%)	21 (2.7%)	0.405
Anxiolytic, sedative, or hypnotic agent		98 (12.5%)	105 (13.4%)	0.598
Alzheimer's disease medications		206 (26.3%)	202 (25.8%)	0.818
Antiparkinson agent		58 (7.4%)	53 (6.8%)	0.622
Estrogen hormone therapy		38 (4.9%)	35 (4.5%)	0.719
Diabetes medication		83 (10.6%)	82 (10.5%)	0.934
APOE genotype	e3,e3	396 (50.6%)	390 (49.9%)	0.995
	e3,e4	242 (30.9%)	245 (31.3%)	
	e3,e2	73 (9.3%)	77 (9.8%)	
	e4,e4	49 (6.3%)	47 (6.0%)	
	e4,e2	20 (2.6%)	20 (2.6%)	
	e2,e2	2 (0.3%)	3 (0.4%)	

Table 1. Selected baseline characteristics of the matched OAB anticholinergic (AC) users and non-users.

FIGURE 2

	Baseline visit	Follow-up visit	Change in score	P value
Non-OAB AC users				
MMSE	26.17 (4.71)	25.26 (5.70)	-1.05 (2.92)	
CDR	2.37 (3.54)	3.21 (4.56)	+0.85 (1.97)	
Boston name test	24.48 (6.06)	24.22 (6.53)	-0.60 (3.05)	
WAIS-R score	37.80 (16.01)	36.57 (17.18)	-1.50 (6.61)	
Trail making test-Part B	133.50 (82.23)	133.18 (85.78)	11.10 (52.12)	
OAB AC users				
MMSE	26.22 (4.57)	25.10 (5.93)	-1.24 (3.21)	0.259
CDR	2.21 (3.25)	3.23 (4.43)	+1.02 (2.19)	0.101
Boston name test	24.83 (5.44)	24.34 (6.21)	-0.67 (2.73)	0.637
WAIS-R score	36.75 (14.83)	35.76 (15.82)	-1.66 (6.97)	0.723
Trail making test-Part B	139.73 (84.88)	142.53 (87.03)	+8.99 (53.50)	0.513

Note: missing data for MMSE (n=207 pairs), Boston naming test (n=272 pairs), for WAIS-R (n=694), and Trail making test part B (n=237 pairs).

Table 2. Primary and secondary outcomes. All results are mean (SD). The p-value is an independent t-test between the change scores of the unexposed and exposed participants.

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BOWEL SYMPTOMS IN THE ELDERLY WOMEN ASSISTED BY PRIMARY HEALTH CARE: A POPULATION-BASED STUDY

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HYPOTHESIS / AIMS OF STUDY

Fecal incontinence and chronic constipation are disabling symptoms that cause a significant public health problem and few studies has focused these pelvic floor dysfunctions in elderly population. The aim of this study was to estimate the prevalence of bowel symptoms in elderly women with pelvic floor dysfunction and to verify associated sociodemographic and clinical factors.

STUDY DESIGN, MATERIALS AND METHODS

It was an analytical, population-based, observational, cross-sectional study that involved women over 60 years of age who were selected through multistage cluster sampling and random draw enrolled in primary health care unit (PHCU) of a specific county, assisted by Community Health Agents (CHA) who belong to the Community Health Agents Program (CHAP) and the Family Health Program (FHP).

The studied population consists of 30.530 people aged over 60 years. Of these, 16.905 (55.4%) are the female population. The city has 465 Community Health Agents (ACS), that cover 84.74% of the population. The sample size was calculated based on a 95% confidence level and a margin of error of 5 %. Then, at least 376 elderly women were necessary.

The selection process was determined through multi-stage cluster sampling, which involved a sequence of stages of random draws from PHCU. The first stage consisted of the random selection of 20 of the 40 PCHU that having a CHAP or FHP. In the second stage, one CHA from each drawn PHCU was randomly selected. In the third stage, each CHA was responsible for visiting 15 elderly women. When the sample size of the specific area exceeded 15 subjects, another CHA was drawn. In case of refusal or exclusion of the volunteer, a new draw was performed. The inclusion criteria were women living in households served by CHA, able to perform the Valsalva maneuver and able to sign the informed consent form. Patients with hearing, verbal, cognitive/mental impairments or neurological conditions that could compromise the interview and complete the questionnaire were excluded as well as women unable to tolerate the physical examination or with a history of pelvic cancer

The FIGO assessment scoring system (FASS) was used to evaluate the bowel symptoms and presence of pelvic organ prolapse. The assessment of the pelvic floor muscle strength was performed using the modified Oxford scale. Physical activity was defined as the performance of physical exercise at least three times a week for a period of not less than one hour.

The chi-square test was used to investigate proportional differences in the prevalence of bowel symptoms based on sociodemographic and clinical variables. Binary logistic regression, including adjusted analysis, was used to evaluate the associations of sociodemographic and clinical variables with the presence of symptoms. For modeling the regression analysis, only the variables that presented a significance level equal to or less than 0.20 in the chi-square test were considered for association with the presence of symptoms of pelvic floor dysfunction. The fit of the model was verified using the Hosmer-Lemeshow test. A significance level of $p < 0.05$ was considered. Data were analyzed using SPSS 22.0 version.

RESULTS

A total of 399 elderly women participated in the study, aged 60 to 93 years-old (68.64 ± 6.65). A high percentage (70.2%) of the elderly women studied had at least one symptom related to pelvic floor dysfunction (PAD). Bowel symptoms were reported by one third of the elderly women, with difficulty in emptying being the most prevalent symptom (90%). However, most of them did not report discomfort (table 1). Initially the presence of bowel symptoms was associated to race, scholarity, physical activity, body mass index (BMI), number of vaginal deliveries, pelvic surgery, and previous hysterectomy ($p < 0.2$). The prevalence analysis of bowel symptoms with the sociodemographic and clinical variables of elderly women using the adjusted regression model demonstrated that the physical activity routine was associated to better bowel emptying but also with anal incontinence. A greater number of vaginal deliveries was also a protective factor for emptying difficulties, but a previous history of abdominal hysterectomy and the presence of obesity were associated with worsening of bowel emptying. The perception of discomfort was proportional to the presence of intestinal symptoms (table 2).

INTERPRETATION OF RESULTS

The FASS, used in present study, defines anal incontinence (AI) as loss of gas, liquid or solid stools and difficulty in emptying as a feeling of incomplete emptying and/or the need to digitation. In this way, 11% of the elderly women surveyed reported symptoms of anal incontinence. The literature indicates that chronic constipation can trigger fecal incontinence in these women, leading to an increase in the prevalence (1). Physical activity may also cause fecal incontinence in younger women (18 and 40 years old), where 14.8% of them who practiced sports for more than 8 hours per week reported incontinence, compared to only 4.9% of less active women (2).

Obesity was also associated with difficulties in bowel emptying, corroborating with other studies who demonstrated an association of BMI with constipation and fecal incontinence. This finding might be justified by the fact that obese women have an abnormal stool consistency (3). Vaginal deliveries had a protective factor for emptying difficulties, despite of obstetric injuries can cause a sphincter rupture in up to 8% of vaginal deliveries or a delivery with forceps can increase this percentage to 35%. Another significant finding was that the previous hysterectomy had a positive association with anal incontinence, suggesting that pelvic floor dysfunctions can also be associated in these cases.

CONCLUDING MESSAGE

The benefits of physical activity and vaginal deliveries in menacme can also extend to the elderly, facilitating bowel emptying, despite increasing the risks of flatus and stool incontinence. The harmful effects of obesity can also extend to the pelvic floor, causing difficulties in bowel emptying in elderly women. Further studies should be performed to confirm the importance of other factors in pelvic dysfunctions.

FIGURE 1

VARIABLES	F	%	I.C. 95%
Scholarity			
Illiterate	165	41.4	36.1-46.4
Incomplete Elementary school	161	40.4	35.6-45.4
Complete Elementary School	29	7.3	4.8-10.0
Complete High School	44	11.0	8.0-14.3
Race			
Black	133	33.4	28.9-37.9
White	125	31.4	26.9-35.9
Mulatto	141	35.2	30.4-39.7
Smoking			
No	301	75,5	71,0-80,0
Yes	48	12,0	8,5-15,1
Ex-smoker	50	12,0	9,3-16,1
Parity			
0 to 2	49	12.3	9.3-15.5
3 to 5	122	30.6	26.6-35.3
More than 5	228	57.1	52.1-61.9
Vaginal deliveries			
0	38	9.5	6.5-12.5
1	18	4.5	2.5-6.8
2 or more	228	86.0	82.5-89.2
IMC			
Normal or under	117	29.4	25.1-33.8
Overweight	139	34.8	30.1-39.6
Obesity	143	35.8	31.1-40.4
Physical activity			
No	304	76.2	71.6-80.2
Yes	95	23.8	19.8-28.4
Physical examination			
Presenting organ above hymen	90	22.6	18.3-27.1
Organ at hymen	181	45.4	40.1-49.9
Organ below hymen	122	30.6	26.3-35.1
Complete eversion	6	1.5	0.5-2.8
Bowel symptoms			
No	259	64.9	60.4-69.4
Yes	140	35.1	30.6-39.6
Anal incontinence (n=140)			
No	124	88.6	82.9-93.6
Yes	16	11.4	6.4-17.1
Emptying difficulties (n=140)			
No	13	9.3	5.0-15.0
Yes	127	90.7	85.0-95.0
Overall bothersome			
No bother	237	59.4	54.6-63.9
Slightly bothered	109	27.2	23.1-31.8
Bothered	31	7.8	5.3-10.3
Very bothered	19	4.8	2.8-7.3
Very much bothered	3	0.8	0.0-1.8
Pelvic floor Strenght (Oxford Scale)			
0	141	35.3	30.8-40.1
1	130	32.6	28.1-36.8
2	73	18.3	14.5-22.3
3 or more	55	13.8	10.5-17.3
Pelvic Surgery			
No	181	45.4	40.4-50.4
Yes	218	54.6	49.6-59.6
Hysterectomy			
No	317	79.4	75.4-83.5
Yes	82	20.6	16.5-24.6

Table 1: Sociodemographic and clinical characterization of the elderly women.

FIGURE 2

Independent variables	OR [C.I 95%]			OR $_{adjusted}$[C.I 95%]		
	Bowel Symptoms	Anal Incontinence	Emptying Difficulties	Bowel Symptoms	Anal Incontinence	Emptying Difficulties
Scholarity						
Illiterate	-	1.00	-	-	1.00	-
Incomplete Elementary school	-	2.105 [0.621-7.132]	-	-	1.782 [0.511-6.213]	-
Complete Elementary School	-	1.437 [0.155-13.339]	-	-	1.394 [0.44-13,.471]	-
Complete High School	-	2.945 [0,.634-13.679]	-	-	1.957 [0.394-9.714]	-
Physical Activity						
No	1.00	1.00	1.00	1.00	1.00	1.00
Yes	0.716 [0.435-1,.180]	**3.402 [1.241-9.329]***	**0.530 [0.309-0.909]***	0.694 [0.414-1.164]	**3.029 [1.018-9.014]***	**0.510 [0.292-0.889]***
BMI						
Under or normal	1,00	-	1,00	1,00	-	1,00
Overweight	0.811 [0.475-1.385]	-	0.890 [0.512-1.547]	0.868 [0.502-1.500]	-	1.000 [0.567-1.764]
Obesity	1.637 [0.984-2.723]	-	**1.737 [1.029-2.930]***	1.660 [0.987-2.793]	-	**1.843 [1.076-3.157]***
Vaginal deliveries						
0	1,00	-	1,00	1,00	-	1,00
1	0.573 [0.183-1.794]	-	0.385 [0.114-1.292]	0.557 [0.173-1.792]	-	0.381 [0.110-1.327]
2 or more	**0.442 [0.225-0.869]***	-	**0.429 [0.218-0.844]***	0.439 [0.219-0.882]	-	**0.406 [0.200-0.821]***
Pelvic surgery**						
Não	1.00	-	-	1.00	-	-
Sim	1.337 [0.882-2.028]	-	-		-	-
Hysterectomy						
No	1.00	1.00	1.00	1.00	1.00	1.00
Yes	1.603 [0.977-2.630]	**3.194 [1.152-8.853]***	1.399 [0.843-2.322]	1.439 [0.862-2.402]	**3.085 [1.088-9.014]***	1.258 [0.741-2.137]

*Significant association ($p < 0.05$); Binary Logistic Regression. OR = *Odds Ratio*; CI = Confidence interval. **Pelvic surgery: Abdominal hysterectomy, tubal ligation e ooforectomy.

Table 2: Prevalence of bowel symptoms, anal incontinence and emptying difficulties according to sociodemographic and clinical variables of elderly women (n = 399)

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Clinical Trial No **Subjects** Human **Ethics Committee** Research **Ethics Committee** HUOC/PROCAPE (UPE) **Helsinki** Yes **Informed Consent** Yes

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10-YEAR FOLLOW-UP OBSERVATION OF IDIOPATHIC DETRUSOR UNDERACTIVITY IN THE ELDERLY LIVING IN COMMUNITY: TREATMENT AND URODYNAMIC CHANGES

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HYPOTHESIS / AIMS OF STUDY

Detrusor underactivity (DU) is not a rare voiding dysfunction associated with lower urinary tract symptoms (LUTS) in the community-dwelling elderly population. However, there have been no urodynamic DU criteria universally applicable in daily practice and the lack of fundamental treatment to restore contractile function of detrusor muscle is an obstacle to establishing a standard strategy for the management of DU. In addition, there is a lack of research on the natural history of the disease and the characteristics of the use of each treatment method, which hinders the establishment of a comprehensive understanding of the disease. Previously, we investigated the prevalence and clinical features of idiopathic DU in the community-dwelling elderly aged over 65 years [1]. In the present study, a cohort of 327 elderly patients with idiopathic DU was followed up over 10 years to investigate the characteristics of the use of each treatment method for DU and urodynamic changes over time.

STUDY DESIGN, MATERIALS AND METHODS

The cohort was prospectively followed up over 10 years with a pre-defined protocol which consists of periodic evaluations with International Prostate Symptom Score (IPSS), 3-day frequency-volume chart, free uroflowmetry, and measurement of post-void residual (PVR) volume. Urodynamic DU was defined as a bladder contractility index (BCI) < 100 for male patients and a maximum flow rate (Qmax) ≤ 12 mL/s combined with a detrusor pressure at Qmax (PdetQmax) ≤ 10 cmH2O for female patients based on a pressure-flow study (PFS). Urodynamic evaluation was conducted repeatedly every 5 or 10 years and additionally after consultation with the patients when the patient's LUTS changed significantly during follow-up. The treatment methods applied to the patients in routine practice were classified into seven categories; medication for the decrease of bladder outlet resistance, endoscopic surgery on the prostate, cholinergics, clean intermittent catheterization, maintenance of indwelling catheter, medication for the improvement of storage symptoms, and observation without treatment. Treatment methods administered at 1 year and 10 years after DU diagnosis were compared, and LUTS, voiding efficacy, and urodynamic index including BCI in male patients and Qmax and PdetQmax in female patients were evaluated at baseline and 10 years after treatment.

RESULTS

The average age of patients was 73.3 years, and 77.7% were male patients. BCI averaged 78.1 in male patients and PFS Qmax and PdetQmax averaged 10.2 mL/s and 7.9 cmH2O in female patients. At 10-year follow-up, evaluation on the treatment methods was performed in 206 (63.0%; male 158, female 48) patients. After 10 years, there was no significant difference in the rate of use of medication for the decrease of bladder outlet resistance, but the use of medication for storage symptoms, cholinergics, and clean intermittent catheterization tended to decrease. On the other hand, the number of observation cases increased significantly to 12.1% (Fig. 1). The storage and voiding score of the IPSS tended to deteriorate. Free Qmax also showed a tendency to decrease from 8.6 mL/s to 7.4 mL/s, and free PVR volume showed a significant deterioration from 78.2 mL to 122.3 mL. Among the patients who repeatedly underwent urodynamic study, BCI deteriorated significantly from 77.5 to 61.7 in male patients, but there were no significant differences in PFS Qmax and PdetQmax in female patients during follow-up.

INTERPRETATION OF RESULTS

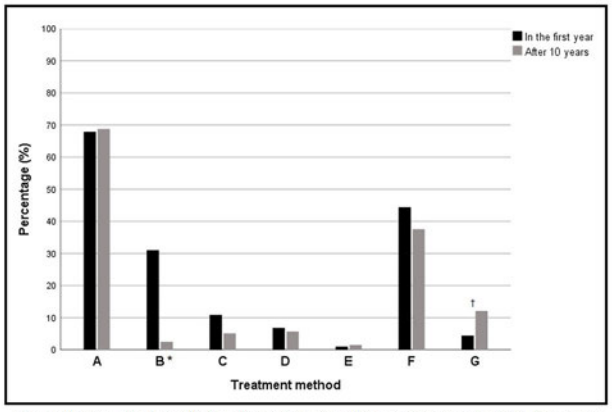
Our study was conducted to improve understanding of natural history of idiopathic DU and to explore what treatment methods are used in actual clinical field. Medications for the decrease of bladder outlet resistance were used in more than 60% of the patients, and, for the same purpose, endoscopic surgery on the prostate was performed on 31% of male patients. Cholinergics were used in 10.9% of the patients during the first year, but its use tended to decrease to 5.1% after 10 years. Presumably, cholinergics may not be an effective medication for the management of idiopathic DU. One of notable findings among the use of treatment methods is that medications for storage symptoms were used in around 40% of the patients both in the first year and 10 years. The number of observation cases without treatment increased significantly from 4.4% to 12.1% and this may imply that there is a group who are reconciled to observation without treatment because all the treatment for idiopathic DU is ineffective. During the 10-year follow-up period, most of LUTS and voiding efficacy tended to deteriorate even though various treatment methods were applied. In particular, free PVR volume showed a significant deterioration over time. Moreover, a significant deterioration in BCI was observed in male patients, while there were no significant differences in PFS Qmax and PdetQmax in female patients during follow-up. Taken together, DU may be a disease condition that progresses slowly and worsens.

CONCLUDING MESSAGE

This study is the first to follow up a cohort of the elderly diagnosed with idiopathic DU over 10 years. The medications for storage symptoms as well as voiding symptoms were often used and free PVR and BCI showed a significant deterioration despite of various treatments. DU is considered a disease that progresses slowly and worsens.

FIGURE 1

Fig. 1. Changes in each treatment method in 206 patients in whom evaluation is available at 10-year follow-up.



The treatment methods applied to the patients in routine practice are classified into seven categories. If multiple treatment methods are applied simultaneously to an individual patient, each treatment method is counted individually. **A**, medication for the decrease of bladder outlet resistance, such as α-blocker and 5α-reductase inhibitor; **B**, endoscopic surgery on the prostate; **C**, cholinergics; **D**, clean intermittent catheterization; **E**, maintenance of indwelling catheter; **F**, medication for the improvement of storage symptoms such as anticholinergics, β3-agonist, and desmopressin; **G**, observation without treatment. * indicates the percentage only in the male patients. † indicates the statistical significance.

Fig. 1. Changes in each treatment method in 206 patients in whom evaluation is available at 10-year follow-up.

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Funding None **Clinical Trial** No **Subjects** Human **Ethics Committee** The Institutional Review Board of the Seoul National University Bundang Hospital **Helsinki** Yes **Informed Consent** No

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VALUE-CREATING CONTINENCE CARE FOR OLDER PERSONS

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HYPOTHESIS / AIMS OF STUDY

This study focuses on what creates value for older persons with incontinence who are provided with toileting assistance and containment strategies. In the older population, and especially for those living in nursing homes, the need for toileting assistance and containment strategies is common.

Several questionnaires are available for the assessment of incontinence as well as for surveying patient-reported outcomes measures (PROMs) to evaluate patients' health status and quality of life, for example. However, there is dearth of questionnaires that focus on patients' experience of receiving care, called "patient-reported experience measures (PREMs)". With a PREM the patient is encouraged to report their actual experience of care, the encounter with health care professionals and the assistance they are provided with.

Having incontinence can be a stigma and needing toileting assistance can be experienced as an intrusion. For this reason, we need more knowledge about what creates value for the older person who is provided with this assistance. The ultimate goal would be to develop a self-report instrument regarding the older person's experiences.

The aim of this study was to describe older persons' and health care professionals' experiences of value-creating continence care.

The research question was: What values are of importance in relation to toileting and containment care for older persons provided with toileting assistance and containment strategies?

STUDY DESIGN, MATERIALS AND METHODS

The study had a descriptive qualitative design using method triangulation (1) to understand the participants' experiences of value-creating continence care in relation to a conceptual framework of value-creating care for older persons with incontinence (2). A critical interpretive synthesis of the literature resulted in the development of the conceptual framework (2). To gain a deeper understanding of older persons' and health care professionals' experiences, qualitative interviews were conducted. The empirical data were compared with and matched to the framework, in order to develop a more complete description of the phenomena (1).

The conceptual framework "the art of connectedness" was based on three themes: co-created care, personalized care, and reflective care, with three subthemes each (see Fig 1).

A purposive sample was used to achieve variations among the participants. Inclusion criteria for older persons (n = 6) were: >65 years of age, living in a nursing home, having incontinence, needing toileting assistance and containment strategies, having reduced physical mobility (measured using the Barthel Index of Activities of Daily Living), and being able to express their needs. The health care professionals consisted of home care staff (n = 4), district nurses with experience and education in incontinence (n = 9) working in municipal care for older persons, and a registered nurse specialized in incontinence care (n = 1).

Data collection was conducted after participants gave their written consent. Individual interviews were conducted with the older persons. The health care professionals were interviewed, either in individual interviews with home care staff or in focus groups with the district nurses and incontinence care nurse.

A thematic analysis with an abductive approach was conducted to search for patterns in the data. Data were analysed in six steps: (i) becoming familiar with the data; (ii) generating initial codes; (iii) searching for themes; (iv) reviewing the themes; (v) defining and naming themes; and (vi) producing the report (3). The data analysis moved between inductive and deductive steps. The first three steps were inductive. In step four, the themes were checked and compared for similarities with and differences from the themes in the conceptual framework. In step five the themes and subthemes were named after their essence, and were found to be in concordance with the framework.

RESULTS

Older persons and health care professionals experience co-created, personalized and reflective care as values of importance in relation to toileting assistance and containment strategies.

In co-created care, the importance of respecting preferences of the older persons was highlighted by the participants, which was in accordance with the framework. This included asking the older persons what assistance they need and how and when they prefer being provided with assistance, and responding to these preferences. The participants rarely mentioned relationships and trust, in contrast to the framework. The health care professionals underlined the need to establish a dialogue with the older person, which was not so prominent in the framework.

Regarding personalized care, meeting the older person's needs was highly valued by all participants. One example of what the older persons valued was not needing to wait for assistance. Promoting the older person's comfort was underlined by the participants and in line with the framework. The importance of assisting the older person in such a way that they can maintain self-determination was described by the health care professionals but not by the older persons. Maintaining self-determination was given more emphasis in the framework than by our study population.

In reflective care, the older persons valued that the health care professionals had a kind approach, which was referred to as "showing empathy" in the framework. The health care professionals stressed the importance of upholding dignity for the older persons, for example by ensuring their privacy while providing assistance, which was also underlined in the framework. The need for health care professionals to have knowledge about and competence in providing assistance was underlined by the participants, and also by the framework

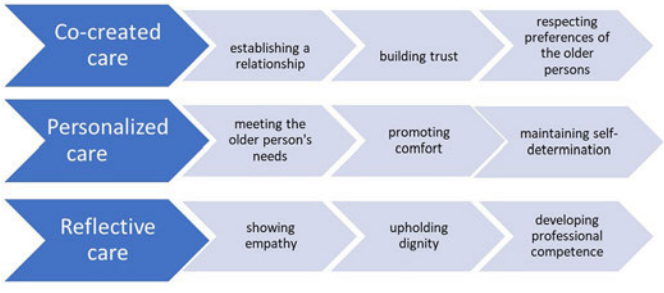
INTERPRETATION OF RESULTS

The results showed that value-creating continence care for older persons provided with toileting assistance and containment strategies can be viewed from different perspectives. The older persons and health care professionals highlighted different aspects (themes) of what creates value. This indicates the need to develop an instrument for the older persons themselves to self-report their experience with the assistance they are provided with. These results, together with the conceptual framework, are envisaged to lay the foundation for suggestions for items to be included in an instrument for evaluating toileting assistance and containment strategies for older persons.

CONCLUDING MESSAGE

Assessing the needs of older persons when provided with toileting assistance and containment strategies is fundamental. Therefore, it is of utmost importance to develop a PREM, to be used by older persons to self-report their own experience and values.

FIGURE 1



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HEALTHY BLADDER STORAGE AND EMPTYING FUNCTIONS IN COMMUNITY-DWELLING WOMEN USING A NOVEL 2-DAY BLADDER HEALTH DIARY.

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HYPOTHESIS / AIMS OF STUDY

To describe the distribution of and factors associated with healthy bladder storage and emptying functions in community-dwelling women using a novel 2-day bladder health diary.

STUDY DESIGN, MATERIALS AND METHODS

We conducted a secondary analysis of participants enrolled in a U.S. cross-sectional study designed to validate a novel bladder health instrument (BHI).(1) Women aged 18+ years were recruited between September 2019 and August 2020 using a delivery sequence file address-based probability sampling frame. Those who completed the primary surveys, which included demographic and medical history, were invited to complete a 2-day bladder health diary. The diary captured bladder storage symptoms (frequency, continence, sensation of urgency and pain), emptying symptoms (initiation, flow, efficacy, relief of urge sensation and pain), and were used to define each individual storage and emptying function (e.g. post void dribbling PVD was captured in column 6, Figure 1.) "Overall healthy bladder function" was defined as up to a mean of 8 voids during waking hours, 0 voids during sleeping hours, and the absence (on both days) of urinary leakage, urinary urgency, or voiding difficulties (including post void dribbling; [PVD]). (2) "Overall healthy voiding experience" was defined as yes responses to "easy starting to pee, continuous stream, feeling the bladder empty and the need to pee feeling is gone;" plus a no response to the item "did you dribble pee when you were done?" Descriptive statistics were used to report overall prevalence of healthy bladder functions. Prevalence of healthy function for each storage and emptying function was assessed. Descriptive statistics were also used to report urinary frequency (waking and sleeping) as well as to describe the prevalence of unhealthy functions including presence and amount of urinary incontinence, frequency of urgency episodes and negative voiding experiences with each void. Presence of pain with storage or emptying and pad usage on either day was also assessed. Means, standard deviations (SD), medians, interquartile ranges (IQR) were used to describe the distribution of voiding frequencies. Stepwise logistic regression models included characteristics associated with healthy function at a $p < 0.2$ on univariate analysis to identify factors associated with healthy bladder function and reported in Odds Ratios (OR) with 95% Confidence Intervals (95%CI). Missing values were handled by single imputation using fully conditional specification methods.

RESULTS

Of 605 respondents in the primary study, 248 returned the 2-day bladder health diary. The mean age was 56.2±15.4 years with 36% being normal weight, 2% underweight and 52% overweight/obese; 53% denied comorbid conditions; 4% were Asian, 6% Black, 88% were non-Hispanic white. Only 12% of women (30/244, 4 missing) had overall healthy bladder function based on our strict definition. Healthy storage function, with voiding frequency during waking hours of 8 or fewer times per day, occurred in 74% (183/248), and 51% (127/248) reported 0 episodes of nocturia. Nocturia occurred once in 30% (74/248), twice in 13% (31/248) and 3 or more times in 6% (16/248). Frequency of urination was 7.6±2.3 (median=7, IQR=3) per 24 hours (7.2±2.2; median=7, IQR=3 during waking hours and 0.8±1.2; median 0, IQR=1 during sleeping hours). A total of 63% (157/248) denied any urine leakage on their 2-day diary; however, those with leakage reported 1.9±1.8 (median=1, IQR=2) leaks per 24 hour period with the majority of leaks being of small volume (68%), and the rest medium (20%) or large (12%) volume. Only 29% (72/248) denied any urgency episodes over 2-days. In those with urgency, the mean daily number of urgency episodes was 3.3±2.5 (median=2.5, IQR=4) and within those women who reported any urgency 39% (IQR=45) of their daily voids were associated with urgency. Overall healthy voiding experience was noted in 47% (91/248) of women. Of those with unhealthy voiding experiences the most common was PVD at 84% (132/157) followed by non-continuous stream (50%, n=80/157), feeling of incomplete emptying (32%, 51/157) and persistent "need to pee" (26%, 40/157). Of those reporting one or more unhealthy voiding experiences on either day of the diary, the median percentage of voids described as unhealthy was 39% (IQR=49). The majority (92%, 225/244, 4 missing) of women denied pain during storage or voiding and of those with pain, 58% (11/19) reported pain with holding, 47% (9/19) pain with peeing and 5% (1/19) pain with both.

Stepwise logistic regression models (Figure 2) identified higher income (OR:95%CI=26.3: 2.8-249.5 for >$150,000 vs. <%50,000), and never previously seeking treatment for bladder problems (OR:95%CI=0.1; 0 -0.9) as associated with overall healthy bladder function. Those with healthy voiding frequency, absence of leakage or PVD were less likely to have sought treatment for bladder problems (OR:95%CI = 0.3: 0.2-0.7; 0.3: 0.1-0.5; 0.2: 0.1-0.5 respectively). Those without leakage, urgency and PVD had fewer comorbidities (OR:95%CI= 0.7: 0.5-0.9; 0.6: 0.4-0.8; and 0.2: 0.1-0.5 respectively. Those working, compared to not working, were more likely to not wake up from sleep to urinate (OR:95%CI: 2.8; 1.3-5.8). There were too few women with pain to evaluate associations between pain free bladder experiences and baseline characteristics.

INTERPRETATION OF RESULTS

The prevalence of overall healthy bladder function for all storage and emptying components, as measured using a 2-day bladder health diary, was very low. Although three in four women void fewer than 8 times during waking and 0 to 1 times during sleeping hours, most community-dwelling women report voiding irregularities and urinary urgency occurring approximately 3 times per day. Two thirds of women deny leakage; however, in those who do report leakage, most have small amounts approximately 2 times a day. Factors associated with healthy bladder functioning include fewer comorbidities, financial security and being a student or working at a job. As expected, having not sought care for bladder problems was associated with healthy storage and emptying functions.

CONCLUDING MESSAGE

A strict definition of overall bladder health based on bladder diaries alone may not represent "normal." The presence of a sudden and urgent need to pee may not be unhealthy, rather a natural response when storage capacity is stressed. Voiding difficulties including PVD and non-continuous stream also occur commonly. Further investigation into whether these clinically defined perturbations in bladder storage and emptying functions are also perceived as unhealthy by women is critical to developing a more informed definition of bladder health and shared treatment goals.

FIGURE 1

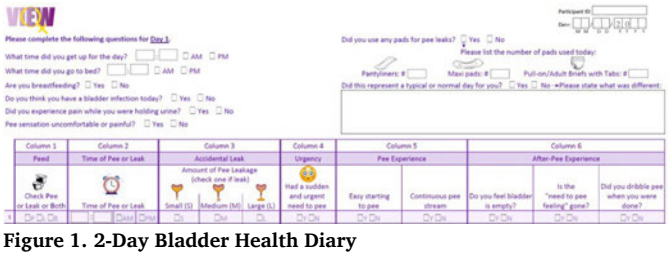
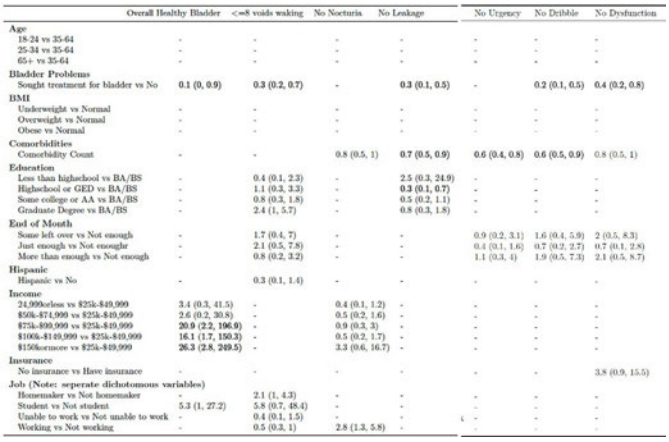


Figure 1. 2-Day Bladder Health Diary

FIGURE 2



	Overall Healthy Bladder	<=8 voids waking	No Nocturia	No Leakage	No Urgency	No Dribble	No Dysfunction
Age							
18-24 vs 35-64	-	-	-	-	-	-	-
25-34 vs 35-64	-	-	-	-	-	-	-
65+ vs 35-64	-	-	-	-	-	-	-
Bladder Problems							
Sought treatment for bladder vs No	**0.1 (0, 0.9)**	**0.3 (0.2, 0.7)**	-	**0.3 (0.1, 0.5)**	-	**0.2 (0.1, 0.5)**	**0.4 (0.2, 0.8)**
BMI							
Underweight vs Normal	-	-	-	-	-	-	-
Overweight vs Normal	-	-	-	-	-	-	-
Obese vs Normal	-	-	-	-	-	-	-
Comorbidities							
Comorbidity Count	-	-	0.8 (0.5, 1)	**0.7 (0.5, 0.9)**	**0.6 (0.4, 0.8)**	**0.6 (0.5, 0.9)**	0.8 (0.5, 1)
Education							
Less than highschool vs BA/BS	-	0.4 (0.1, 2.3)	-	2.5 (0.3, 24.9)	-	-	-
Highschool or GED vs BA/BS	-	1.1 (0.3, 3.3)	-	**0.3 (0.1, 0.7)**	-	-	-
Some college or AA vs BA/BS	-	0.8 (0.3, 1.8)	-	0.5 (0.2, 1.1)	-	-	-
Graduate Degree vs BA/BS	-	2.4 (1, 5.7)	-	0.8 (0.3, 1.8)	-	-	-
End of Month							
Some left over vs Not enough	-	1.7 (0.4, 7)	-	-	0.9 (0.2, 3.1)	1.6 (0.4, 5.9)	2 (0.5, 8.3)
Just enough vs Not enough	-	2.1 (0.5, 7.8)	-	-	0.4 (0.1, 1.6)	0.7 (0.2, 2.7)	0.7 (0.1, 2.8)
More than enough vs Not enough	-	0.8 (0.2, 3.2)	-	-	1.1 (0.3, 4)	1.9 (0.5, 7.3)	2.1 (0.5, 8.7)
Hispanic							
Hispanic vs No	-	0.3 (0.1, 1.4)	-	-	-	-	-
Income							
24,999orless vs $25k-$49,999	3.4 (0.3, 41.5)	-	0.4 (0.1, 1.2)	-	-	-	-
$50k-$74,999 vs $25k-$49,999	2.6 (0.2, 30.8)	-	0.5 (0.2, 1.6)	-	-	-	-
$75k-$99,999 vs $25k-$49,999	**20.9 (2.2, 196.9)**	-	0.9 (0.3, 3)	-	-	-	-
$100k-$149,999 vs $25k-$49,999	**16.1 (1.7, 150.3)**	-	0.5 (0.2, 1.7)	-	-	-	-
$150kormore vs $25k-$49,999	**26.3 (2.8, 249.5)**	-	3.3 (0.6, 16.7)	-	-	-	-
Insurance							
No insurance vs Have insurance	-	-	-	-	-	-	3.8 (0.9, 15.5)
Job (Note: seperate dichotomous variables)							
Homemaker vs Not homemaker	-	2.1 (1, 4.3)	-	-	-	-	-
Student vs Not student	5.3 (1, 27.2)	5.8 (0.7, 48.4)	-	-	-	-	-
Unable to work vs Not unable to work	-	0.4 (0.1, 1.5)	-	-	-	-	-
Working vs Not working	-	0.5 (0.3, 1)	2.8 (1.3, 5.8)	-	-	-	-

Figure 2. Multivariable regression models for each healthy bladder definition, OR (95% CI)

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ASSOCIATION OF THIGH MUSCLE STRENGTH, AREA, AND SPECIFIC FORCE WITH INCIDENT URINARY INCONTINENCE IN OLDER ADULTS: THE BALTIMORE LONGITUDINAL STUDY OF AGING

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HYPOTHESIS / AIMS OF STUDY

Urinary incontinence (UI) in older adults is common and associated with mobility limitations.[1] Lower extremity muscle health is critical for maintaining mobility in older age. Therefore, age-related thigh muscle changes are potential, yet unexplored, shared mechanisms of both UI and mobility limitations.

STUDY DESIGN, MATERIALS AND METHODS

This analysis includes 227 women and 231 men enrolled in the Baltimore Longitudinal Study of Aging. We restricted the analysis to community-dwelling older adults age ≥60 years with no history of stroke or Parkinson's disease and no missing UI or muscle measures seen between February 2011 and September 2015. UI severity and type were assessed by asking "During the past week (7 days), how many times did you leak urine under the following conditions?" and "In the past 12 months, how often have you leaked urine?" Stress UI was defined by "With an activity like coughing, lifting, or exercise", urgency UI was defined by "When you had a sense of urgency and could not get to a toilet fast enough", other UI was defined by "Unrelated to an activity or urge to urinate", and mixed UI as the presence of both urgency and stress UI. We excluded participants who reported at least weekly UI at analytic baseline. Given the limited number of events for individual UI subtypes, our primary outcome was new at least weekly UI of any subtype. Thigh muscle strength (Nm) was defined as maximum concentric 30˚/s knee extensor torque. Thigh muscle area (cm2) was estimated using mid-femur cross-sectional 10-mm CT images. Thigh muscle specific force (Nm/cm2) was defined as strength divided by area. We used multivariable interval censored cox regression to model associations between tertiles of thigh muscle measures (strength, area, specific power) and incident at least weekly UI. Associations were stratified by sex and adjusted for age, race, height, weight, height*weight, and physical activity. We conducted sensitivity analyses further adjusting for number of live births or hormone replacement therapy among women.

RESULTS

Baseline characteristics of the analytic study population are reported in Table 1. Mean follow-up time was 3.2 years. Overall, the incidence of at least weekly UI was 9.1/100 person-years for women and 7.8/100 person-years for men. Among the 75 women with incident UI, 53% developed urgency UI, 31% stress UI, and 16% other/mixed UI. Among the 82 men with incident UI, 50% developed urgency UI, 19% stress UI, and 31% other/mixed UI. Compared to women in the lowest tertile of thigh muscle area, the hazard ratio for incident UI was 49% lower among women in the middle tertile (hazard ratio = 0.51, 95% CI 0.27, 0.97) and 54% lower among women in the highest tertile (hazard ratio = 0.46, 95% CI 0.20, 1.07; Figure 1). Conversely, after multivariable adjustment thigh muscle area was not significantly associated with incident UI in men and thigh muscle strength or specific force were not significantly associated with incident UI in women or men (95% CI included 1.0 for all). Further adjusting for number of live births or hormone replacement therapy among women did not meaningfully impact the results.

INTERPRETATION OF RESULTS

In this prospective cohort study of community-dwelling older adults, we observed an association between greater thigh muscle area and lower risk of incident UI in older women but not older men. Thigh muscle strength and specific force were not associated with incident UI in either sex. This study extends existing cross-sectional data suggesting that older women with UI have poorer lower extremity strength and function.[2] Although we are not aware of other longitudinal studies that have examined this relationship, our findings are also consistent with prior literature demonstrating that older women with incident UI have increased risk of lower extremity functional decline.[3] Although prospective studies with larger sample sizes are needed to confirm our findings, low thigh muscle area may reflect emerging sarcopenia, an unexplored mechanism of UI that could partially explain why older women with UI have increased risk of mobility limitations.

CONCLUDING MESSAGE

This novel study provides preliminary evidence for a relationship between thigh muscle area and risk of UI in older women. While we did not observe statistically significant associations between thigh muscle measures and incident UI in older men, our power may have been insufficient to detect modest but clinically meaningful effects. These relationships should be evaluated in larger prospective cohort studies of older adults with detailed assessments of UI subtypes.

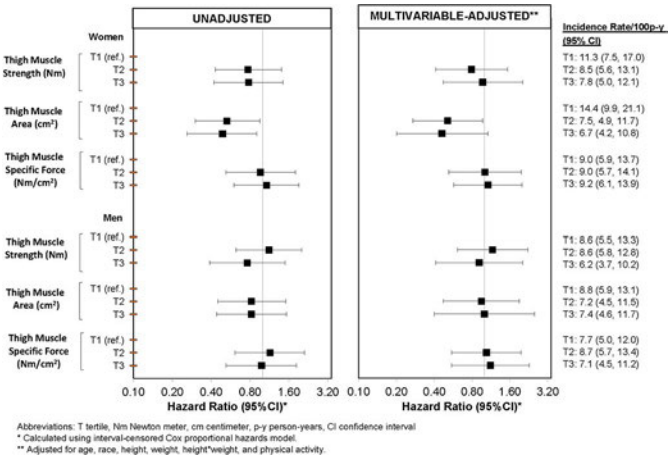
FIGURE 1

	Women		Men	
	Lowest Tertile (n=76)	Highest Tertile (n=75)	Lowest Tertile (n=77)	Highest Tertile (n=77)
Age, years, mean ± SD	75.6 ± 7.5	67.6 ± 6.0	78.7 ± 7.1	67.0 ± 5.8
Race, n (%)				
White	52 (68)	26 (34)	63 (82)	45 (59)
Black	14 (18)	47 (62)	7 (9)	28 (37)
Asian, Other Race, or Multiracial	10 (13)	3 (4)	7 (9)	3 (4)
Height, cm, mean ± SD	160 ± 5	163 ± 6	173 ± 8	176 ± 6
Weight, kg, mean ± SD	62 ± 10	79 ± 13	76 ± 11	94 ± 14
BMI, kg/m², mean ± SD	24.1 ± 3.6	29.9 ± 4.6	25.3 ± 2.7	30.5 ± 4.1
Waist circumference, cm, mean ± SD	77 ± 11	88 ± 10	90 ± 9	101 ± 11
CES-D, mean ± SD	4.9 ± 5.2	4.6 ± 4.6	4.7 ± 4.2	4.8 ± 5.3
California Verbal Learning Test, mean ± SD	51 ± 14	53 ± 10.4	43 ± 12	49 ± 11
Trails-Making Test Part A, mean ± SD	35 ± 12	31 ± 12	36 ± 16	31 ± 11
Alcohol Intake, n (%)				
0 to <1 drink/week	40 (53)	33 (45)	30 (39)	31 (41)
1-7 drinks/week	27 (34)	32 (43)	32 (42)	33 (43)
≥8 drinks/week	9 (12)	9 (12)	15 (20)	12 (16)
Smoking, n (%)				
Never	52 (68)	57 (76)	47 (61)	51 (66)
Quit ≥10 years ago	23 (30)	16 (21)	29 (38)	24 (31)
Current or quit <10 years ago	1 (1)	2 (3)	1 (1)	2 (3)
Vigorous physical activity, min/week, mean ± SD	84 ± 104	104 ± 173	101 ± 134	98 ± 186
Comorbidities and Medication Use, n (%)				
Diabetes Mellitus	11 (15)	16 (21)	19 (25)	18 (23)
Hypertension	35 (46)	42 (55)	36 (47)	40 (53)
High Cholesterol	51 (67)	44 (59)	52 (70)	53 (70)
Chronic Obstructive Pulmonary Disease	5 (6.6)	0 (0)	4 (5)	0 (0)
Diuretic Medication Use	4 (5.3)	15 (20)	8 (10)	5 (7)
Anti-cholinergic Medication Use	1 (1.3)	0 (0)	0 (0)	1 (1)
Female-Specific Factors				
Ever Pregnant, n (%)	61 (80)	65 (86)	-	-
Number of Live Births, mean ± SD	2.4 ± 1.7	2.2 ± 1.5	-	-
Hormone Replacement Therapy, n (%)	44 (60)	35 (46)	-	-
History of Hysterectomy, n (%)	23 (30)	22 (29)	-	-
Thigh Muscle Strength, Nm, mean ± SD	80 ± 21	109 ± 28	122 ± 27	167 ± 39
Thigh Muscle Area, cm², mean ± SD	68 ± 7	104 ± 10	99 ± 9	152 ± 17
Thigh Specific Force, Nm/cm², mean ± SD	1.18 ± 0.3	1.05 ± 0.3	1.23 ± 0.3	1.11 ± 0.3

Abbreviations: SD standard deviation; n sample size; cm centimeter; kg kilogram; m meter; CES-D Center for Epidemiologic Studies Depression Scale; Nm Newton meter

Table 1. Characteristics of Older Women and Men Without Urinary Incontinence at Baseline, by Sex and Extreme Tertile of Thigh Muscle Area (cm2).

FIGURE 2



Abbreviations: T tertile, Nm Newton meter, cm centimeter, p-y person-years, CI confidence interval
* Calculated using interval-censored Cox proportional hazards model
** Adjusted for age, race, height, weight, height*weight, and physical activity.

Figure 1. Unadjusted and Multivariable-adjusted Associations of Baseline Thigh Muscle Strength, Area, and Specific Force with Incident At Least Weekly Urinary Incontinence among Older Adults, Stratified by Sex.

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ANTICHOLINERGIC BURDEN DECREASES VOIDING EFFICIENCY IN THE ELDERLY FACILITIES.

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HYPOTHESIS / AIMS OF STUDY

Some studies have estimated that in nursing homes more than 30 % of older residents take more than two anticholinergic drugs, and 5 % take more than five. Furthermore, an estimated 51 % of the general population use anticholinergic drugs. The Anticholinergic Cognitive Burden (ACB) scale is an index that classifies anticholinergic drugs with an anticholinergic effect (which may affect mortality and worsening cognitive function) into scores of 1 to 31. A one-point increase in the mean total daily ACB scale was associated with a 16% increased risk of cognitive impairment, and it increased the likelihood of inpatient admission by 11% and the number of outpatient visits2. An increased anticholinergic burden is also likely to affect bladder, defecation, and swallowing functions. Herein, we investigated the influences of the anticholinergic burden on the lower urinary tract functions of elderly subjects.

STUDY DESIGN, MATERIALS AND METHODS

We analyzed the cases of elder-care facility residents whose bladder capacity were evaluated by abdominal ultrasonography or a Lilium α-200 Bladder Volume Ultrasound System (Lilium Otsuka Co., Sagamihara, Japan)3. Residents were excluded if they were unable to respond to various questionnaires such as frailty score, barthel index, IPSS, IPSS-QOL, and OABSS, had a prostate volume of ≥35 ml, or had an indwelling urethral catheter. For the residents who could urinate in a toilet, the voided volume and residual urine volume were measured three times, and the average values were calculated. For those who urinated in a diaper all day, the bladder capacity and residual urine volume were measured continuously for 24 hr with the Lilium α-200 because the urination time could not be identified. The nadir of the bladder capacity was defined as the residual urine volume, and the difference between the maximum bladder capacity and the nadir of the bladder capacity was defined as the voided volume. Furthemore, we divided residents into two groups depending on ACB score, and examined the difference of both groups with respect to voided volume, residual urine volume, and voiding efficacy. All statistical analyses were performed using IBM SPSS 28.0 （SPSS Inc., Chicago IL, USA）. Differences between the paired measurements were evaluated by paired t tests when distribution was normal, or by Mann - Whitney U tests otherwise. All tests were two-sided, with $P<0.05$ considered statistically significant.

RESULTS

Of the 342 residents in four elder-care facilities, the evaluable cases were 202 residents (43 men, 159 women). The average age was 87.7 ± 7.1 years. The comorbidities were hypertension in 133, dementia in 119, stroke in 73, chronic heart failure in 68, and diabetes in 45 cases. Median frailty score is 3, barthel index is 35, IPSS is 5, IPSS-QOL is 5, and OABSS is 5. The mean values of voided volume, residual urine volume, and voiding efficiency were 140.8 ml, 109.5 ml, and 57.6%, respectively. Since the median ACB score was 2 points, we divided the residents into two groups: those with an ACB score ≤2 points (n=119) and those with ≥3 points (n=76). Among the comorbidities, percentage of patients with hypertension was significantly higher in the group with ACB ≥3 points than that with ≤2 points (77.6% vs. 52.9%; p=0.026). The mean value of residual urine volume was significantly higher (130.1 ml) in the ≥3-points group compared to 96.3 ml in the ≤2-points group (p=0.007). Voiding efficiency was significantly lower in the ≥3-points group than in the ≤2-points group (49.2% vs. 62.3%, respectively; $p<0.001$). However, no significant difference was found in average voided volume between the ≥3-points and ≤2-points groups (124.9 vs. 141.6 ml; p=0.265).

INTERPRETATION OF RESULTS

These results suggest that the long-term burden of drugs with anticholinergic effects in the elderly was associated with a decrease in voiding efficiency. Hypertension was more frequent in the group with ACB ≥3 points because many patients were taking drugs classified as ACB score 1, such as Nifedipine, Captopril, Triamterene, and Furosemide.

CONCLUDING MESSAGE

Clinicians must keep in mind that the anticholinergic burden already reduces the voiding efficiency of elderly individuals.

FIGURE 1

Table.1 : Demographic and clinical characteristics of two groups.

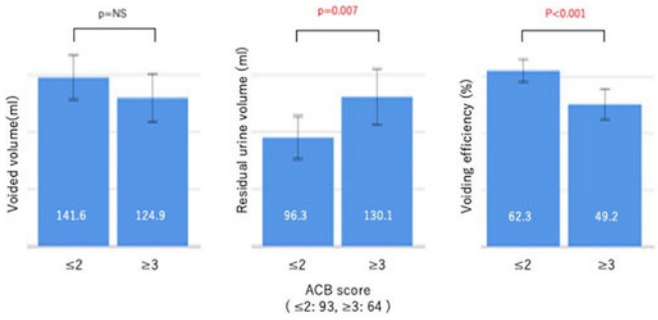
	ACB score ≤2	ACB score ≥3	P-value
Total	123	79	-
Age (y/o)	88.3	88.5	NS
Male	30	13	NS
Female	93	66	NS
Body weight (kg)	44.3	43.5	NS
BMI (kg/m²)	20.3	20.6	NS
Systlic BP (mmHg)	119.9	124.4	NS
Diastlic BP (mmHg)	67.9	70.5	NS
【Comorbidity】			
Hypertension	74	59	0.026
Dementia	65	54	NS
After stroke	39	24	NS
Chronic heart failure	39	29	NS
Diabetes melitus	21	24	NS
Overactive bladder	11	12	NS
Benign prostatic hyperplasia	15	10	NS
Neurogenic bladder	8	2	NS

	ACB score ≤2	ACB score ≥3	P-value
【General condition】			
Frailty index	2.4	3.0	NS
Barthel index	34.9	35	NS
NQOL			
【LUTS】			
IPSS	6.7	9.7	NS
IPSS-QOL	2.6	2.3	NS
OABSS	5.1	5.3	NS
【Urinary condition】			
Residents who can urinate in a toilet	32	23	NS
Residents urinating in a diaper only at night	33	20	NS
Residents urinating in a diaper all day	28	21	NS
【Medication】			
Number of drugs	4.5	6.7	<0.001

percentage of patients with hypertension was significantly higher in the group with ACB ≥3 points than that with ≤2 points (77.6% vs. 52.9%; p=0.026).

FIGURE 2

Figure.1 : Correlation between ACB score and voiding function.



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OUTCOMES OF INTRADETRUSOR INJECTION OF ONABOTULINUMTOXINA (BTX-A) FOR OVERACTIVE BLADDER IN THE ELDERLY POPULATION.

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HYPOTHESIS / AIMS OF STUDY
Overactive bladder (OAB) is a common condition in patients older than 70 years of age and its prevalence increases with age. AUA guidelines recommend oral anticholinergics and b-3 agonists as second line therapy. However, these medications have been associated with negative cognitive effects and may negatively affect the blood pressure in elderly respectively. Furthermore, b-3 agonists do not have an acceptable formulary medication coverage, additional concern for elderly with limited insurance coverage. Currently there is lack of evidence assessing the outcomes of OnabotulinomtoxinA (BTX-A) injection as a third line OAB therapy, evaluating its efficacy and safety in the elderly population.

STUDY DESIGN, MATERIALS AND METHODS
A retrospective chart review of patients seen at the Urology and Urogynecology clinic who underwent intradetrusor BTX-A from May 2015 to September 2021 was obtained. Patients older than 70 years of age at the time of their first injection were selected. Baseline characteristics, assessment of overactive bladder symptoms based on self-reported symptoms before and after injection were retrieved.

RESULTS
141 patients over 70 years of age who had intradetrusor BTX-A were selected. 124 (88%) were female. Prior to injection 94% (132) were voiding spontaneously. Urinary urgency was the most common symptom in 97.3%, followed by urinary incontinence, daytime frequency in 93% and 85% respectively. The most common medications initially prescribed were anticholinergic in 74%, followed by b-3 agonist in 19%. The amount of BTX-A injected was 100U (89%) and 200U (6%).

Subgroup analysis by OAB symptom domain after BTX-A showed that patients noted a significant improvement in 73% for incontinence, 77% for urinary urgency, 72.5% daytime urinary frequency and 68% in nighttime frequency. Temporary de novo intermittent catheterization was initiated in four patients and one needed indwelling catheter placement. 57% returned for repeated injections due to good symptom response. Twenty-six (18%) had a symptomatic UTI at follow-up and 73% were not needing OAB medications after follow-up.

Subgroup analysis of patients who were over 80 years of age (n = 26/141) at the time of first BTX-A injection was performed. Twenty-two (85%) were female, 92% were voiding spontaneously, on initial presentation urinary urgency was reported in 26 (100%), urinary incontinence 96%, daytime urinary frequency in 73%. Medications initially prescribed were Anticholinergics in 50% and Beta 3 Agonists in 38%. The most common cause for undergoing BTX-A was no response to oral medications. Urinary urgency showed marked improvement on 81% and urinary incontinence of 73% of patients after injection. Symptomatic urinary tract infection was seen in 3 (12%) of this group of patients.

INTERPRETATION OF RESULTS
BTX-A is well tolerated in patients older than 70 with significant improvement in all OAB symptom domains and significant reduction of their oral OAB medication needs. This provides an option for patients to limit oral medications with unwanted side effects for this special population potentially at an earlier time in the OAB management algorithm.

CONCLUDING MESSAGE
Use of intradetrusor BTX-A injection for elderly patients is safe, effective and will avoid detrimental cognitive and blood pressure changes caused by oral OAB medications in patients with overactive bladder over 70 years of age.

Funding N/A **Clinical Trial** No **Subjects** Human **Ethics Committee** Houston Methodist IRB **Helsinki** Yes **Informed Consent** No

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EFFECT OF ANTIMUSCARINIC DRUGS ON COGNITIVE FUNCTIONS IN THE MANAGEMENT OF OVERACTIVE BLADDER IN ELDERLY

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HYPOTHESIS / AIMS OF STUDY
Overactive bladder (OAB) affects 17-41% of older adults in community dwelled settings. For several years, antimuscarinics have been validated as the first-line medical treatment for OAB. Despite abundant data obtained from clinical trials provisions the use of antimuscarinics, investigation about the effect of this drug on cognitive function in the elderly remains scarce. This study aims to investigate the effect of antimuscarinics therapy on cognitive functions in OAB geriatric patients.

STUDY DESIGN, MATERIALS AND METHODS
This study design is a systematic review and meta-analysis. Studies were collected using several search engines; those were PubMed, Science Direct, Cochrane, and EBSCOhost using predetermined MeSH keywords with Boolean operators. The selection of studies was done by three reviewers. Studies that fulfilled the inclusion and exclusion criteria underwent a full-text review. For every selected full text, we extracted the following data is available: patients demographics, types of antimuscarinics used, placebo, dose, follow-up period, and Mini-Mental State Examination (MMSE) total score

RESULTS
A total of 146 publications were initially retrieved (Figure 1). Of these, 106 studies were excluded due to duplication. Moreover, 28 were excluded during title and abstract screening. Eight studies underwent full-text appraisal, both qualitative and quantitative analysis. There were 8 antimuscarinic agents evaluated in the studies, including Oxybutynin, Darifenacin, Tolterodine, Trospium, Imidafenacin, Propiverine hydrochloride, Fesoterodine, and Solifenacin.

INTERPRETATION OF RESULTS
Esin et al investigated the effect of antimuscarinic medications on elderly cognitive functions. It was shown that no cognitive impairment was observed in the patients involved in the study who were using these medications. No cognitive impairment was observed in the study population who had dementia at the beginning of the study. From the antimuscarinic medications being used in the study, the oxybutynin and darifenacin group was shown to significantly decrease MMSE scores.

CNS adverse effects such as cognitive impairment might occur because many antimuscarinics can cross the blood-brain barrier. This issue is addressed as a serious consideration in antimuscarinic therapy for elderly OAB patients. The guidelines often recommended oxybutynin. However, a high incidence of cognitive impairment is noted with the administration of this drug. Therefore, administration of oxybutynin is not recommended in frail elderly OAB patients.

Oxybutynin is a highly lipophilic compound, which allows it to cross the blood-brain barrier and causes effects on the central nervous system (CNS). The high lipophilicity, neutrality, and small molecular size of oxybutynin may allow the drug to cross the blood-brain barrier and skin more easily relative to other antimuscarinic agents.

CONCLUDING MESSAGE
The use of most but not all antimuscarinics medication has little to no effect on the cognitive function in the management of overactive bladder in elderly patients. However, Oxybutynin, Darifenacin, and Tolterodine was shown to have significant decrease in cognitive functions, as shown in the decline of total MMSE score.

Funding The first author of the paper (E. Rangganata) received a scholarship from Indonesia Endowment Fund for Education (LPDP scholarship) from the Ministry of Finance, Republic of Indonesia. **Clinical Trial** No **Subjects** Human **Ethics not Req'd** This study was written in the form of systematic review and meta-analysis **Helsinki** not Req'd This study was written in the form of systematic review and meta-analysis **Informed Consent** No

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THE DAILY EXPERIENCE OF URINARY INCONTINENCE IN PEOPLE LIVING WITH DEMENTIA AND THEIR CARE PARTNERS: A QUALITATIVE EXPLORATORY STUDY

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HYPOTHESIS / AIMS OF STUDY

People living with dementia (PLWD) are twice as likely to be diagnosed with urinary incontinence (UI) than those without dementia. UI becomes increasingly common as the disease progresses (1). Both dementia and UI impair the health and well-being of the individual, but these conditions also affect care partners (CP), spouses or family members who provide day-to-day care for the individual, who may experience stress and depression (2). Furthermore, the burden of managing UI has been associated with the CP's choice to move the PLWD from the community to a care home (1). There is a paucity of evidence informed UI management for PLWD so trial and error is often employed (1). This exploratory study aimed to gain an understanding of the daily experience of UI, its management and impact on community dwelling PLWD and their CPs via semi-structured interviews. With a deeper understanding of how UI affects PLWD and their CP, management strategies tailored for PLWD can be developed.

STUDY DESIGN, MATERIALS AND METHODS

Qualitative description design. Between September, 2021 and January 2022, participants were recruited in dyads from a secondary care continence clinic, comprising a community dwelling PLWD and their CP. PLWD with either moderate or severe UI on the Sandvik severity index were included (3). After reviewing participant information sheets, verbal consent was given to take part in a semi-structured interview, lasting up to 45 minutes, conducted either over the phone or by Zoom. Due to the virtual nature of the interview, this approach was approved by the local ethics board. The PLWD and their CP were interviewed together, and each were asked questions pertaining to their experiences with dementia and UI management. Topics of enquiry included the nature, extent, duration and likely underlying nature of the UI and the history of healthcare seeking or self management of UI. Using a semi-structured interview guide, participants were asked to identify UI management strategies they had employed and their experience with them. Additionally, the impact of dealing with dementia and UI on the CP, the PLWD, and the relationship between the dyad was explored. The interviews were digitally recorded, de-identified and transcribed verbatim. Data were analyzed using a content analysis approach. The first two transcripts were independently coded by three researchers who then met to compare notes and develop the coding framework. The remaining transcripts were coded by a single researcher, and any new codes were reviewed with the other researchers. Data for each code were reviewed by the team and collapsed into categories and themes.

RESULTS

Eight dyads, consisting of married male and female partners were interviewed. Data analysis resulted in 17 categories and 5 themes. The themes included 1) What brings it on, 2) Trying to manage, 3) Asking for help, 4) Relationship and 5) Burdens (Table 1).

What brings it on:

UI was described by the CP and or the PLWD in terms of UI triggers, cause, timing and severity. UI triggers were physical and auditory, such as laughing, coughing and running water. Washroom accessibility related to dementia symptoms (e.g. not remembering to go to the washroom), particularly at night, was discussed as a contributor to UI. PLWD and their CP described UI in terms of timing and severity, with emphasis on the fluctuation of severity over time.

Trying to manage:

PLWD and their CP spoke about how they managed UI. This included how they initially addressed UI and a variety of strategies that either worked or didn't work. PLWD and their CPs were unsure how to address UI, and they believed that when they identified leakage as being UI, it made it more of a concrete problem. Dyads discussed 3 main types of management strategies: preventative/anticipatory strategies, aids and devices, and social strategies. Preventative measures included strategies such as setting a reminder timer for the washroom and using the washroom whenever they had access to prevent UI. Aids and devices were containment products (e.g. pads, depends or plastic bedding) or physical aids (e.g. a walker or a raised toilet seat). Social strategies, including hiding UI from others, were used in an effort to reduce the social impact of UI. Management strategies had varying efficacy. Some dyads felt that advice about UI management strategies were limited or non-existent or that healthcare professionals were not sure how to address UI. PLWD and CP discussed hypothetical management strategies they believed would be beneficial, such as something to stop leaks or control their urgency.

Asking for help:

PLWD and their CP's talked about seeking information or additional assistance from a variety of sources to manage dementia and UI, such as their children and hired help. The CP and or the PLWD spoke about wanting information from healthcare professionals, including physicians and nurse practitioners, on how to control UI and some of the barriers to accessing this information, such as waiting for healthcare and unclear or conflicting information.

Relationship:

Dealing with UI and dementia changed the relationship between the PLWD and the CP in both positive and negative ways. The CP spoke of supporting the PLWD beyond assisting with tasks through being attentive and encouraging independence. Dyads experienced changes due to dementia and UI, but they were able to accept these changes.

Burdens:

The PLWD and their CP experienced considerable burdens as a result of dealing with dementia and UI. Some aspects, like sleep interference and having to change clothes following an accident were specific to the PLWD, and others such as fatigue and an increase in responsibility were unique to the CP. Additionally, a diminishing social life, frustration and the possibility of relocation to a care home were felt by both PLWD and CP.

INTERPRETATION OF RESULTS

According to PLWD and UI and their CP, dementia symptoms were implicated in the occurrence of UI. Although PLWD and their CP were unsure about how to manage UI and information on how to do so was difficult to obtain, some dyads were able to adopt management strategies that were beneficial. On the other hand, some dyads discussed management strategies, such as medication, that were minimally effective, and felt that choices for UI management were limited. Additionally, some dyads found healthcare professionals unsure about how to address UI. Dyads expressed multiple effects as a result of dementia and UI, including both positive and negative consequences for their relationship and the impact of specific burdens.

CONCLUDING MESSAGE

For PLWD and their CP, UI is associated with relationship changes and burdens. Although some PLWD and their CP were able to find effective ways of managing their UI, others did not and some felt that this was due to shortcomings of the healthcare system.

To improve the situation, dementia specific UI management information should be created to address the factors illustrated here, means to ensure wide information availability ensured, and clinical management strategies for UI specific to PLWD developed.

FIGURE 1

Table 1. Themes, categories and sample quotes

Themes	Categories	Exemplar quotes
What brings it on	- UI triggers - Dementia-related washroom accessibility - UI timing and severity	**SI-4:** "*CP:* I think sometimes you know, with dementia, she forgets you know, how long she's been sitting and by the time she realizes she has to go to the bathroom, it's too late."
Trying to Manage	- Preventative/anticipatory UI management strategies - Aids and devices as UI management strategies - Social UI management strategies - Nothing they could do - Wish they had - Addressing UI	**SI-4:** "*CP:* well, she tries to, I'll try and help her speak to it just so she … she tries to get up more often like uh if she's sitting and watching TV or whatever and during the day and uh, and we, she watches like if we're out should she go to the bathroom before we leave and uh how long the trip is gonna be and whatever. And I guess at times she watches what she drinks."
Asking for help	- Asking for outside help - Accessing information	**SI-3:** "*CP:* That would always be good to know how to, how to control- …how can we limit the problem … I don't think you'll ever eliminate it but it's the management"
Relationship	- Dyad relationship - Emotional support - Changes	**SI-1:** "*CP:* and I think it may be uh maybe there's some irritation every now and again. *PLWD:* there's bound to be… *CP:* no I'm not bossy but I do direct [laughing] I definitely direct him."
Burdens	- PLWD burdens - CP burdens - Dyad burdens	**SI-8:** "*CP:* well, it's there is stress because the children feel we should go into a um retirement home or something and I'm not prepared for that, yeah and I don't think [PLWD] wants it either. *PLWD:* no far from it."

Table 1. Themes, categories and sample quotes

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THE INFLUENCE OF AGE AND HEALTH STATUS FOR OUTCOMES AFTER MID-URETHRAL SLING SURGERY – A SWEDISH NATIONAL REGISTER STUDY

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HYPOTHESIS / AIMS OF STUDY

Despite being safe and less invasive than traditional surgery for stress urinary incontinence (SUI), proportion of mid-urethral sling surgeries performed in older women has decreased [1]. SUI prevalence increases with age and incurs a high cost for the individual and society [2]. However, evidence of the efficacy of mid-urethral sling surgery in older women and women with a significant disease burden is limited. This study in women, grouped according to the American Society of Anesthesiologists Physical Status (ASA) class, examined the influence of chronological age and disease burden on satisfaction, improvement, cure, and adverse events at a 1-year follow-up following mid-urethral sling surgery.

STUDY DESIGN, MATERIALS AND METHODS

This cohort study was based on the Swedish National Quality Register of Gynecological surgery (GynOp) [3]. 5200 women aged 55-94 years had surgery (2010-2017) and were divided into three age cohorts: 55-64, 65-74, and 75-94 years of age. The preoperative questionnaire included height, weight, parity, prior abdominal and gynecological surgery, comorbidity, and physical performance. An anesthesiologist performed an ASA classification at the time of the intervention. Women in ASA class 1-2 (healthy or mild systemic disease) were categorized as healthy, and those with ASA class 3-4 (severe systemic disease with/ without a constant threat to life) were classified as having a significant disease burden. One year postoperatively, women were asked to complete a questionnaire about cure (defined here as SUI never or 1-4 times per month), change in urinary frequency, satisfaction, impact, and adverse events after surgery. Given the size of the study cohorts, an alpha level of 0.05, and a power value of 80%, the minimum significant difference in prevalence of outcomes was 5% in pairwise comparisons between groups using Fisher's exact test for the analysis.

RESULTS

In Sweden 2007-2017, the proportion of mid-urethral sling surgeries performed in women ≥75 years more than halved (Trend $P<0.0001$). The response rate to the 1-year postoperative questionnaire was similar among age groups (>86%), resulting in a study population of 4581 women. The overall estimated probability of cure, improvement of SUI, and satisfaction with the procedure was similar and decreased by OR10yr 0.48 for cure to OR10yr 0.54 for satisfaction (all $P<0.0001$). Women with a significant disease burden had lower rates of cure and satisfaction compared with healthy women (65.5% vs. 83.7% and 65.7% vs. 80.6%, both $P<0.0001$). Women with prior incontinence surgery had a lower cure rate than first-time surgery (73.5% versus 84.3%, $P<0.0001$) (Figure 1). A low preoperative rate of leakage was associated with being unchanged or worse at follow-up ($P<0.0001$). Cure and satisfaction were also lower in women with diabetes ($P<0.0001$). Younger (55-74 years) and older women (≥75 years) were equally satisfied if they experienced a decrease of at least one step in the frequency of leakage. Older age was more likely to be associated with de novo urgency ($P=0.0022$) and nocturia ≥2 ($P<0.0001$), and women with a significant health burden experienced greater de novo urgency ($P=0.0018$). Body mass index ≥30 (kg/m2) was associated with a higher rate of de novo urgency and nocturia ≥2/night ($P<0.0214$ and $P<0.015$) (Figure 2). Adverse events, readmission, and 30-day mortality rates were low.

INTERPRETATION OF RESULTS

Older age, prior incontinence surgery, and a significant disease burden were associated with a less satisfactory outcome, whereas adverse events were few and similar across ages. Disease burden seemed more important than chronological age for all outcomes. Older women and those with a significant disease burden were satisfied with the procedure if they experienced a reduction of leakage episodes.

CONCLUDING MESSAGE

Despite mid-urethral sling surgery in older women and those with significant disease burden being associated with a lower cure rate and less satisfactory outcome, a majority of the women were satisfied provided they experienced a reduction in incontinence episodes.

FIGURE 1

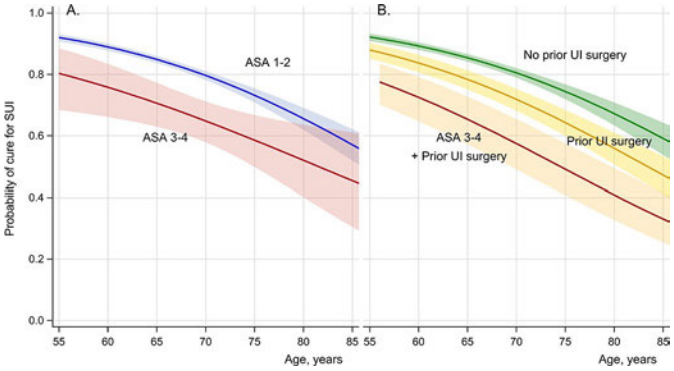

Figure 1. The probability of cure of stress urinary incontinence A. According to age and ASA-class B. According to age and prior surgery

FIGURE 2

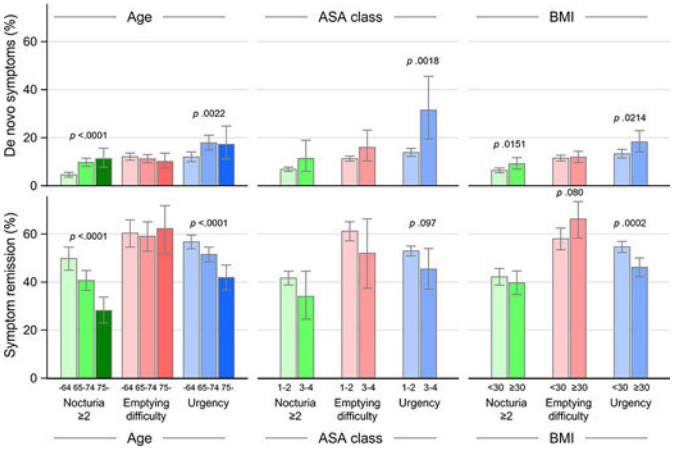

Figure 2. Remission and de novo lower urinary tract symptoms

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SESSION 12 - BIOMECHANICS AND APPLIED SCIENCE

Abstracts 192-203
16:30 - 18:00, Hall D
Chair: Dr Jennifer Kruger (New Zealand)

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COMPUTATIONAL BIOMECHANICS AS A TOOL TO IMPROVE SURGICAL PROCEDURES FOR PELVIC ORGAN PROLAPSE: EFFECT OF MESH ANCHORING TECHNIQUE IN REPAIR SURGERY

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HYPOTHESIS / AIMS OF STUDY
Many surgical procedures to repair pelvic organ prolapse (POP) have been proposed, but their long-term benefits have been poorly evaluated, particularly regarding native tissue repair techniques (with recurrence rates around 29%) [1]. Alternatively, surgeons began to augment native tissue repairs with synthetic meshes. Initially, mesh-augmented repair using polypropylene was introduced taking into consideration the high success rates in correcting abdominal hernias, based on the concept that POP also results from fascial defects.

Several post-operative complications such as infections, chronic pain and voiding dysfunction symptoms were previously described, as well as mesh erosion, a phenomenon whereby soft tissues become damaged as a result of contact with the prosthetic mesh. These mesh-related complications prompted the Food and Drug Administration (FDA) to issue safety communications regarding its use [2]. Therefore, the development of innovative tools to increase the biomechanical knowledge associated with POP may be crucial to carry out effective and viable therapeutic procedures.

The study of pelvic biomechanics is still a relatively new field of research. It relies on translational knowledge, from advances in medical imaging, improved tissue modelling and also noninvasive biomechanical measurement methods and increased computational power, which make in silico analysis very relevant in this field.

Recently, a biomechanical study simulated a laparoscopic surgery to correct an apical prolapse using synthetic meshes computational models, concluding that different meshes provide different support to the vaginal wall.

The main objectives of this study are (1) to simulate the effect of the process of the transvaginal reconstructive surgery to reinforce/replace the apical ligaments and (2) to simulate the effect of mesh anchoring technique, and compare the displacement magnitude of the pelvic tissues, during Valsalva maneuver. Previous studies showed that POP recurrence is common after vaginal mesh implantation that may be related to a strong attachment point for mesh anchorage [3]. These authors showed that mesh anchoring failure was observed in 38% of patients on average 1.8 years after mesh implantation.

The suturing technique with two different anchoring points (simple stich - a set of four nodes and continuous stitch - a line of nodes) was simulated. The effect of this technique was verified on the pelvic structures, namely the displacement magnitude and supero-inferior displacement of the uterus and vaginal wall.

STUDY DESIGN, MATERIALS AND METHODS
In this work, one commercial synthetic mesh (to transvaginal repair of POP) was subjected to experimental uniaxial tensile tests: three specimens were tested, estimating the experimental mechanical behavior of the uniaxial nominal stress-stretch response and their mechanical properties.

To mimic the apical ligaments (cardinal ligaments (CLs) and uterosacral ligaments (USLs), after impairment (90%) and total rupture, computational models of the synthetic implants were developed (see Figure 1a) and b)). The geometric dimensions of these synthetic implants were based on existing literature specifications. These implants have been used in the surgical repair of POP, mimicking the functional component of the CLs and USLs.

Biocomputational model of the female pelvic cavity (Figure 1c)), used in the present study, corresponding a nulliparous 24 years old healthy female - (1) symphysis pubis, (2) bladder, (3) uterus, (4) rectum, (5) levator ani muscle, (6) pelvic fascia, (7) arcus tendineous fasciae pelvis, (8) lateral ligaments of the rectum, (9) uterosacral ligaments (USLs), (10) cardinal ligaments (CLs), (11) pubourethral ligaments, (12) urethra, (13) vagina, (14) anus. This model was adapted, including the impairment (90%) (changing the stiffness of the apical ligaments) and the total rupture of the apical ligaments (CLs and USLs).

Regarding to anchoring technique, two anchoring points (simple stich (Figure 1d)) and continuous stitch (Figure (1e))), corresponding to the fixation between the USLs implant and the sacrum and CLs implant and the arcus tendineous fasciae pelvis, were considered fixed.

The Valsalva maneuver was simulated without muscle activation, considering an IAP of 4kPa.

RESULTS
Impairment and total rupture of the USLs and CLs cause variation in the supero-inferior displacement (SI-disp) of the vaginal wall. The Table c) of the Figure 2 shows the SI-disp of the vaginal wall, measured on the red point of the Figure 2b), when impairment of 90% and total rupture of the USLs and CLs occurs. The simulations showed that there was an increase of the displacement when impairment or rupture of the CLs and USLs occurs and the incorporation of the implants (with a continuous stitch) caused a reverse impact, decreasing the vaginal wall displacement. The non-existence/existence of the synthetic implant, when total rupture of the CLs and USLs occurs, caused a variation of the vaginal displacement (9% for the CLs and 27% for the USLs).

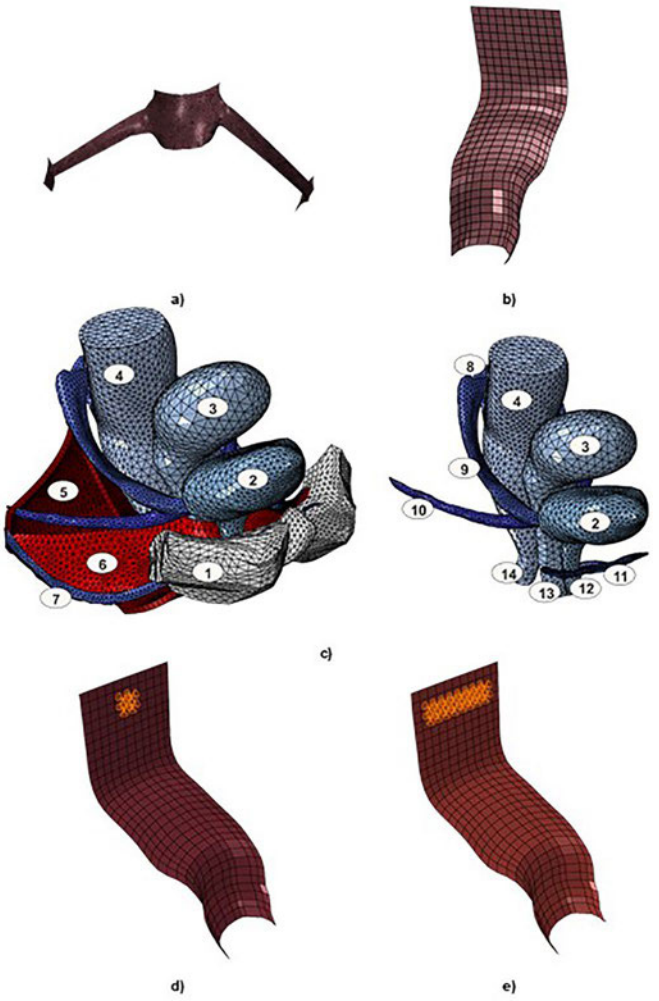
The Table of the Figure 2d) shows the variation of the supero-inferior displacement of the vaginal wall between different anchoring points, showing a difference of approximately 10% for the simulation USLs and CLs implant.

INTERPRETATION OF RESULTS
The supero-inferior displacement (SI-disp) of the vagina, when a total rupture of USLs and CLs occurs, increased approximately 4.98mm and 0.84mm, respectively, when compared to healthy numerical cases, being more pronounced when USLs rupture occurs. This result is consistent with literature showing a strong relationship between impairment of apical support and anterior vaginal wall prolapse descent.

The proposed methodology also showed that the simple suture (simple stich) causes a higher supero-inferior displacement of the vagina than the continuous suture, because this allows more freedom of the implant since it is only fixed in a set a loose point rather than a continuous suture (continuous stitch). These results showed that different types of sutures influence the numerical results and probably the outcomes of the surgery.

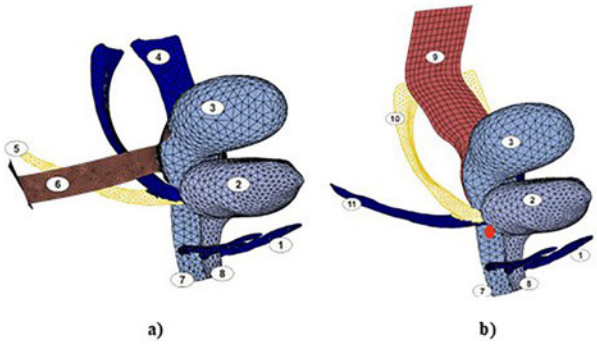
CONCLUDING MESSAGE
The development of in silico computational simulations can be used to predict the outcome of a pelvic surgery, with native tissues and/or synthetic meshes, and has the potential to change the way the clinicians manage surgical treatment for women with POP and prevent post-operative complications. The simulation of the pelvic cavity can also be an important tool in the design and development of new meshes, shortening the lead time of launching novel, safer and more effective meshes. The computational outcomes will also contribute to developing new methodologies to get more rigorous clinical data for premarket approval of the new materials.

FIGURE 1



Development of the computational models of the surgical implants to mimic the CLs (a) and USLs (b). c) healthy 3D computational model. d) and e) different anchoring points (simple stich and continuous stitch, respectively).

FIGURE 2



Variable		*Supero-inferior displacement of the vagina (mm)*		
		USLs	*CLs*	*Variation USLs/CLs (%)*
Healthy	Rest	.....	.....	.....
	Valsalva	7.69	7.69	.....
Impairment 90%		11.98	8.17	32%
Total rupture		12.67	8.53	33%
		USLs Implant	*CLs Implant*	*Variation USLs/CLs (%)*
Impairment 90%		7.90	7.05	11%
Total rupture		9.25	7.78	16%
Total Rupture Variation (%)		27%	9%	.....

c)

	Simple	*Continuous*	*Variation (%)*	*Simple*	*Continuous*	*Variation (%)*
Impairment 90%	8.78	7.90	10%	7.73	7.05	9%
Total rupture	10.17	9.25	9%	8.49	7.78	8%

d)

Implantation of the CLs a) and USLs b) implant after rupture. c) SI-disp of the vagina when impairment and total rupture of the USLs and CLs occurs and after implantation. d) SI-disp of the vagina after implantation with different anchoring points.

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3. K. L. Shek et al., “Anterior compartment mesh: A descriptive study of mesh anchoring failure,” Ultrasound Obstet. Gynecol., vol. 42, pp. 699–704, 2013.

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STANDARDIZATION OF SIMULATION- BASED FUNDAMENTAL FUNCTIONAL UROLOGIC SURGERY TRAINING MODELS AND CURRICULUM: EUROSOMT EXPERIENCE

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HYPOTHESIS / AIMS OF STUDY

Recently, the use of technological teaching modalities in functional urological surgery education has increased significantly. It is essential for these technological products to be standardized so that they can be integrated into the education curriculum. The School of Modern Technology works to deliver gold standard educational resources and project proposals in Modern Technology to ICS members through e-Learning and work placements at international centers of excellence. Our working group has been working under the umbrella of IEEE since 2017 as IEEE 3D Based Medical Application Working Group (EMB/Stds Com/3333.2) sponsored by IEEE Engineering in Medicine and Biology Society Standards Committee mainly focusing on 3D Medical Printing including soft and hart tissue, implant, surgical guide printing and bio-printing. Main aim of this study is the creation of Standard Simulation-Based Functional Urologic Surgery Training Syllabus and Curriculum under umbrella of ICS with using 3D solutions (3D virtual surgical models, medical printing). We would like to share our preliminary results with this abstract which includes 17 surgical procedures (10 female, 7 male), enrolled for preparation of procedure-based simulators.

STUDY DESIGN, MATERIALS AND METHODS

The steps of the preparation of simulation-based training syllabus and curriculum in the scope of EuroSOMT project are; production of patient-specific CT-reconstructed 3D printed models with using patient/cadaver radiological data, creation of VR/AR models with using the same 3D modeling scans, establishment appropriate syllabus and preparation evaluation documents, assessment of skills (technical and cognitive) in learning-training and teaching activities, preparation of e-learning videos. Working group was created by 20 participants from various disciplines and countries, mostly within the body of ICS. We know that there are many different surgical procedures on functional urological surgery with various degree of difficulty. For this reason, we chose the basic procedures for training purposes to enroll the study and possible training curriculum.

The 17 surgical procedures were graded in terms of difficulties and complexities from level 1 to 9. For each of them; 10 surgical steps including important anatomical landmarks through tissue dissection, 2 difficult techniques/anatomic challenges, short e-learning surgical video were included into the curriculum. However, for quality assessment of training sessions (knowledge and learning degree of trainees / realistic and usefulness of 3D simulators), 5 questions related surgical anatomy and surgical skills, evaluation of practical skills and cognitive skills and parameters of simulators were prepared as well.

RESULTS

Learning&Teaching&Training activities were programmed in accordance with the proposed curriculum. The program of the first of these is shared as an attachment.

INTERPRETATION OF RESULTS

Until now, functional urological surgery did not have a curriculum based on 3D digital and physical models created from real patient radiological data. Our working group worked with both ICS as School of Modern Technologies and IEEE as 3D Based Medical Application Working Group (EMB/Stds Com/3333.2) to prepare step-by-step and reproducible syllabuses based on anatomical landmarks.

CONCLUDING MESSAGE

When technologically standardized models and a new curriculum covering them are created, it will be easier to receive training for inexperienced surgeons and surgeon candidates in functional urological surgery, which is difficult to perceive and implement.

FIGURE 1

The program of the first LTT activity

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EFFECTS OF PERINATAL MESENCHYMAL STROMAL CELLS ON STRESS URINARY INCONTINENCE IN VIVO IN A RAT MODEL AND IN VITRO IN A COCULTURE SYSTEM

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HYPOTHESIS / AIMS OF STUDY
Urinary incontinence (UI) is a common problem the older adults affecting to 200 million people worldwide, and it affects about 25% of adult women. There are three types of UI: stress UI, urgency UI, and mixed UI. Stress urinary incontinence (SUI) is the most common type among women and it affects to 50% of women with UI. Several non-surgical and surgical treatment options are available for SUI, such as pelvic floor muscle training, vaginal pessary, urethral bulking agents, and surgery. For severe SUI, surgical interventions is the most recommended treatment option, although it present post-operative complications. In this context, the search and development of less invasive therapies as treatment for SUI continues to be a main requirement and stem cell-based therapy may be an important option for treating these disorders. Mesenchymal stem cells (MSC) are adult stem cells and one of the most attractive sources for stem cell research and therapy. The aim of this study is to use MSc obtained from perinatal tissues and study their use of the treatment of SUI using in vitro and in vivo models.

STUDY DESIGN, MATERIALS AND METHODS
Cell cultures: SUI patients and pregnant women were recruited at the Department of Obstetrics and Gynecology under informed consent approved by the Ethics Committee. Suburethral tissues were obtained by biopsy and cell cultures were established by enzymatic digestion. Isolated cells were cultured in Dulbecco Modified Eagle Medium (DMEM) supplemented with 10% fetal bovine serum. Human placentas were obtained during natural or cesarean births and decidua-derived mesenchymal stromal cells (DMSC) were isolated from placental membranes by enzymatic digestion. Isolated cells were cultured in DMEM supplemented with 2 mM glutamine, 0.1 mM sodium pyruvate, 55 μM β-mercaptoethanol, 1% non-essential amino acids, 1% penicillin/streptomycin, 10% fetal bovine serum and 10 ng/ml epidermal growth factor (EGF). All steps of tissue processing were performed in a biosafety cabinet using appropriate aseptic techniques. For trans-well co-culture assays, DMSC were placed on top of the trans-wells and SUI-isolated cells were placed at the bottom of the well at a ratio 1:2 or 1:5. After 24-48 hours of co-culture, migration, proliferation and the cytokines present in the coculture supernatants were studied. Migration was evaluated by the CytoSelectt 24-Well Cell Migration Assay. Proliferation was evaluated by Alamar blue assay. Cell culture supernatants were analyzed by the Procarta-Plex™ Multiplex Immunoassays.

Animal model of stress UI caused by childbirth: Vaginal distention in female Sprague-Dawley rats was used to simulate the maternal injuries of childbirth. Animal experiments were performed meeting the animal protection requirements and the approval of the Animal Experimentation Ethics Committee. The animals were divided in two groups, control and DMSC-treated animals. Two doses of DMSC (1 million DMSCs suspended in phosphate-buffered saline) were injected into the periurethral area of the rats. The sham injection was performed with the same volume of phosphate buffered saline without cells. UI was assessed by measurement of the leak point pressure (LPP). To evaluate the engrafment of DMSCs, cells were labeled with VivoTrack before injection. Labeled cells were infused into the periurethral area and visualized by Bruker In Vivo Xtreme animal imaging system once a week.

Data analysis: The data were analyzed using the t-Student test to obtain the significance of the data between groups and data in which a $p < 0.05$ is shown as statistically significant.

RESULTS
We have developed a SUI rat model consisting of vaginal distension which mimics the maternal injuries of childbirth. In this model there is a consistently decrease in the abdominal leak point pressure (LPP) indicative of SUI. After periurethral injection of saline or DMSC, LPP value was significantly higher in the DMSC group when compared to that of the control group ($p < 0.05$). The existence of VivoTrack-stained DMSCs in the injected periurethral tissue was verified by using an animal imaging system. We have observed that the cells remain in the ventral area, that they are still alive at least for 14 days after the injection, and they do not produce tumors or adverse reactions such as graft-versus-host syndrome.

To assess the possible mechanism involved in the regenerative potential of DMSC in SUI, we performed several in vitro assays by coculturing DMSC and SUI isolated cells. It is important to note that DMSCs are able to migrate and home at injured sites with high efficiency. The results showed that DMSC have a significant increase in their in vitro migration toward SUI cells when compared with control media used as negative control.

To examine whether DMSC can modify SUI cell proliferation, coculture of both cell types was stablished. DMSC significantly increased the proliferation of SUI cells as compared with untreated cells at the two examined ratios.

The possible interaction between DMSC and SUI cells was examined by evaluating cytokines, chemokines, and growth factors expression on coculture supernatant using multiplex immunoassays that allows to simultaneously quantitate many proteins. Preliminary results showed that anti-inflammatory cytokines such as IL6, IL8, and MCP3 were significantly reduced in coculture, when expressed as a relative ratio to the secretion of those proteins by both cells cultured separately. In addition, angiogenic growth factors such as VEGF and metalloproteinases MMP-2, MMP-3 and MMP-9 were significantly decreased in the coculture supernatant.

INTERPRETATION OF RESULTS
This original work shows that DMSC injection into periurethral tissue after vaginal distension in rats led to increased LPP suggesting that DMSC can be used as one of the possibly effective cell therapies for SUI. This effect is likely to be mediated by cellular secretions acting through fibroblasts proliferation from pelvic floor tissue and modifying the fibroblast microenvironment after vaginal distension which may lead to improved continence.

CONCLUDING MESSAGE
The data obtained are providing the basis for further studies of the effect of perinatal MSC in in vitro and in vivo studies in the rat model. Translational investigation of SUI using animal models could potentially lead to an understanding of the pathophysiology of SUI and enable preclinical testing of potential treatments such as cell therapy treatments. The outcomes of this investigation indicated that the application of perinatal mesenchymal stromal cells could be associated with higher therapeutic value in stress urinary incontinence patients compared with used treatments. The stem-based therapy could be the next step in the treatment of SUI. However, there are still many elements of this type of therapy such as effectiveness or long-term side effects, which need to be researched.

Funding This work was funded by project PI 15/01803 and PI18/01278, from the Instituto de Salud Carlos III (Ministry of Economy, Industry and Competitiveness) and cofunded by the European Regional Development Fund **Clinical Trial** No **Subjects** Animal **Species** Rat **Ethics Committee** Comité de Experimentación y Bienestar Animal del Hospital 12 de Octubre (CEBA)

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EXTRACELLULAR MATRIX ANALYSIS TO IMPROVE TISSUE ENGINEERING FOR URETHRAL RECONSTRUCTION

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HYPOTHESIS / AIMS OF STUDY
Tissue engineering is the field of medicine in which cells, (bio)materials and biochemical signals are used to repair or replace biological functions. Our research focus is tissue engineering for urethral reconstruction in patients with complicated urethral stricture disease or hypospadias.

In more severe urethral stricture, besides fibrotic changes of the urethral wall and obstruction of the lumen, also tissue surrounding the urethra, i.e. corpus spongiosum (CS), is affected by fibrosis. In hypospadias , the distal CS is absent to a greater or lesser extent. In urethral reconstruction using oral mucosal or preputial grafts, only the urethral epithelium and subepithelium is replaced. Currently, no substitution for the surrounding CS is provided. We hypothesize that replacement of CS-like tissue in urethral reconstruction might improve outcomes of urethral reconstruction.

To recreate CS that mimics healthy native CS the best possible, the exact structure and composition of healthy native CS should be known. The CS is composed of several layers, which could be mimicked using 3D-bioprinting. For this, a hydrogel is required as printing ink. Existing hydrogels like Gelatin Methacryloyl (GelMA) have good mechanical properties for printing, but lack the required biochemical cues for cells. By enriching the biomaterials with natural components of the extracellular matrix (ECM), regeneration is enhanced [1]. The ECM is the essential non-cellular component of the tissue microenvironment of cells, comprised of a network of macromolecules including polysaccharide glycosaminoglycans (GAGs) and proteins such as collagens, laminins, and fibronectin. Ideally, the graft used in urethral reconstruction promotes healthy healing. By studying the difference of ECM proteins in spongiofibrosis and in healthy CS, a hydrogel can be developed with relevant ECM proteins steering towards healthy healing.

Our hypothesis is that understanding the composition of the ECM in healthy and diseased CS can lead to a tissue specific hydrogel. Here we focus on the molecular composition of the ECM using liquid chromatography coupled to tandem mass spectrometry (LC-MS/MS) to analyze tissue on protein level. We compare ECM components both qualitatively and quantitatively in healthy and fibrotic CS tissue.

STUDY DESIGN, MATERIALS AND METHODS
Surgical waste was collected under local biobank protocol. Both fibrotic lesions obtained from excision and primary anastomosis urethral surgery and resected penile urethra after gender conformation surgery were used. Decellularization was performed using Sodium Dodecyl Sulphate (SDS). Decellularized tissue was stored in phosphate buffered saline before processing to LC-MS/MS analysis. The differences in amounts of ECM protein were investigated for three groups: healthy CS, fibrotic CS and normal-looking CS that was located next to the fibrotic part.

Samples were processed as described before [2]. MS/MS spectra were extracted out of raw data files and were analyzed by using MaxQuant software. Results were analyzed using Perseus (version 1.6.0.7). By cross referencing with the Human Matrisome Project the results were analyzed using gene ontology analysis (geneontoly.org) and Search Tool for the Retrieval of Interacting Genes/Proteins (STRING) network analysis (string-db.org).

In parallel, surgical waste was fixated and embedded in paraffin. Tissue sections of 3 μm were stained with 4′,6-diamidino-2-phenylindole (DAPI), Hematoxylin-Eosin and used in immunohistochemistry for ECM components.

RESULTS
Elastin (ELN) was found in all three comparisons, it was highest expressed in fibrotic tissue, lower in normal-looking tissue and the lowest in transgender tissue. The proteins fibrilin 2 (FBN2) and emilin 2 (EMILIN2) were expressed higher in healthy (transgender) tissue. TNC, COMP, CILP, FGB, COL8A1, THBS4, AEBP1, ELN, FGF7, WNT9A and CHRDL1 were expressed higher in fibrotic tissue. No clear interaction between this group of proteins was found in the GO analysis nor the STRING. A few proteins were identified up in the two other comparisons (transgender - normal looking and fibrotic - normal looking). Expression of FBN2 was low in fibrotic tissue, ITIH1 was low in normal-looking tissue, and TNC, COMP, CILP and FGB were expressed low in transgender tissue. Findings from the MS/MS could be confirmed by immunohistochemistry. Most striking was the aberrant distribution of ELN in fibrotic samples, in contrast to healthy tissue, no bundles could be identified.

INTERPRETATION OF RESULTS
Some differences were found between the protein distribution, however, despite the different origin of the samples, the overall protein intensities were comparable. FBN2 and EMILIN2 are candidates for a scaffold to stimulate generation of healthy CS, whereas TNC, COMP, CILP, FGB, COL8A1, THBS4, AEBP1, ELN, FGF7, WNT9A and CHRDL1 are higher in fibrotic tissue, indicating these should be downregulated for regeneration of healthy CS. ELN was highest expressed in fibrotic tissue, this was unexpected as elastin is a protein that establishes strength and flexibility in tissues. ELN and FNB2 are interacting proteins in the formation of the elastic ECM network, low expression of FNB2 could contribute to the aberrant distribution of ELN in fibrotic tissue. Limitation of our research is the use of waste material from gender conformation surgery. This tissue is hormone treated and may not represent healthy tissue. On the other hand, only few significant differences were found when this tissue was compared to healthy tissue from urethroplasty. In addition, there are few other ways to obtain healthy human penile tissue for research purposes.

CONCLUDING MESSAGE
In this study we compared ECM components of healthy and fibrotic CS in order to be able to compose the ideal hydrogel for 3D-bioprinting for tissue engineering of the urethra and CS.

We suggest that FBN2 and EMILIN2 may stimulate regeneration, whereas TNC, COMP, CILP, FGB, COL8A1, THBS4, AEBP1, ELN, FGF7, WNT9A and CHRDL1 should be downregulated for regeneration of healthy CS.

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Funding None **Clinical Trial** No **Subjects** Human **Ethics Committee** Local medical and ethical committee **Helsinki** Yes **Informed Consent** Yes

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FACTORS IMPACTING VAGINAL MUSCULARIS IN MESH IMPLANTATION

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HYPOTHESIS / AIMS OF STUDY
Urinary incontinence and pelvic organ prolapse are common debilitating gynecologic conditions in postmenopausal women. It is estimated that the lifetime risk of undergoing a single operation for incontinence or prolapse by age 80 was about 11.1%. Urogynecologic meshes, including mid-urethral slings and prolapse meshes, are important implantable devices that have been used to overcome the high failure rates of native tissue repair. However, the use of mesh is hampered by mesh-related complications, typically mesh exposure into vaginal lumen with the vaginal wall continuity breached. The impact of mesh on the vagina and the mechanism underlying the pathogenesis of complications are not completely understood.

Vaginal muscularis, composed of smooth muscle fascicles is key to the integrity of vaginal wall and plays important roles in vaginal tone maintenance and sexual function, thus having important implications for a women's quality of life. Our group and others have shown that the vaginal smooth muscle (VSM) is highly sensitive and responsive to mechanical cues, undergoing degenerative changes following the implantation of stiffer and heavier meshes [1, 2]. In addition, menopausal estrogen decrease induces vaginal atrophy including both molecular and functional changes of VSM. Considering that women who receive mesh implantation are mostly post-menopausal, it is important to understand how the VSM is impacted by both mesh implantation and menopause. While these factors have been individually studied, scarce data is available on their combined effect. In addition, diabetes is a pandemic affecting approximately 1/5 of aging women 45 years or older. Women with diabetes experience ~5-fold increase of risk of mesh exposure, the mechanism of which is unknown. While studies have shown that diabetes negatively impact vascular smooth muscle [3], its impact on the VSM in the context of mesh implantation and/or menopause is unclear.

In this study, we aimed to define the impact of mesh implantation on the VSM in the situation of menopause and/or diabetes by comparing the VSM thickness using a rat model. We hypothesized that mesh implantation, menopause-associated estrogen decrease, and hyperglycemia have a synergistic negative impact on the VSM.

STUDY DESIGN, MATERIALS AND METHODS
A rat model was used. Three interferences were introduced: (1) bilateral ovariectomy (OVX); (2) diabetes; (3) mesh implantation. Based on a power analysis using our previous data comparing stiffness of vagina between rats with vs. without OVX [3], at least 4 animals in each group were needed to achieve 80% power to detect meaningful differences with $p<0.05$. All animal studies were approved by the University Institutional Animal Care and Use Committee. In total, 100 middle-aged (9 – 12 mos) female Wistar rats were used, 80 with OVX, 52 with diabetes, and 60 with mesh implantation. In the OVX groups, outcomes were evaluated at 3- (very early, $n=23$), 7- (early, $n=28$), and 42-days (late, $n=29$) post-surgery. In the no-OVX groups, the outcomes were evaluated at 42 days due to the chronic effect of estrogen ($n=20$).

Specifically, a polypropylene mesh (Restorelle) was implanted on the anterior and posterior vagina via a modified sacrocolpopexy following supracervical hysterectomy with or without bilateral OVX. Sham surgeries were performed following the same procedures without mesh implantation. Diabetes was induced using a single iv of streptozotocin (STZ) at 45mg/kg. OVX and mesh implantation were performed 2 weeks following the development of hyperglycemia. At different time points following surgery, proximal vaginal tissues were collected for gross morphology and histological analysis. Briefly, the cross-sectional tissue sections at 7μm were obtained following embedding and cryo-sectioning. Masson Trichrome procedures were performed and large images at 100x were taken for overall morphological observation and VSM thickness quantification. The VSM thickness was measured at intervals of approximately 100μm. In samples with mesh implantation, the VSM thickness was measured in areas between mesh fibers and beneath the mesh fibers (mesh impacted) (Figure 1).

Mann-Whitney U, Kruskal-Wallis, and related samples Wilcoxon signed rank tests were used for statistical analysis with $p<0.05$ set as significance.

RESULTS
All three interventions were successfully implemented. Diabetes was effectively induced with the development of hyperglycemia ($\geq$300mg/dL), polydipsia, and polyuria at 3 days following STZ injection.

Without mesh implantation, OVX induced a decrease of VSM thickness over time in the normoglycemic groups, starting from 7 days post-surgery (Figure 2). Specifically, the VSM thickness at 3 days was not different between the OVX and no-OVX groups with median at 183μm. The value was decreased 45% at 7 days and 49% at 42 days following OVX. In contrast, the change of VSM under the impact of OVX was not significant in the diabetic groups (Figure 2).

Mesh implantation generally induced thinning of VSM in areas beneath the mesh fibers as compared to areas at fiber intervals ($p<0.001$), with the decrease being 16% and 19% at 7- and 42-days post- implantation ($p=0.015$, 0.002, respectively). This effect was not significant at 3 days ($p=0.721$). No differences between VSM thickness at mesh fiber intervals and Shams were observed (all $p>0.05$). With OVX, the VCM thickness in the normoglycemic rats was decreased 50% in areas at fiber intervals ($p=0.039$) and 51% in areas beneath the fibers ($p=0.003$) at 42 days post-surgery, as compared to the no-OVX rats (Figure 1). This effect was not observed in the diabetic rats (all $p>0.05$). Interestingly, under the impact of diabetes, the VCM thickness in the no-OVX rats was decreased 61% in both areas at fibers intervals ($p=0.013$) and beneath the fibers ($p=0.020$) at 42 days post-surgery, as compared to the normoglycemic rats (Figure 1). This effect was not observed in the OVX rats (all $p>0.05$).

INTERPRETATION OF RESULTS
This is the first study demonstrating the interactive effect of mesh implantation, menopause, and diabetes on the vaginal smooth muscle structure. Consistent with literature, our findings showed that mesh implantation had a negative impact on the VSM thickness, predominantly affecting the areas directly beneath the mesh fibers. This scenario provides additional evidence that stress shielding, incurred by a soft tissue (vaginal VSM) in contact with a stiff material (polypropylene mesh), might be an underlying mechanism for the mesh implantation associated VSM degeneration. With the longitudinal study design, we further showed that the negative impact of mesh occurred early following the mesh placement and lasted for a long term, supporting a high sensitivity of VSM to mechanical stimulation.

In addition, our results showing that OVX induced VSM atrophy is in line with the literature. Importantly, we showed that the negative impact of OVX on the VSM was deteriorated with mesh implantation in the long term (42 days), suggesting that estrogen plays a protective role in maintaining vaginal structural integrity and that an abrupt decrease of estrogen had a synergistic negative impact on the VSM with mesh implantation.

Interestingly, diabetes did not affect the gross morphology of VSM in both no-OVX and OVX conditions without mesh implantation. The negative impact of diabetes was exhibited only when mesh was implanted under no-OVX condition in the long term. Thus, it is likely that the adverse influence of diabetes on the VSM was executed through a mechanism attenuating the protective effect of estrogen. As a result, the benefits of topical estrogen on the vaginal tissue structure might be compromised in women with diabetes.

CONCLUDING MESSAGE
Implantation of polypropylene mesh and surgical menopause have a synergistic negative impact on the VSM, while diabetes demonstrates negative effect only when mesh is implanted under normoestrogenic condition.

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FIGURE 1

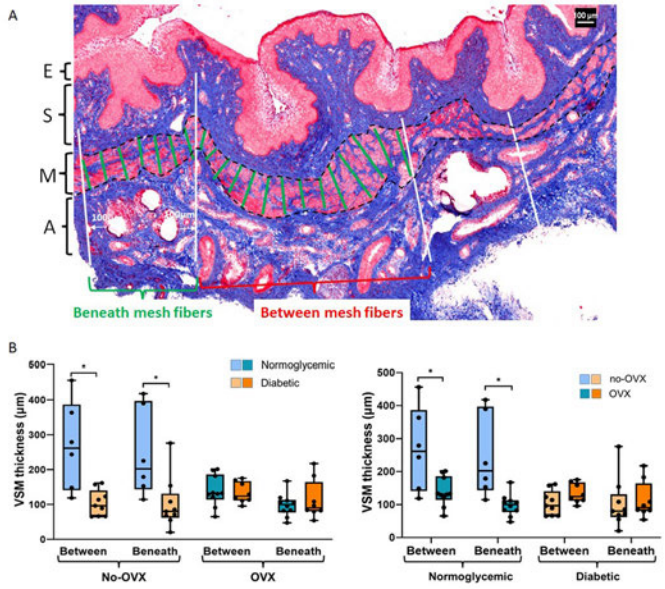

Figure 1. (A) Measurement of vaginal smooth muscle (VSM) thickness in areas between mesh fibers and beneath mesh fibers. In the image, the muscularis layer is delineated with dashed lines. Measurements (green bars) were made at 100µm intervals. Area beneath mesh fibers was defined as 100µm apart from mesh borders at both sides. E = epithelium, S = sub-epithelium, M = muscularis, A = adventitia. (B) Comparisons of VSM thickness in areas between fibers (Between) and beneath fibers (Beneath) in OVX vs. no-OVX and diabetic vs. normoglycemic groups at 42 days post-mesh implantation. Quantitative data are presented using box-whisker plots with medians, minimum, and maximum. Dots represent individual samples. * p<0.05.

FIGURE 2

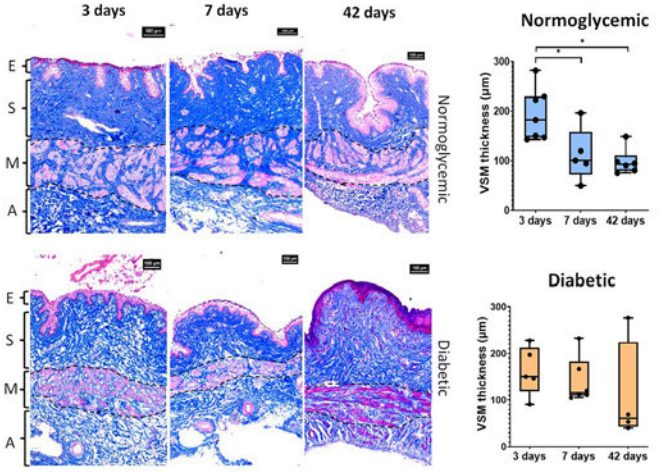

Figure 2. Longitudinal impact of OVX on the thickness of vaginal smooth muscle without mesh implantation from 3 days to 42 days in normoglycemic and diabetic conditions. In the images, the muscularis layer is delineated with dashed lines. E = epithelium, S = sub-epithelium, M = muscularis, A = adventitia. Quantitative data are presented using box-whisker plots with medians, minimum, maximum. Dots represent individual samples. * p<0.05.

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PRE-OPERATIVE PROLAPSE PHENOTYPE IDENTIFIED THROUGH MACHINE LEARNING PREDICTS SURGICAL OUTCOMES IN WOMEN WITH POPQ STAGE 3-4 UTEROVAGINAL PROLAPSE UNDERGOING SACROCOLPOPEXY

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HYPOTHESIS / AIMS OF STUDY

Apical vaginal support is referred to as the “keystone” to pelvic organ support and up to 50% of anterior vaginal wall support loss has been attributed to vaginal apical support loss. [1,2] Sacrocolpopexy, whether abdominal or minimally invasive, has been considered the “gold standard” treatment for advanced pelvic organ prolapse and a recent study has shown that laparoscopic supracervical hysterectomy compared to total hysterectomy (vaginal or minimally invasive) at time of sacrocolpopexy resulted in a higher incidence of prolapse recurrence. [3] We aimed to develop a clinical prediction model to determine the vaginal apical support, as assessed in centimeters using the Pelvic Organ Prolapse Quantification (POPQ) examination, needed to address anterior and posterior vaginal wall support loss in women undergoing minimally invasive sacrocolpopexy utilizing a large surgical database. The hypothesis of this study is that pre-operative biodemographic variables can be used to determine the surgical apical support needed to address anterior and posterior vaginal wall prolapse and result in POPQ stage <2 post-operative support.

STUDY DESIGN, MATERIALS AND METHODS

A large multi-institutional surgical database of minimally invasive sacrocolpopexies including pre- and post-operative variables was utilized. Unsupervised machine learning was used to categorize participants and investigate the association between the cluster and outcome. The K-means clustering analysis was performed with pre-operative POPQ points and stratified by prior hysterectomy status (yes/no). Analysis was limited to women with "advanced” prolapse (pre-operative POPQ stage 3-4 in this study). The dichotomous “ideal” outcome was defined as (“1”) if there was a ≥ 3 stage change vs (“0”) if there was a <3 stage change by the POPQ system between pre- and post-operative POPQ stage. In women with pre-operative POPQ stage 3-4, this definition resulted in the “ideal” postoperative outcome of POPQ stage <2 support. Demographic variables were compared by cluster groups using Student’s t-test and Chi-squared tests. Odds ratios were calculated to determine if clusters based on pre-operative POPQ points could predict the outcome. The age at surgery and Body Mass Index (BMI) were used for adjusted odds ratio.

RESULTS

There were 698 participants that had POPQ stage 3-4 prolapse pre-operatively (401 uterovaginal prolapse, 297 vaginal vault prolapse). In those with POPQ stage 3-4 prolapse, 3 statistically distinct prolapse clusters (subsequently referred to as prolapse phenotype) were identified by POPQ points in those who had uterovaginal prolapse and 3 distinct clusters in those who had vaginal vault prolapse (Figure 1). In women with uterovaginal prolapse (UVP), there was a statistically significant difference only in ethnicity, pre-operative POPQ stage and OR time by anatomic phenotype (Table 1). In women with vaginal vault prolapse there were no statistically significant differences in bio demographical variables except for pre-operative POPQ stage.

For women with UVP, pre-operative prolapse phenotype was predictive of surgical outcome by minimally invasive sacrocolpopexy. Phenotype 1 is anterior vaginal wall-predominant with the apex near the introitus, Phenotype 2 is anterior wall-predominant with some preserved apical and posterior vaginal wall support, and Phenotype 3 is apical-predominant with loss of both anterior and posterior vaginal wall support (Figure 1). Post-operatively, participants with prolapse phenotype 1 (cluster 1) were more likely to have POPQ stage ≤ 1 support (95.7%, aOR = 1) compared with phenotype 2 (86.7%, aOR = 0.29, 0.09-0.89, $p = 0.02$) and phenotype 3 (83.9%, aOR = 0.23, 0.06-0.78, $p = 0.02$). By “ideal” surgical outcome, participants with POPQ stage 0-1 support post operatively had, on average, ~1cm better support at points Aa and Ba (-2.50 vs -1.53, and -2.49 vs -1.50, respectively, $p < 0.001$), >0.5cm better support at points Ap and Bp (-2.65 vs -2.15, and -2.65 vs -1.97, respectively, $p < 0.001$), a GH ~1cm smaller (2.86 vs 3.70, $p < 0.001$), and were 7.0-fold more likely to have had a midurethral sling (RR = 6.97, $p = 0.01$) compared to those with stage ≥ 2 support (worse support). There was not a statistically significant difference between postoperative point C or TVL between phenotypes but there was a statistically significant difference between the delta of the POPQ point pre-C to post-C for phenotypes 1 vs 2 vs 3 (-8.17 vs -6.84 vs -13.55cm, respectively, $p < 0.001$). Perineorrhaphy rates were very low and were not significant between outcome groups. For women with prior hysterectomy, anatomic phenotype was not predictive of outcome after minimally invasive sacrocolpopexy.

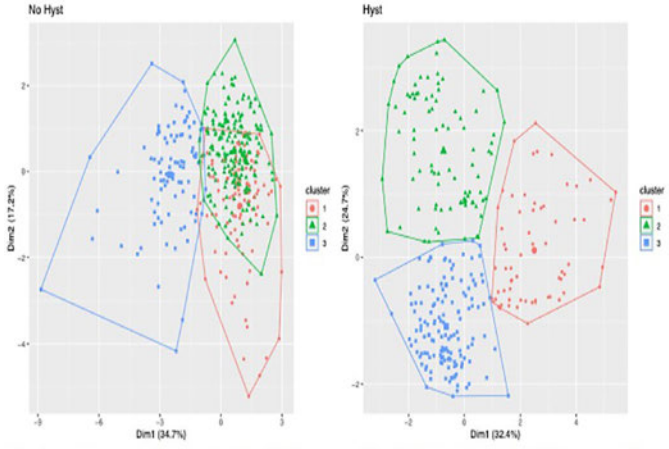
INTERPRETATION OF RESULTS

In a large surgical database of women with pelvic organ prolapse, 3 distinct anatomic phenotypes based on pre-operative POPQ points were found in women with advanced uterovaginal prolapse who underwent minimally invasive sacrocolpopexy. Phenotype 3 represented the most advanced prolapse with all 3 compartments prolapsed >4cm on average past the hymenal remnant. Phenotype 2 had anterior-predominant vaginal prolapse with more preserved apical support compared to Phenotype 1 which was also anterior-predominant but had more apical and posterior wall prolapse compared to 2. These phenotypes were found to be predictive of post-operative support with different odds of obtaining the “ideal” surgical outcome of stage <2 support based on the phenotype. Concomitant midurethral sling at time of minimally invasive sacrocolpopexy was significantly associated with the “ideal” outcome of stage ≤ 1 support, likely due to addressing distal anterior vaginal wall support. For women with pre-operative POPQ stage 3-4 vaginal vault prolapse, three phenotypes were identified but they were not predictive of the postoperative surgical outcome.

CONCLUDING MESSAGE

In women with POPQ stage 3-4 uterovaginal prolapse, there appear to be 3 anatomic phenotypes that can be determined using the pre-operative POPQ and which are associated with different odds of anatomic surgical success when treated with minimally invasive sacrocolpopexy. Further work needs to confirm the presence and predictive nature of these 3 POPQ-based anatomic phenotypes and whether the 3 phenotypes represent merely a progression of prolapse or if they represent 3 discrete prolapse presentations resulting from different anatomic and life course risk profiles. Ultimately, this information may be useful in surgical counseling and planning.

FIGURE 1



	PreAa	PreBa	PreC	PreGH	PrePB	PreTVL	PreAp	PreBp	PreD
Cluster1	-0.4	1.6	0.1	4.5	3.4	8.8	-1	0.3	-2.6
Cluster2	2.3	2.8	-1.3	4.8	3.5	8.9	-2.1	-1.7	-5.1
Cluster3	2.7	5.4	5.5	6.3	3.1	8.9	-1	4.8	2

	PreAa	PreBa	PreC	PreGH	PrePB	PreTVL	PreAp	PreBp
Cluster1	2.3	5.1	5.3	6.1	3.2	8.9	-0.9	4.9
Cluster2	-1.4	0.4	-0.4	4.4	3.5	8.2	0.9	2.3
Cluster3	2	2.6	-2.6	4.5	3.5	8.1	-2.1	-1.6

Figure

FIGURE 2

Table 1. Baseline demographics in women with POPQ stage 3-4 prolapse *without a hysterectomy*

		Phenotype 1	Phenotype 2	Phenotype 3	p
n		108	202	91	
Age (mean (SD))		60.58 (10.14)	61.28 (9.30)	61.06 (8.72)	0.823
Race (%)					0.027
Caucasian		101 (93.5)	195 (96.5)	78 (86.7)	
African American		6 (5.6)	5 (2.5)	9 (10.0)	
Asian		1 (0.9)	0 (0.0)	2 (2.2)	
American Indian		0 (0.0)	0 (0.0)	1 (1.1)	
Other		0 (0.0)	2 (1.0)	0 (0.0)	
Gravity (mean (SD))		3.16 (1.65)	3.06 (1.45)	3.14 (1.72)	0.857
Parity (mean (SD))		2.70 (1.33)	2.67 (1.19)	2.73 (1.27)	0.929
BMI (mean (SD))		28.36 (4.61)	27.47 (4.90)	27.26 (5.07)	0.209
Vag Deliveries (mean (SD))		2.61 (1.32)	2.59 (1.19)	2.58 (1.30)	0.985
PreOp POPQ Stage (%)	3	106 (98.1)	201 (95.5)	55 (60.4)	<0.001
	4	2 (1.9)	1 (0.5)	36 (39.6)	<0.001
Pre-OP POPQ point (mean (SD)	Aa	-0.39 (1.17)	2.27 (0.73)	2.74 (1.38)	<0.001
	Ba	1.58 (1.72)	2.75 (0.85)	5.40 (1.73)	<0.001
	C	0.13 (3.20)	-1.27 (2.97)	5.45 (2.06)	<0.001
	D	-2.57 (3.63)	1.96 (4.89)	-5.14 (2.30)	<0.001
	GH	4.54 (1.19)	4.76 (1.04)	6.25 (1.42)	<0.001
	PB	3.40 (0.86)	3.49 (0.98)	3.11 (0.80)	0.005
	TVL	8.84 (1.07)	8.87 (1.25)	8.93 (1.42)	0.871
	Ap	-1.04 (1.67)	-2.12 (0.80)	-1.03 (2.52)	<0.001
	Bp	0.25 (2.11)	-1.74 (1.37)	4.79 (2.69)	<0.001
OR time (mean (SD))		219.99 (91.08)	270.39 (79.88)	276.10 (90.02)	<0.001
Post-OP POPQ point (mean (SD))	Aa	-2.61 (0.45)	-2.31 (0.78)	-2.23 (0.91)	0.002
	Ba	-2.60 (0.45)	-2.30 (0.78)	-2.19 (0.92)	0.001
	C	-8.24 (1.39)	-8.24 (2.52)	-8.23 (2.02)	0.999
	D	-9.08 (2.32)	-9.54 (2.34)	-8.89 (4.02)	0.342
	GH	2.98 (0.72)	2.90 (0.86)	3.06 (0.85)	0.404
	PB	3.26 (0.82)	3.57 (0.92)	3.47 (0.86)	0.028
	TVL	9.44 (1.45)	9.53 (1.93)	9.23 (3.62)	0.688
	Ap	-2.58 (0.57)	-2.63 (0.70)	-2.49 (0.65)	0.357
	Bp	-2.58 (0.57)	-2.61 (0.74)	-2.44 (0.72)	0.267
Post-Op POPQ Stage (%)	0	35 (37.6)	37 (25.9)	15 (24.2)	0.052
	1	54 (58.1)	87 (60.8)	37 (59.7)	
	2	4 (4.3)	19 (13.3)	9 (14.5)	
	3	0 (0.0)	0 (0.0)	1 (1.6)	

Table

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THE EFFECT OF SERICIN ON UNDERACTIVE BLADDER MODEL FOLLOWING LUMBAR CANAL STENOSIS

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HYPOTHESIS / AIMS OF STUDY

Underactive bladder (UAB) is characterized by a slow urinary stream, hesitancy, and straining to void, with or without a feeling of incomplete bladder emptying, sometimes with storage symptoms. The International Continence Society (ICS) defines DU as “a diagnosis based on urodynamic investigations, generally (but not always) with relevant symptoms and signs, manifest by low detrusor pressure or short detrusor contraction in combination with a low urine flow rate resulting in prolonged bladder emptying and/or a failure to achieve complete bladder emptying within a normal time span (a high post-void residual may be present)” (1).

There is currently no proven treatment for treating UAB. Sericin is a natural hydrophobic polymer produced by silkworms. It has several biological properties including antioxidant, anti-tumor, anti-inflammatory, antibacterial, moisturizing, wound healing, and protective effect on neurons (2). Several studies have reported that sericin prevents lipid peroxidation and eliminates ROS, and enhances the enzymatic antioxidant activities such as superoxide dismutase (SOD), catalase (CAT), glutathione reductase, and glutathione (GSH) in the brain and peripheral tissues (3). In addition, several experimental studies have shown that sericin protects dopaminergic and cholinergic neurons primarily through its antioxidant effects. Sericin has also been shown to have an anticholinesterase effect. The enzyme acetylcholinesterase (AChE) is involved in the hydrolysis of the neurotransmitter acetylcholine (ACh) and helps maintain the integrity and permeability of synaptic membranes during neurotransmission. Excessive activity of this enzyme has toxic effects and can lead to the death of neurons. We aimed to investigate the effect of sericin on the expression of RhoA, ROCK-α, ROCK-β, and M2, M3 muscarinic receptor expression, and to measure apoptotic markers in the bladder tissue of UAB following lumbar canal stenosis (LCS) model.

STUDY DESIGN, MATERIALS AND METHODS

In the present study, a total of 24 female Wistar rats (12-13 weeks and a weight of 220-270 g), were enrolled. Animals were housed in the Neuroscience Research Center's animal shelter at 25 ˚ C with a 12-hour light / dark cycle and unrestricted access to food and drinking water.

Rats were randomly divided into 6 groups (6 in each) as follows;

S200 sericin 200 mg/kg /daily/14 days/P.O + underactive bladder model

S250 sericin 250 mg/kg /daily/14 days/P.O + underactive bladder model

S300 sericin 300 mg/kg /daily/14 days/P.O + underactive bladder model

Model NS 2 ml/kg/daily/14 days/P.O + underactive bladder model

Sham NS 2 ml/kg/daily/14 days/P.O + sham surgery

Control NS 2 ml/kg/daily/14 days/P.O

Due to the solubility of sericin in normal saline, the solutions were prepared immediately before administration.

Model Preparation

To induce UAB model, we used LCS model which previously was established by Sekido et al. Animals were anesthetized with isoflurane. For this purpose, animals were placed in a closed box, gassed with isoflurane 5% in pure oxygen (1 L/min). After the induction of anesthesia, the drug levels were maintained at the appropriate level by a small mask with 0.8–1 L/min oxygen and 1–1.5% isoflurane. Under anesthesia, the L5-L6 vertebral arches were exposed, and a small hole (1.5-2 mm in diameter) were drilled at the fifth vertebral arch, and a rectangular piece (3.5 mm * 5.0 mm * 0.5 mm) of silicone rubber were inserted into the epidural space. The layers of skin, subcutaneous, and muscle were closed using sutures. The urinary bladder was compressed twice daily for emptying in the following days post-procedure, and an antibiotic (ciprofloxacin (1 mg/kg, i.p.) were administered.

Western blot analysis

Western blot was used to quantitatively assess the expression of RhoA, ROCK-α, ROCK-β, and M2, M3 muscarinic receptor expression, and to measure apoptotic markers, including the levels of caspase 3, 9, Bcl2 and Bax proteins in the bladder tissue.

RESULTS

Western blot results showed that M2 receptor expression decreased significantly following LCS compared to control and sham groups ($P < 0.01$). Expression increased in rats who were treated with sericin. However, the increment of expression in rats with LCS + sericin at doses of 250 and 300 mg was statistically significant compared to the LCS group receiving normal saline ($P < 0.01$). M3 receptor expression decreased in rats with LCS compared to the rats in the control and sham groups ($P < 0.001$). Rats receiving different doses of sericin had higher expression of M3 receptor in the bladder compared to rats in the LCS group receiving normal saline, which was statistically significant ($P < 0.01$).

Our results showed that the expression of Rho A, ROCK-β, and ROCK-α in control and sham groups was higher compared to model groups ($P < 0.05$). Following LCS, they were reduced, and treatment with different doses of sericin increased their expression of them. The results of Tukey post hoc tests showed that the expression of Rho A in the bladder of the groups receiving doses of 250 mg ($P < 0.05$) and 300 mg ($P < 0.01$) compared with the model group of LCS receiving normal saline was significantly higher.

Also, the expression of ROCK-β (ROCK-1) was significantly higher only in the group receiving 300 mg sericin compared to the LCS group receiving normal saline ($P < 0.05$) (Figure 1).

The results of Tukey post hoc tests showed that the expression of ROCK-α (ROCK-2) in the bladder of groups receiving different doses of sericin was not statistically significant compared to the LCS group receiving normal saline.

The analysis of apoptotic factors results showed that the Bax index in LCS groups increased significantly compared to control and sham groups and treated with different doses of sericin reduced this amount in bladder tissue. However, compared to the LCS group receiving normal saline, only the sericin 300 group receiving it was statistically significant ($P < 0.05$). Our results showed that the expression of Bcl-2 in the LCS groups was significantly reduced compared to the control and sham groups ($P < 0.001$). Treatment with different doses of sericin increased the amount that was highest in the group receiving sericin 300 compared to the LCS group receiving normal saline ($P < 0.01$). The ratio of cleaved caspase 3 / Pro-caspase 3, and also cleaved caspase 9 / Pro-caspase 9 increased significantly in the LCS group receiving normal saline compared to the control and sham groups ($P < 0.001$). Treatment with different doses of sericin reduced this amount. However, this decrease in expression was statistically significant in LCS receiving doses of 250 and 300 ($P < 0.001$) (Figure 2).

INTERPRETATION OF RESULTS

There is currently no proven treatment for treating UAB. our results revealed that various doses of sericin which has several biological properties may increase the expression of muscarinic receptors, and the expression of Rho A, and ROCK-β (ROCK-1) after decrement of them in LCS rats. In addition, our findings provide evidence for the protective effect of sericin therapy against apoptotic changes in bladder tissue of the underactive bladder model.

CONCLUDING MESSAGE

Our results revealed the promising role of sericin in the management of the underactive bladder model following the LCS model. It may increase the expression of muscarinic receptors expression after decrement of them in the bladder tissue of LCS rats as well as the expression of Rho A, and ROCK-β (ROCK-1). In addition, our findings provide evidence for the protective ef-

fect of sericin therapy against apoptotic changes in bladder tissue of the underactive bladder model.

FIGURE 1

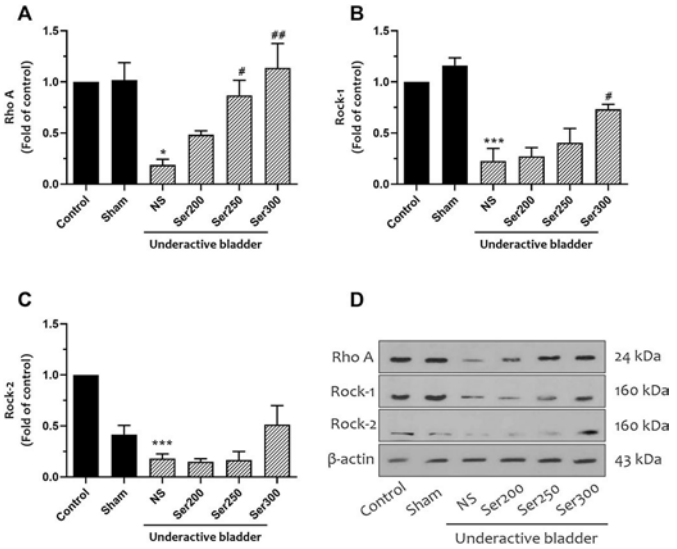

Figure 1. expression of Rho A, ROCK-β, ROCK-α in bladder tissue of study groups

FIGURE 2

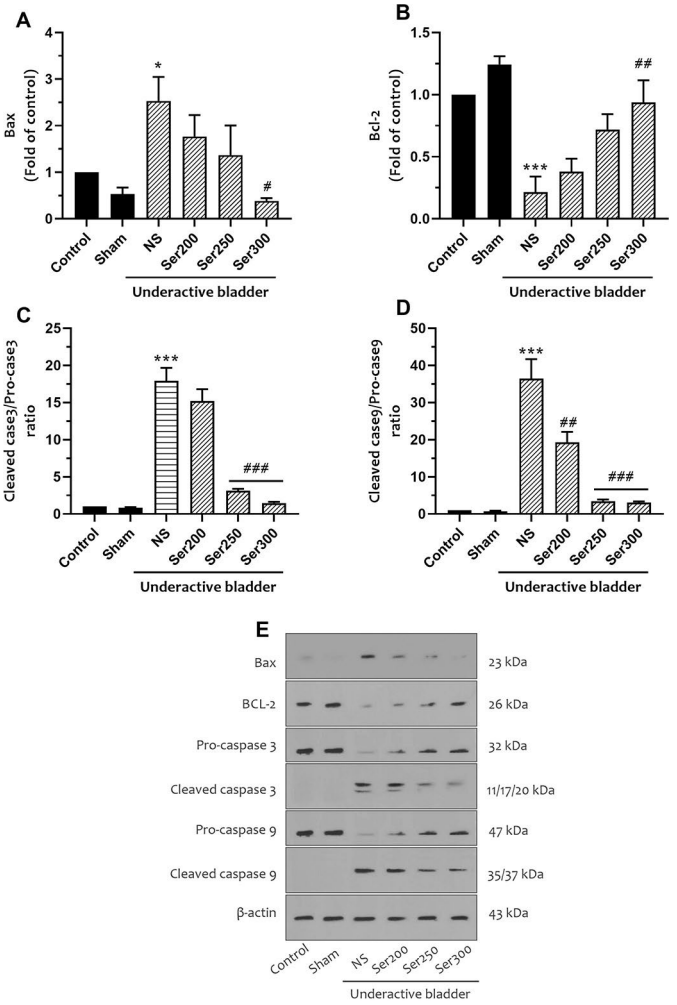

Figure 2. Analysis of apoptotic factors results in bladder tissue of study groups

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CENTRAL ABNORMAL SPROUTING OF BLADDER AFFERENTS LEADING TO NDO REFLECTS NGF-INDUCED CHANGES THE EXPRESSION OF REGULATORS OF AXONAL GROWTH

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HYPOTHESIS / AIMS OF STUDY
Neurogenic detrusor overactivity (NDO) emergence following spinal cord injury (SCI) courses with abnormal lumbosacral extension of bladder afferents. Mechanisms regulating this aberrant sprouting are unresolved, but may involve changes at the lumbosacral cord in the expression of inhibitory cues that block axonal growth, including myelin-associated inhibitors (MAIs), such as Nogo-A, and chondroitin sulphate proteoglycans (CSPGs), such as Phosphacan. It is presently unclear whether bladder afferents recognize these repulsive cues and respond to them, regulating the expression of their receptors and adjusting growth responses, and how this process could be regulated. Here, we investigated changes in the expression of Nogo-A and Phosphacan and their specific receptors NgR1/Lingo1/p75 and/or TROY, NgR1/NgR3 and Rptps/Lar at the lumbosacral cord and dorsal root ganglia (DRG) neurons, respectively, following SCI. We also investigated whether these alterations were NGF-dependent.

STUDY DESIGN, MATERIALS AND METHODS
Female Wistar rats ($n = 8$/group) were left spinal intact (controls) or underwent a largely incomplete spinal cord transection (SCT) at T8/T9 segments and left to recover for 7 or 28 days. At each endpoint, lumbosacral cords (L5-S1) and associated ganglia (DRG) were collected. Lumbosacral cords were processed by Western Blotting to evaluate the expression of Nogo-A, Phosphacan and GAP43, a marker of axonal sprouting. Total RNA from lumbosacral DRG neurons was extracted, reverse-transcribed and analyzed by qPCR to evaluate the expression of Nogo-A receptor complex NgR1/Lingo1/p75 and/or TROY and Phosphacan receptor complexes NgR1/NgR3 and Rptpσ/Lar. L5-S1 DRG neurons from other control and SCT animals were collected and cultured for 22h in the presence of 0, 50 or 100 ng/mL of NGF.

RESULTS
Lumbosacral cord expression of Nogo-A and Phosphacan had a 3-fold increase at 7 days post-injury (dpi), compared to controls (Phosphacan: $p \leq 0.05$ vs. controls; Nogo-A: $p \leq 0.001$ vs. controls), returning to baseline at 28 dpi. A significant increase in GAP43 expression at the lumbosacral cord was also found following SCI.

In lumbosacral DRG, the expression of the Nogo-A receptor complex NgR1/Lingo1/TROY was time-dependently decreased, compared to controls (NgR1: $p \leq 0.05$ controls vs. 7 dpi, $p \leq 0.001$ controls vs. 28 dpi). Phosphacan receptor complexes NgR1/NgR3 and Rptps/Lar also showed time-dependent decreases in expression, compared to controls (NgR1: $p \leq 0.05$ controls vs. 7 dpi, $p \leq 0.001$ controls vs. 28 dpi; NgR3: $p \leq 0.05$ controls vs 7 and 28 dpi; Rptps and Lar: $p \leq 0.05$ controls vs. 28 dpi). To assess whether the alterations in RNA levels of these receptor complexes were dependent on NGF exposure, lumbosacral DRG were cultured in 0, 50 or 100 ng/ml of NGF. Preliminary results indicate that after 22h in culture, neurite length and branching increased in an NGF concentration-dependent manner, particularly in SCT groups. In contrast, RNA levels of receptor complexes decreased in an NGF concentration-dependent manner in all groups, in tandem with in vivo observations.

INTERPRETATION OF RESULTS
We observed alterations in the expression of known inhibitors of axonal growth, Nogo-A and Phosphacan, at the lumbosacral cord following thoracic SCI. Both proteins were overexpressed at the lumbosacral cord 7 dpi, even though axonal sprouting significantly increased at this site following thoracic SCT, as indicated by GAP43 levels. This process appears to be dependent on exposure to NGF, known to occur in vivo in peripheral tissues after spinal injury.

CONCLUDING MESSAGE
These results indicate that, despite the presence of a highly repulsive spinal environment, bladder sensory afferents can grow from the periphery into the lumbosacral spinal cord. This reflects a time-dependent down-regulation of the expression of receptors for those repulsive cues. This process appears to be NGF-dependent, suggesting that peripheral NGF control could be used to regulate abnormal axonal sprouting and, consequently, block NDO emergence.

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200 | www.ics.org/2022/abstract/200

SOLUBLE GUANYLATE CYCLASE ACTIVATOR, CINACIGUAT, PROMOTES REVASCULARIZATION OF THE CONTUSED SPINAL CORD TO TREAT SPINAL CORD INJURY INDUCED DYSFUNCTION

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HYPOTHESIS / AIMS OF STUDY

Neurogenic injury can have severe consequences to multiple physiological functions including mobility, autonomic regulation of the urinary bladder and vascular dysfunction, which is believed to occur in response to inflammation, oxidative stress, and vascular endothelial cell damage. A hallmark of vascular damage is the impaired responsiveness to nitric oxide (NO•), a key mediator of vascular smooth muscle relaxation. NO• activates soluble guanylate cyclase (sGC) to generate cyclic guanosine monophosphate (cGMP) that stimulates a multitude of downstream pathways. There are indications that increasing NO•-cGMP signaling can be beneficial in ameliorating spinal cord injury (SCI) induced detrusor overactivity [1]. However, approved agents such as phosphodiesterase (PDE) type 5 inhibitors have limited efficacy due to decreased NO• bioavailability and/or oxidative stress-induced inhibition of sGC, preventing cGMP generation. Small molecule sGC activators can circumvent these pathological changes as they are heme mimetics that allosterically activate sGC in the absence of its heme prosthetic group and NO• (Fig 1). We have measured the benefits of cinaciguat on the mitochondrial respiration and spinal cord regrowth in spinal cord contused (SCC) mice.

STUDY DESIGN, MATERIALS AND METHODS

Mitochondria were isolated from the spinal cords of control, SCC and SCC C57Bl/6 mice treated with cinaciguat (10 mg/kg/day/7 days). The mitochondria were mechanically dissociated, isolated by differential centrifugation, and placed in a gas-tight vessel containing a Clark-type oxygen microelectrode to measure state 3 (succinate + ADP) and state 4 (succinate alone) respiratory rates. The respiratory control ratio (RCR), a measure of the "tightness of coupling" between electron transport and oxidative phosphorylation, was determined from the ratio of state 3 to state 4 respiration rates. A RCR of 2-4 is considered good for complex II substrates [2]. Measures were expressed as mean ± standard deviation (SD). Between group differences were assessed by a one-way ANOVA with Tukey's post-hoc multiple comparison analysis (Prism 9, GraphPad) and significance was determined as $p < 0.05$.

RESULTS

The neuroprotective effect of cinaciguat in the spinal cord was assessed by measuring the respiration of mitochondria isolated from the spinal cords of female sham, SCC, and SCC mice given cinaciguat (Fig 2). These experiments showed that a decrease in the RCR following SCC (1.9 ± 0.6 vs 4.3 ± 1.1 in controls) was normalized by cinaciguat (4.6 ± 1.4, n ≥ 5 for all groups). Improved RCR values with cinaciguat treatment correlated with the higher density of blood vessels around the spinal cord lesion.

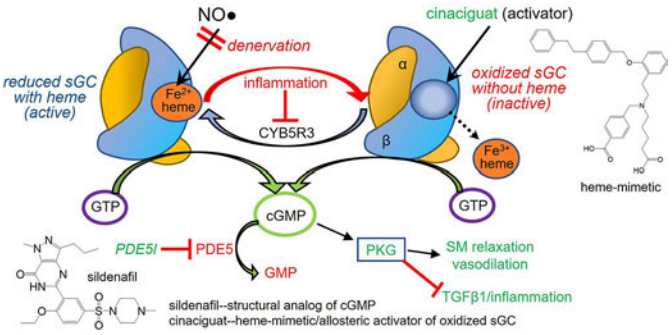
INTERPRETATION OF RESULTS

The unique feature of sGC activators is their ability to induce cGMP generation when the heme moiety is oxidized or absent and the NO• signaling pathway is compromised. This is especially important in SCI accompanied by systemic inflammation and chronic oxidative stress that promotes heme oxidation and inactivation of sGC. Our data show SCC resulted in significant alterations in mitochondrial RCR in spinal cord tissue which was normalized by treatment with cinaciguat.

CONCLUDING MESSAGE

Angiogenesis around the spinal cord lesion occurs slowly, leading to chronic ischemia and cellular metabolic dysfunction. Cinaciguat promotes angiogenesis as demonstrated by the improved RCR.

FIGURE 1



sGC-cGMP signaling pathway.

FIGURE 2

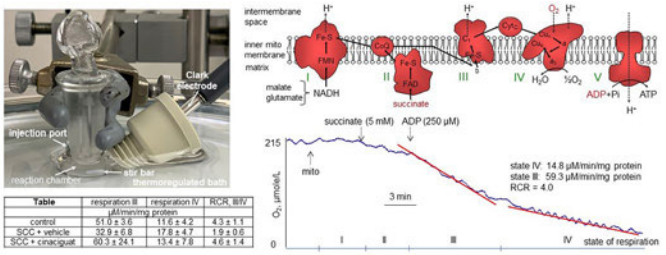


Table	respiration III	respiration IV	RCR, III/V
	µM/min/mg protein		
control	51.0 ± 3.6	11.6 ± 4.2	4.3 ± 1.1
SCC + vehicle	32.9 ± 6.8	17.8 ± 4.7	1.9 ± 0.6
SCC + cinaciguat	60.3 ± 24.1	13.4 ± 7.8	4.6 ± 1.4

Chamber for mitochndrial respiration measurements, representation of mitochondrial respiratory chain, oxidative phosphorilation and RCRs of spinal cord mitochondria isolated from control, contused and contused mice treated with cinaciguat.

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201 | www.ics.org/2022/abstract/201

IMPROVEMENT OF URETHRAL DYSFUNCTION BY 5-HT(1A) RECEPTOR AGONIST NLX-112 IN DIABETIC RATS

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HYPOTHESIS / AIMS OF STUDY

To examine the effects of the selective 5-HT1A receptor agonist, NLX-112, on urethral function in streptozotocin-induced diabetic rats.

STUDY DESIGN, MATERIALS AND METHODS

Female Sprague-Dawley rats (n = 32) were divided into two groups: rats with type 1 diabetes mellitus (T1DM) and age-matched normal control rats (NC). T1DM was induced by intraperitoneal injection of streptozotocin (65 mg/kg). Isovolumetric cystometry and urethral perfusion pressure (UPP) were evaluated 10 weeks post-injection in rats (n = 9 per group). The selective 5-HT1A receptor antagonist, WAY-100635 maleate salt, was administered after NLX-112 hydrochloride dose-response curve was generated (intravenously). The remaining rats were used for immunofluorescence and Western blot assays.

RESULTS

Compared to controls, type 1 diabetic rats (T1D rats) had lower maximal intravesical pressure (IP max) and UPP changes. In NC group, there was no significant change in UPP nadir, UPP change, IP max and HFOs amplitude with the application of NLX-112 hydrochloride. While all of these parameters, except IP max, showed no significant differences after the administration of WAY-100635 maleate salt (0.3 mg/kg). As Fig.1 shown, in T1D rats, NLX-112 hydrochloride (0.003-1.0mg/kg) induced dose-dependent decreases in UPP nadir, IP max, high-frequency oscillations (HFOs) rate; and increases in UPP change and HFOs amplitude. WAY-100635 maleate salt (0.3mg/kg) partially or completely reversed the NLX-112-induced changes. As shown in Fig.2, immunofluorescence revealed that 5-HT1A receptors were found in the L6-S1 spinal cord Onuf's nucleus, but the expression was significantly higher in the T1D rats (Fig.2A,2C). Additionally, Western blot showed there were significantly more 5-HT1A receptors in the ventral L6-S1 spinal cord of T1D rats.

INTERPRETATION OF RESULTS

It's universally acknowledged that Onuf's nucleus regulates the activity of external urethral sphincter (EUS). Long-lasting hyperglicemia is associated with a decrease in cerebral concentration of serotonin and other studies have already confirmed the existence of compensatory mechanisms in the serotonergic system of diabetic rats. Therefore, the discrepant expression level of 5-HT1A receptors in Onuf's nucleus may lead to different effects of NLX-112 on HFOs in NC and T1D groups. Along with the increase of EUS bursting activity, urethral relaxation function was improved. In addition, the decrease of bladder contraction may result from the activation of the central 5-HT1A receptors which inhibited the parasympathetic excitatory input to the bladder.

CONCLUDING MESSAGE

Taken together, these results suggested that in urethane-anesthetized T1D rats, i.v. administration of NLX-112, a selectivity 5-HT1A receptor agonist could improve the urethral function by enhancing EUS activity in T1D rats. The expression of 5-HT1A receptors was significantly greater on the dorsolateral nucleus of L6-S1 spinal cord in T1D rats, which might be the binding site of the drug. The findings may be a reference for the development of pharmacotherapy for voiding dysfunction in diabetic patients.

FIGURE 1

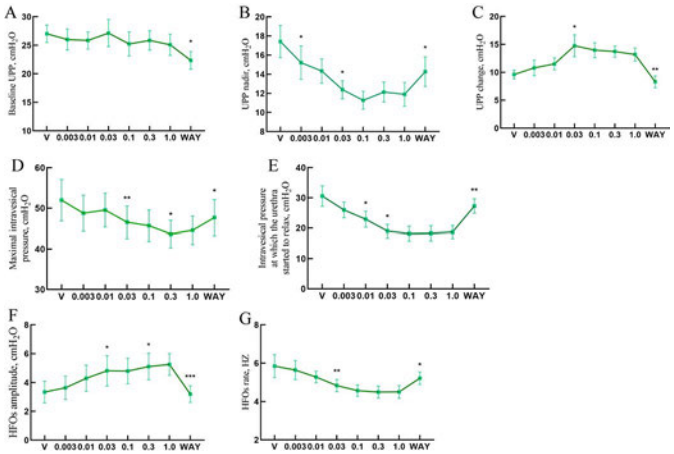

Figure 1. Effects of i.v. NLX-112 hydrochloride in rats with type 1 diabetes mellitus.

FIGURE 2

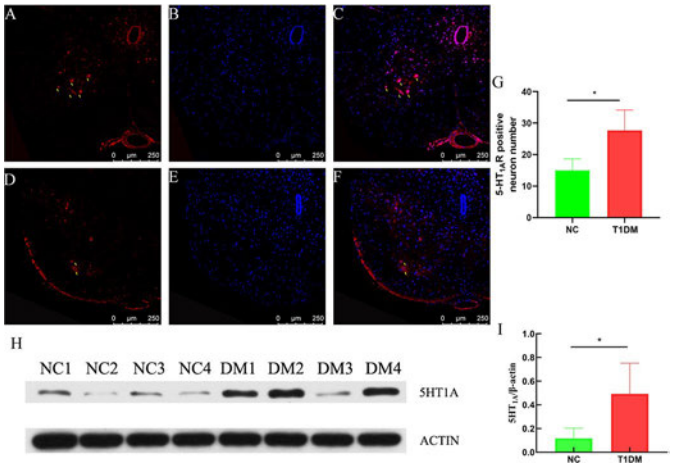

Figure 2. Results of immunofluorescence and Western Blot.

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2. Diabetes-induced changes in 5-hydroxytryptamine modulation of vagally-induced bradycardia in rat heart
3. Influence of central serotonergic mechanisms on lower urinary tract function

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202 | www.ics.org/2022/abstract/202

MAPPING THE SPINAL CIRCUITRY COORDINATING NEURAL CONTROL OF BLADDER FUNCTION IN A SEMI-CHRONIC SPINAL CORD INJURY ANIMAL MODEL

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HYPOTHESIS / AIMS OF STUDY

A traumatic spinal cord injury (SCI) causes lasting damage to sensory and motor circuitry, resulting in partial or complete paralysis, loss of sensation, autonomic dysreflexia, pain, and bowel and bladder dysfunction [1]. While there has been significant investment and focus on mechanisms and methods to improve mobility of the SCI community, neurogenic lower urinary tract dysfunction (NLUTD) is a much less studied co- morbidity. This is remarkable, given that patients designate the restoration of voiding as a top priority [2]. The lower urinary tract (LUT) has two principal functions: storage and voiding. These processes rely on the synchronized activity of the LUT, which is elaborately regulated by supraspinal centers [3]. After a SCI, supraspinal control of voiding is disrupted leading to development of NLUTD. Prevailing intervention focuses on symptom relief such as chronic catheter utilization, which is associated with altered voiding dynamics and can result in infection or mal-adaptive plasticity of the spinal circuitry. Recent advances in our understanding of the potential for plasticity or regeneration of damaged micturition circuitry will not only have a dramatic impact on patients with SCI, but more broadly, in the global population for those that suffer NLUTD as well. In this study we propose an innovative approach by applying ventral epidural spinal stimulation (VES) to map the spinal circuitry involved in the neural control of micturition in a semi-chronic injury model. Understanding the adaptive nature of neural circuitry can help us better understand NULTD pathologies as well as identify potential therapeutic targets to restore bladder function.

STUDY DESIGN, MATERIALS AND METHODS

Long Evans rats underwent a laminectomy at T9 and received a moderate contusion injury with an Ohio State Impactor. Four weeks post-SCI, we conducted terminal electrophysiology evaluations (n = 4), along with age matched controls (n = 3). During terminal electrophysiology experiments, a laminectomy at T9 was performed to allow for insertion of a custom spinal stimulation electrode. Next, a suprapubic catheter was inserted through the bladder dome and coupled to a three-way valve for controlled infusion of intravesical saline, and to monitoring changes in bladder pressure via an in-line pressure transducer. Subsequently, flexible microelectrodes were fitted to regions of the bladder identified as dome, mid, and base, as well as the external urethral sphincter (EUS) to record electromyographic (EMG) signals. Once all LUT electrodes were in place, the spinal stimulating electrode was inserted ventrally until reaching the L1 spinal segment. Additionally, needle electrodes were placed in the gastrocnemius and tibialis anterior muscles in both hindlimbs to record motor evoked potentials. Stimulation was delivered at each spinal segment between L1 and S1 (0.1-0.5mA and 1-20Hz) with a D8SR Bipolar Constant Current Stimulator (Digitimer Ltd.), and evoked potentials from the LUT and hindlimb muscles were recorded with a PowerLab 16/35 DAQ (ADInstruments Inc.).

RESULTS

Analysis of the LUT recruitment curves (bladder dome, mid bladder, bladder base, and EUS) showed significantly higher ($p < 0.01$) amplitudes of response as stimulation intensity increased in both control and SCI animals. Preliminary results also demonstrate distinct trends in response to stimulation between control and SCI groups in both bladder and EUS. More specifically stimulation at L6 recorded the strongest response at both 0.4mA and 0.5mA throughout the bladder in control animals. But this trend was not seen in SCI animals with bladder dome showing the highest response at L4, while mid bladder and bladder base both showing the highest response to S1 stimulation. Overall, each location in the bladder displayed distinct responses to not only stimulation intensity, but also with respect to the spinal level stimulated. Evoked potentials of the EUS showed significantly divergent patterns between controls and SCI groups. Amplitude of the EUS response was highest when the spinal cord was stimulated at L4-L6 in controls, with SCI animals demonstrating significantly higher response amplitudes with S1 stimulation, followed by L4-L6 (Figure 1).

INTERPRETATION OF RESULTS

Our lab has previously demonstrated the ability to record EMG signals from the LUT of SCI rodents. These results have reflected that graduated levels of bladder dysfunction are proportional to injury severity, with overall attenuated EMG activity throughout the LUT of all SCI animals when compared against controls (Figure 2). With this study we further characterize the activity seen in the LUT and the contribution of each spinal segment between L1/S1 with respect to bladder function. Our results show there is a distinct response to stimulation between SCI rats and uninjured controls. These differences could be derived from an innate plasticity of the central nervous system (CNS) to adjust after traumatic injury. By understanding how spinal circuitry adapts after a SCI, we can determine more effective targets for neuromodulation with the potential to improve storage and/or voiding, and thus restore bladder function.

CONCLUDING MESSAGE

Although these are preliminary results, our data suggest that CNS plasticity after a moderate thoracic SCI leads to significant reorganization of the spinal circuitry coordinating neural control of bladder function. Understanding these mechanisms will allow us to more accurately determine targets for therapeutic spinal stimulation depending on the type of NLUTD present.

FIGURE 1

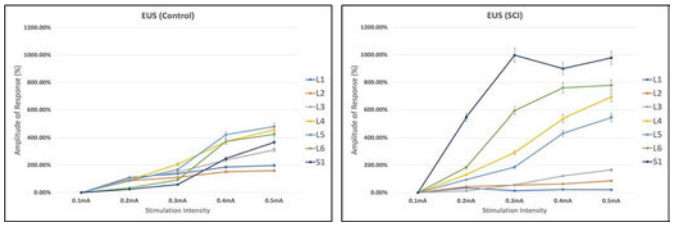

Figure 1. Changes in recruitment curves during lumbosacral stimulation in uninjured controls vs SCI rats.

FIGURE 2

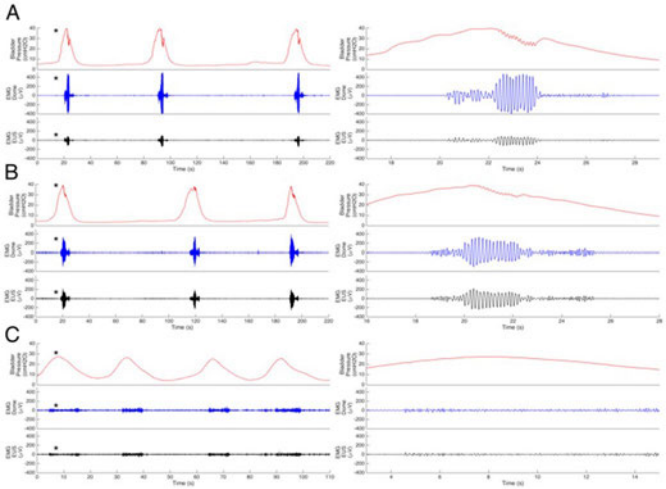

Figure 2. Correlation between SCI severity and LUT EMG characteristics

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203 | www.ics.org/2022/abstract/203

ANTIFIBROSIS TREATMENT IMPROVES DETRUSOR OVERACTIVITY AND CHRONIC BLADDER PAIN ASSOCIATED WITH NEURAL REMODELING OF CENTRAL NERVOUS SYSTEM IN A MOUSE MODEL MIMICKING INTERSTITIAL CYSTITIS.

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HYPOTHESIS / AIMS OF STUDY

Several studies have been reported that the interruption of bladder fibrosis may be associated with improvement of interstitial cystitis (IC) [1, 2]. In our previous study, nintedanib, which has been clinically approved as a therapeutic agent in idiopathic pulmonary fibrosis, showed an antifibrotic effect on the bladder and an improvement of detrusor overactivity in spinal cord injured mice associated with improvement of C-fiber hyperexcitability [3]. Therefore, we investigated whether antifibrosis treatment using nintedanib can improve the IC-like pathologic conditions.

STUDY DESIGN, MATERIALS AND METHODS

Female C57BL/6 mice were divided into 3 groups (each N = 8): (A) Sham, (B) IC mice treated with vehicle, and (C) IC mice treated with nintedanib. For inducing an IC-like model, one-hour intravesical instillation of hyaluronidase (5 mg/ml) and lipopolysaccharide (5 mg/ml) mixed with 0.9% saline was conducted 3 times once a week. From the last instillation, vehicle or nintedanib (50mg/kg) was subcutaneously administered daily for 3 weeks. Then, the pain assessment using Von-Frey filaments and cystometry was conducted. Trichrome staining, RT-PCR of the bladder, and immunohistochemistry of L6-S1 dorsal root ganglia (DRG) and L6 spinal cord were performed to investigate the improvement of bladder fibrosis, inflammation, nociception, and central sensitization.

RESULTS

In pain assessment, 50% thresholds of target force were significantly reduced in group B vs. A ($p = 0.001$), but recovered in group C vs. B ($p = 0.001$). In cystometry, non-voiding contractions (NVCs, numbers/min; 0.39 ± 0.11 vs. 0.13 ± 0.07) and voiding efficiency (VE, %; 72.1 ± 8.6 vs. 87.1 ± 9.5) were worsened in group B vs. group A, but restored in group C (NVCs 0.15 ± 0.09/min, VE 84.0 ± 4.8%) (Fig 1-a). Bladder fibrosis increased in group B was improved in group C in trichrome staining (Fig.1-b). mRNA levels related to inflammation (IFN-r, CCR2), nociception (TACR2), P2X purinergic (P2X3, P2X4, P2X7), muscarinic (M2), and β-adrenergic receptors (β2, β3) in the bladder mucosa were increased in group B vs. group A, but decreased in group C vs. group B (Fig 1-c). In immunohistochemistry, TRPV1 in L6-S1 DRG and CX3CR1, GFAP, and CCR2 in L6 spinal cord were upregulated in group B vs. group A, but reduced in group C vs. group B (Fig 1-d).

INTERPRETATION OF RESULTS

The increased expressions of proinflammatory cytokines, M2-muscarinic, β2- and β3-adrenergic, P2X-purinergic, and TACR2 receptors in the bladder mucosa and upregulated TRPV1 in L6-S1 DRG indicate that bladder inflammation induced by repetitive damage is closely related to detrusor overactivity, afferent sensitization of bladder, and chronic bladder pain. In addition, neural remodeling at the central nervous system (CNS) level, which is evidenced by the enhanced signals of CX3CR1 and GFAP in L6 spinal cord, seems to be implicated in this mechanism, too.

Antifibrosis treatment using nintedanib improved detrusor overactivity and afferent hyperexcitability evidenced by improved cystometric parameters and decreased M2-muscarinic, β3-adrenergic, and P2X-purinergic receptors. Moreover, antifibrosis treatment also improved chronic bladder pain, and this mechanism seems to be implicated in the anti-inflammatory effect of nintedanib and interruption of neural remodeling in CNS although it was not corroborated whether nintedanib directly affects CNS or not.

CONCLUDING MESSAGE

Antifibrosis treatment using nintedanib improved detrusor overactivity and chronic bladder pain in the IC mouse model. Therapeutic effects seem to be mediated by inhibitions of bladder afferent hyperexcitability as well as central sensitization.

FIGURE 1

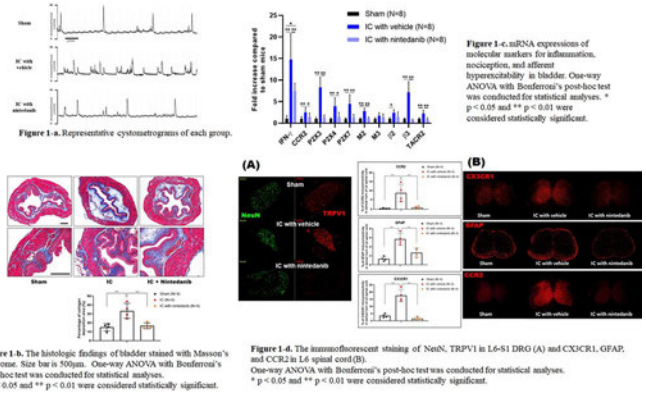

Figure 1-a. Representative cystometrograms of each group.

Figure 1-c. mRNA expressions of molecular markers for inflammation, nociception, and afferent hyperexcitability in bladder. One-way ANOVA with Bonferroni's post-hoc test was conducted for statistical analyses. * $p < 0.05$ and ** $p < 0.01$ were considered statistically significant.

Figure 1-b. The histologic findings of bladder stained with Masson's trichrome. Size bar is 500μm. One-way ANOVA with Bonferroni's post-hoc test was conducted for statistical analyses. * $p < 0.05$ and ** $p < 0.01$ were considered statistically significant.

Figure 1-d. The immunofluorescent staining of NeuN, TRPV1 in L6-S1 DRG (A) and CX3CR1, GFAP, and CCR2 in L6 spinal cord (B). One-way ANOVA with Bonferroni's post-hoc test was conducted for statistical analyses. * $p < 0.05$ and ** $p < 0.01$ were considered statistically significant.

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Funding National Research Foundation of Korea (2020R1C1C1012208) **Clinical Trial** No **Subjects** Animal **Species** mouse **Ethics Committee** Institutional Animal Care and Use Committees

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SESSION 13 - IMAGING

Abstracts 204-215
16:30 - 18:00, Hall K
Chair: Miss Manjula Annappa (United Kingdom)

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MULTIMODAL MEASUREMENT OF LEVATOR BOWL VOLUME: TRANSVAGINAL ULTRASOUND VERSUS MRI

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HYPOTHESIS / AIMS OF STUDY
Direct assessment of levator musculature integrity during pelvic exam is both subjective and difficult. Many have proposed that measurements of levator bowl volume using advanced imaging, may be predictive of pelvic floor muscle function[1,2]. However, these methods require the use of MRI (monetarily and time expensive) to calculate volume. Conversely, transvaginal pelvic floor ultrasound (TVU) is a faster and more readily available method for capturing images of the pelvic floor musculature. A potential drawback when using TVU in this manner is that it captures data in a significantly smaller region. However, if TVU can capture enough of the pelvic floor muscles to accurately calculate levator volume it could potentially be used as a tool to diagnose pelvic floor dysfunction.

The aim of this study was to quantify and compare the volume of the levator ani musculature using both magnetic resonance imaging (MRI) and TVU. While we anticipate that MRI volumes will be larger based on the increased field of view, we hypothesized that a correlation between volumes measured by the two modalities could be established that may demonstrate clinical utility of TVU. Additionally, we intended to map the non-captured landmarks with TVU when compared with MRI.

STUDY DESIGN, MATERIALS AND METHODS
We performed a prospective cohort study including asymptomatic subjects who volunteered to undergo MRI and TVU of the pelvic floor. All participants underwent a comprehensive interview with completing PFDI-20 questionnaire, pelvic exam including POP-Q evaluation, MRI exam, and TVU. Women who answered “no” to all PFDI-20 questions and had a normal POP-Q exam (stage 0) were included in this study.

Levator bowel landmarks:

Using Slicer (v. 4.11) each patient’s TVU was translated and rotated such that the pubic bone was aligned with the patients MRI in all three anatomical planes. Once aligned by bony landmarks, five anatomical landmarks were identified on the midsagittal plane of the MRI. The most inferior-posterior point on the pubic symphysis, point along the curvature of the pubic symphysis 1/3 of the long-axis from the distal pubic point (~ the level of the pubovisceral muscle, refer to as the OT point, the most inferior-anterior point on the perineal body, anorectal junction, and ischial spine (projected to the midsagittal plane) were identified. Additionally, the pubococcygeal line, H-line, M-line, line connecting the OT point to the ischial spine (OTIS line), and line connecting the inferior-posterior pubic symphysis to the perineal body point (PSPB line) were drawn. Finally, the length perpendicular to the top of the TVU’s FOV to the PSPB line was also measured. Figure 1 shows all identified landmarks, their context with respect to the MRI segmentation, and the alignment of the MRI and TVU.

Levator bowel volume measurements:

After all landmarks were identified the levator ani muscles were segmented in both MRI and TVU using Slicer. The segmentations were conducted by one author then reviewed and edited by the remaining authors. The MRI volumes were standardized to the patient anatomy using two methodologies. In the first method we removed any musculature superior to the OTIS line or inferior to the PSPB line. This method allowed for calculation of the volume that was inclusive of the levator muscle attachments. The second method removed any portion of the segmented MRI that were outside the TVU’s FOV, this allowed us to determine whether the ultrasonic probe caused any change in the observed volume or was unable to capture some of the musculature.

The shapes were then individually imported into Blender (v. 3.0.1) to measure their volume. Using Blender’s built in shrinkwrap function – which allows an object to project itself on to the surface of another object by transforming each vertex of the targeting object to its closest vertex on the targeted object – a cylindrical shape was created and fit to interior surface of the muscles. Then using Blender’s 3D printing toolkit, the volume of the fitted shape was measured.

RESULTS
Twenty subjects were initially recruited for this study. However, one patient became pregnant during the study and was thus excluded. The remaining 19 patients (age = 29.7 ± 8.2, BMI = 24.3 ± 4.5) were included in the final analysis.

We found the levator volume measured via MRI to be larger than that measured in TVU (46.1 ± 7.9 cm¬3 v. 25.6 ± 6.0 cm3, $p < 0.001$). However, when the MRI segmentation was limited to the FOV of the TVU, we observed volumes much closer to the volumes observed in TVU (35.5 ± 3.3 cm3 v. 25.6 ± 6.0 cm3, $p < 0.001$). Although statistically different these two groups of volumes were highly correlated ($r2 = 0.808$, $p < 0.001$).

INTERPRETATION OF RESULTS
Our findings confirmed that MRI captures all portions of levator bowl while TVU captures ~ 60% of it. After overlaying these two measured volumes, it was shown that the TVU includes all distal subdivisions (levator ani muscles) but misses apical sections of iliococcygeus muscles. This difference plus anal sphincter and muscle bulk behind it that are included in MRI segmentation but missed in ultrasound segmentation explains the ~ 40% smaller volume captured by TVU (Figure 2).

CONCLUDING MESSAGE
In conclusion, we were able to compare levator volume measured in TVU to levator volume measured using MRI and identify uncaptured landmarks by ultrasound that accounts for the differences. Levator volume is being used as a new metric for evaluating pelvic floor dysfunction symptoms and also will be a valuable variable assessing childbirth related trauma. This study demonstrates that volumes measured via TVU may are easy and safe and also may provide clinical utility associated with this measurement.

FIGURE 1

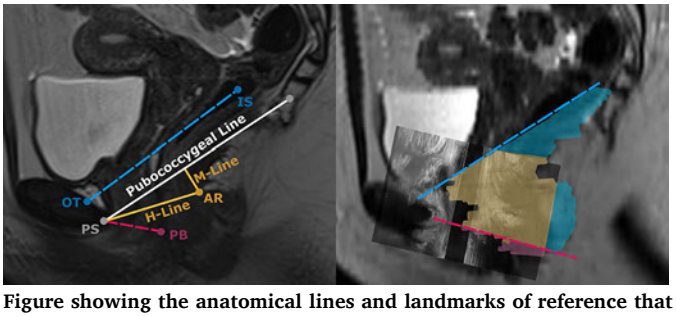
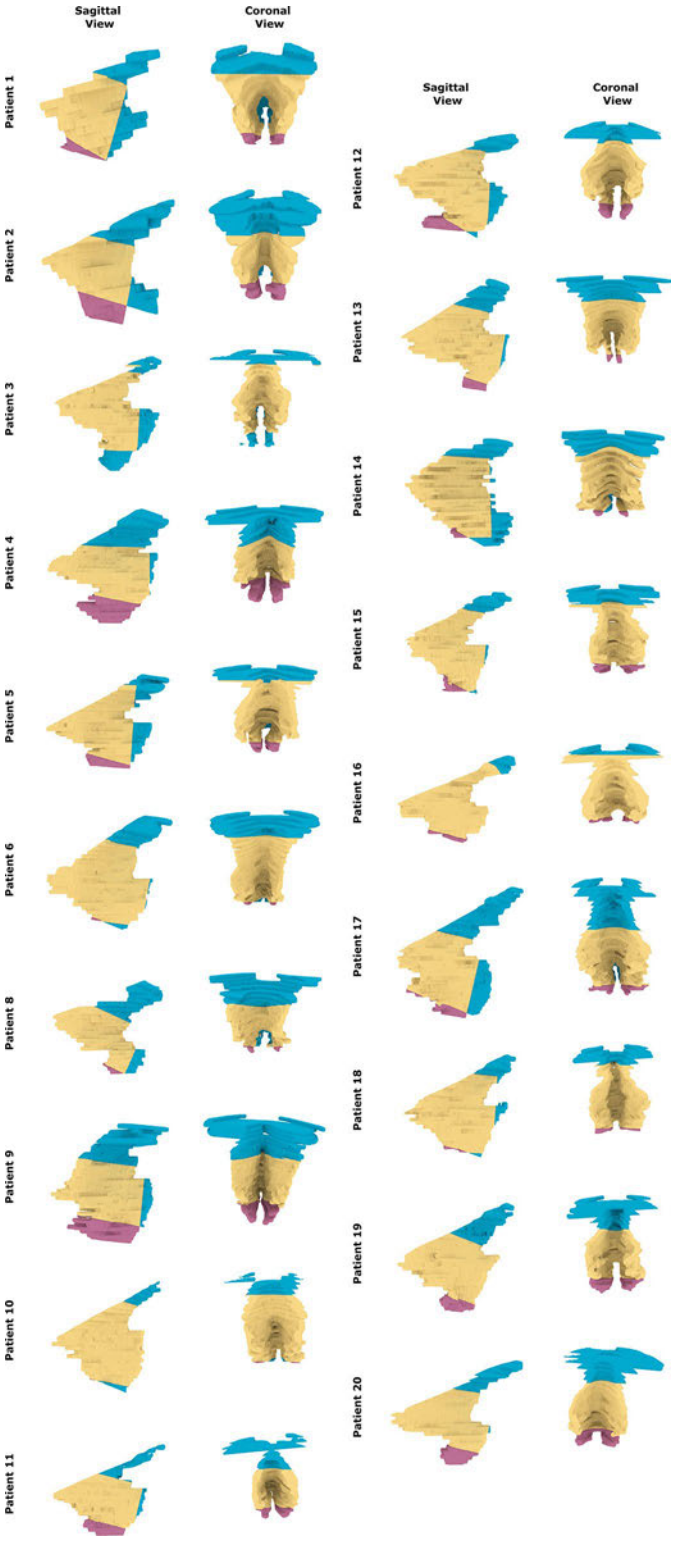


Figure showing the anatomical lines and landmarks of reference that were used to trim the segmentations. A) Blue line represents the superior edge of the levator ani musculature. Drawn by connecting the point on the pubic bone at the level of the pubovisc

FIGURE 2



All patients included in this study colored by the modality that was able to capture the potion of the musculature. Blue = only captured on MRI and part of the levators, Yellow = captured by both ultrasound and MRI and part of the levator ani, and Red = c

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PELVIC FLOOR MUSCLE DYSFUNCTION AT 3D TRANSPERINEAL ULTRASOUND IN MATERNAL EXPOSURE TO GESTATIONAL DIABETES MELLITUS

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HYPOTHESIS / AIMS OF STUDY

According to translational research, the pelvic floor (PFM) and rectus abdominis muscles (RAM) showed a myopathic process1 presence of hyperglycemia in pregnant rats and GDM women. These investigations, however, did not look at changes in the contractility and distensibility of the levator hiatus. Our hypothesis was that GDM women will exhibit PFM dynamic abnormalities indicating of lower strength compared to pregnant women without GDM using 3D-TPUS. 2 Our major aim was to investigate and compare the dynamic morphometry of PFM using 3D-TPUS, as well as the development at two third-trimester time periods in women with and without GDM.

STUDY DESIGN, MATERIALS AND METHODS

This was prospective cohort study approved by the Institutional Ethical Committee (Protocol Number CAAE 82225617.0.0000.5 411). The main inclusion criteria were: pregnant women between 24-30 weeks of gestation in the first assessment; singleton pregnancy; 18–40 years of age; primigravida or primiparous with previous c-section. The participants were allocated in GDM group if they presented fasting glycemic levels ≥92 mg/dL or 1 hour ≥180 mg/dL or 2 hours ≥153 mg/dL. In addition, participants who had lower levels composed the Non-GDM group. Participants were evaluated at two time points: 24–30 weeks of gestation (T1), at 36–38 weeks of gestation (T2). The same procedures were followed at each time point. During first step of the investigation the participants answered a questionnaire, followed by instructions about pelvic floor contraction. After the confirmation that they were prepared to perform the main acquisition, the 3DUS data collection were performed. After confirming that the participants understood and performed all functions correctly, an experienced 3D-TPUS investigator obtained the PFM images. The participants had two predetermined times to perform the previously instructed pattern. The AGE Voluson I system was employed, along with a RAB 2-6RS (2-6 MHz) curved array 3D transducer (GE Healthcare, Zipf, Austria). The condom-covered probe was positioned on the perineum in the sagittal plane. The sagittal plane's field of view angle was set to 70°, while the coronal plane's field of view angle was set to 85°.3 In terms of the 3D-TPUS protocol acquisition, three separate images were gathered in the following order and colors: 1) One gray picture was collected at rest with no pelvic floor movement to be utilized as a reference basal measurement to determine the index from rest to functional activity; 2) One sepia image at maximum voluntary PFM contraction; 3) and one blue image at maximum distension obtained during the Valsalva maneuver.

RESULTS

PDRC recruited and tracked a total of 110 pregnant women over the study period. The study's eligibility criteria were met by 104 people (94%). In the end, 83 participants (80%) were included in the study, 38 in the GDM group and 45 in the non-GDM group. Table 1 shows the sociodemographic and clinical characteristics of the individuals. As expected, the non-GDM and GDM groups revealed significant differences on the OGTT-75g, fasting (p < .001), after 1 hour (p < .001) and after 2 hours (p < .001). Furthermore, there were still variations in glycemic levels between the groups at 38-40 weeks of gestation (p = .002) (Table 1). Table 2 summarizes the results of static (at rest) and dynamic (PFM contraction and distension) morphometry. Comparisons of PFM contraction, distension, and mobility dimensions between GDM and non-GDM groups at 24-30 weeks of gestation revealed no significant changes in the LH dimensions.The LHarea (P < .000) showed reduced constriction in the GDM group compared to the non-GDM group at 38-40 weeks of gestation. In the GDM group,

LHap (P < .001), LHrl (P = .001), and LHarea (P < .001) had less distension. In terms of mobility, LHap (P < .001), LHrl (P = .001), and LHarea (P < .001) dimensions were less mobile in the GDM group.Table 3 shows the comparison of PFM at the two gestational stages in all LH dimensions in each group. The GDM group experienced a significant decrease (P = .000) in LHarea contraction, distension, and mobility during pregnancy. The non-GDM group, on the other hand, showed higher distension in transverse diameter (LHrl) (P = .046) and LHarea (P = .000), as well as more mobility in LHap (P = .032), LHrl (P = .048), and LHarea (P = .000). from 24 to 28 weeks through 36 to 40 weeks of gestation.

INTERPRETATION OF RESULTS

The maternal PFM dynamic 3D-TPUS evaluation in GDM women at two time periods during the third trimester of pregnancy was compared between women with and without GDM in this hypothesis-generating analysis; Thus, GDM women had lower PFM contractility, distensibility, and mobility at 38-40 weeks of gestation compared to non-GDM women. Our findings of less functional PFM using 3D-TPUS assessment include GDM as an epidemiological factor for the development of PFD in pregnancy, which warrants further investigation.

CONCLUDING MESSAGE

Our data indicate that maternal GDM exposure may lead to a loss of PFM functioning, as measured by decreased PFM contractility, distensibility, and mobility compared to non-GDM women. Furthermore, as these muscles move to a lower functional muscle near the end of pregnancy, GDM may decompensate the PFM maternal adaption for normal delivery.

FIGURE 1

TABLE 1 Baseline variables of the study population.

Variable	non-GDM (n=45)	GDM (n=38)	*P-value
Ethnicity			
Caucasian	38 (84.4)	29 (76.3)	.349
Others	7 (15.6)	9 (23.7)	
Smoking in pregnancy	0 (0.0)	1 (2.6)	.457
Physical activity in pregnancy	5 (11.1)	3 (6.3)	.477
Education level –min. high school	40 (88.9)	36 (75.0)	.083
Previous C-section	14 (33.0)	11 (29.0)	.668
Age (years)[1]	29.00 (18.00-39.00)	28.00 (18.00-40.00)	.912
BMI (kg/m²) [1]	25.10 (18.00-37.20)	27.20 (17.70-37.00)	.079
Weeks of gestational[1]	26.90 (24.70-30.00)	26.50 (24.70-30.00)	.426
Weeks of gestational[2]	39.10 (37.90-40.10)	38.90 (37.70-39.20)	.653
Maternal weight gain (kg) [2]	9.10 (0.50-24.80)	7.40 (-0.20-21.90)	.187
Newborn weight at birth (grams)	3160 (2675 - 4180)	3175 (2560 - 4585)	.306
Blood glucose (mg/dL)[1]	78.00 (64.00-91.00)	85.00 (72.00-99.00)	<.001
OGTT-75g (mg/dL) - fasting[1]	74.00 (58.00-85.00)	85.00 (69.00-163.00)	<.001
OGTT-75g - 1h (mg/dL)[1]	108.0 (58.00-163.00)	160.0 (88.00-213.00)	<.001
OGTT-75g - 2h (mg/dL)[1]	101.0 (58.00-135.00)	144.0 (72.00-189.00)	<.001
Blood glucose (mg/dL)[2]	78 (58.00-135.00)	83 (72.00– 99.00)	.002

Non-GDM, Non-Gestational Diabetes Mellitus; GDM, Gestational Diabetes Mellitus; BMI, Body Mass Index; OGTT, Oral Glucose Tolerance Test. [1]Evaluation at 24-30 weeks of gestation. [2]Evaluation at 38-40 weeks of gestation. Data are the median (minimum, maximum) or n (%). *Based on Mann–Whitney U and Chi-square test.

TABLE 1 Baseline variables of the study population.

FIGURE 2

TABLE 2 Comparison of levator hiatal (LH) dimensions of pelvic floor muscle (PFM) on rest, contraction, distension, and mobility, considering the resting state, between the gestational diabetes mellitus (GDM) and non-GDM (non-GDM) groups at 24-30 and 38-40 weeks of gestation.

Variables	24-28 weeks of gestation			38-40 weeks of gestation		
	GDM (38)	non-GDM (45)	*P-value	GDM (38)	non-GDM (45)	*P-value
Rest						
LHap (cm)	5.78 (4.33-8.12)	5.61 (4.23-7.31)	.112	5.37 (4.03-7,01)	5.83 (4.01-6.83)	.044
LHrl (cm)	3.98 (2.99-4.96)	4.05 (3.30-5.24)	.583	4.02 (3.09-4.88)	4.10 (3.23-5.32)	.708
LHarea (cm²)	13.50 (11.23-21.32)	13.73 (8.35-17.60)	.175	13.61 (10.26-19.19)	14.57 (10.25-17.62)	.162
Contraction						
LHap (cm)	-0.82 (-3.01-0.79)	-1.09 (-2.53-0.53)	.357	-0.83 (-6.28-3.26)	-1.09 (-2.70-0.38)	.125
LHrl (cm)	-0.28 (-1.01-1.47)	-0.37 (-1.4-0.8)	.246	-0.23 (-1.13-0.79)	-0.26 (-1.21-0.85)	.206
LHarea (cm²)	-2.71 (-6.65- -0.50)	-2.70 (-6.63-2.95)	.924	-0.90 (-15.10-3.51)	-2.53 (-6.37-4.08)	<.000
Distension						
LHap (cm)	-0.03 (-1.36-1.82)	-0.02 (-1.80-1.87)	.685	-0.10 (-5.40-3-37)	0.26 (-1.43-1.71)	.012
LHrl (cm)	0.14 (-0.77-1.85)	0.13 (-0.96-0.97)	.867	0.05 (-4.21-1.06)	0.35 (-1.44-9.91)	.007
LHarea (cm²)	2.16 (0.76-5.09)	1.89 (-5.70-8.46)	.097	0.93 (-14.03-3.63)	3.37 (-3.98-9.65)	<.001
Mobility						
LHap (cm)	0.88 (-1.25-3.42)	0.95 (-0.48-3.16)	.561	0.54 (-1.66-1.99)	1.25 (-0.21-2.94)	.001
LHrl (cm)	0.43 (-2.24-2.16)	0.39 (-0.43-1.38)	.957	0.32 (-1.46-1.29)	0.60 (-0.43-10.31)	.001
LHarea (cm²)	5.16 (2.34-9.60)	3.93 (-1.27-11.14)	.060	1.90 (-0.81-5.07)	5.85 (-0.39-9.99)	<.001

LHap, anteroposterior diameter; LHrl, transverse diameter from right to left; LHarea, levator hiatal area. Contraction was calculated by (C = C –R); distension by (D = D –R), and mobility by (M = D – C).Data are the median (minimum, maximum). *Based on Mann–Whitney U test.

TABLE 2 Comparison of levator hiatal (LH) dimensions of pelvic floor muscle (PFM) on rest, contraction, distension, and mobility, consider-

ing the resting state, between the gestational diabetes mellitus (GDM) and non-GDM (non-GDM) groups at 24-30 and 38-4

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BEST IN CATEGORY PRIZE: IMAGING

DO WOMEN AND MEN HAVE DIFFERENT BRAIN AND BRAINSTEM ACTIVATION PATTERNS AT THE INITIATION OF VOIDING? A 7-TESLA BRAIN-BLADDER PARADIGM STUDY

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HYPOTHESIS / AIMS OF STUDY

With advances in neuroimaging over the last two decades, such as functional magnetic resonance imaging (fMRI), the evaluation of supraspinal control over the lower urinary tract has become feasible. However, imaging of significant structures in the brainstem has been met with challenges due to relative size, physiological noise from nearby arteries, and the limited resolution of 1.5 and 3 Tesla MRIs. Measuring activity in the brainstem has become a critical component in understanding the fundamental mechanisms of bladder function as the periaqueductal gray (PAG) and pontine micturition center (PMC) known to be involved in the voiding reflex are housed in this area. As imaging techniques and protocol designs have improved in just the last couple of decades, Blood Oxygen Level-Dependent (BOLD) studies of the brain and more specifically the brainstem have become a pragmatic reality. In this study, we evaluated brain and brainstem activation during initiation of voiding in healthy men and women utilizing a 7 Tesla MRI scanner and a non-invasive brain-bladder paradigm.

STUDY DESIGN, MATERIALS AND METHODS

Twenty healthy adult volunteer men and women with no history of urinary symptoms or neurological diseases were invited to participate. Uroflow was obtained, and those who failed to meet all inclusion and exclusion criteria were removed from the study. Volunteers were instructed to practice voiding and holding 4 times for a day prior to the day of the MRI scan. For the brain-bladder protocol, each volunteer was asked to consume 500mL to 750mL of water and empty their bladder prior to entering the scanner. Post-void residual (PVR) volume was measured. Next, volunteers were placed within the 7T MRI. An anatomical scan and diffusion tensor imaging (DTI) image were obtained. Volunteers then remained in the scanner until they felt the urge to void, prompting a functional scan during the full bladder phase. Once completed, another function scan began where volunteers began five cycles, consisting of fifteen seconds of attempting to void, followed by thirty seconds of rest. The first 7.5 seconds of each void cycle identified as “initiation of voiding” were analyzed. Activation of regions of interest (ROIs) including brainstem structures were obtained for all men and women enrolled in the study. ROIs with a t-value greater than 2.1 were statistically significant and BOLD maps of the brain and brainstem were generated.

RESULTS

The average age of each participant was 27.45 years with males averaging 26 and a females averaging 28.9 years of age. Five distinct regions of interest within the PAG and PMC yielded statistically significant activation according to BOLD analysis of initiation of voiding. These included 3 distinct PAG regions and 2 distinct PMC regions (Table 1). Additionally, there were several other Talairach regions in the brain (consistent with prior neuroimaging literature) beyond our scope that showed statistically significant activation (Figure 2a). Interestingly, when comparing BOLD activation in men and women, women had overall lower BOLD activation compared to men with the exception of the caudate (Figure 2b).

INTERPRETATION OF RESULTS

We again see significant BOLD activation in specific brainstem structures that have been shown to play an active role in the voiding cycle, including the PAG and PMC [1]. Beyond our ROIs, many of the significantly activated Talairach regions fit nicely within Griffiths et al’s Working Model of Lower Urinary Tract Control. Specifically, the left and right superior frontal gyrus contribute to Circuit 1, the left and right anterior cingulate gyrus contribute to Circuit 2, and the left and right parahippocampal gyrus contribute to Circuit 3 [1]. Next, activation of certain regions such as the left and right thalamus seem appropriate, as the thalamus is the ‘relay center’ for all sensory information. Others, such as the caudate and putamen are part of the basal ganglia, which is critical for coordinating voluntary movements and making postural adjustments. As this is the first study using a 7-Tesla to evaluate voiding and micturition in both men and women, subsequent studies are needed to clarify how previously unidentified Talairach areas may fit into the current working model of higher neural control of bladder. Interestingly, the results with respect to lower BOLD activation in women as compared to men is particularly notable; prompting further investigation in both the cause of this difference in activation, as well as other differences that may exist between genders and its impact on initiation of voiding.

CONCLUDING MESSAGE

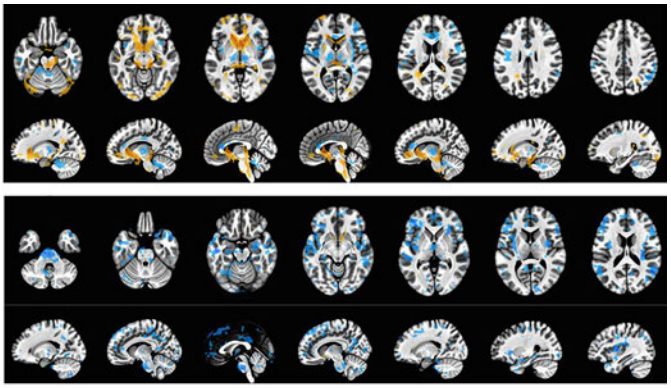
To our knowledge, we have conducted the first study of its kind to implement a non-invasive fMRI protocol to evaluate brainstem involvement during initiation of voiding in real-time in both men and women utilizing a 7-Tesla MRI . Our findings support the critical role of the PAG and PMC in the initiation of voiding, previously studied in animals, incorporating the complex social, emotional, and mechanical criteria needed for voiding in humans.

FIGURE 1

Brain Region	x	y	z
PAG	-6	-15	-6
PAG	4	-33	-19
Right PAG	12	-22	-12
PMC	2	-34	-32
PMC	6	-30	-24

A Priori ROIs with significant activation at voiding initiation as defined by their Montreal Neurological Institute (MNI) coordinates

FIGURE 2



a) fMRI BOLD activation during initiation of voiding – all participants (top). b) fMRI BOLD activation during initiation of voiding – women versus men (bottom)

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THE RELATIONSHIP BETWEEN PELVIC FLOOR MUSCLE STRENGTH AND MORPHOLOGICAL FEATURES MEASURED BY MRI IN MEN

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HYPOTHESIS / AIMS OF STUDY

Pelvic floor muscles (PFM) are innervated by branches of the pudendal nerves arising from the S2–S4 nerve roots of the sacral plexus, which has an important role in maintaining continence and pelvic support. Also, PFM strength can be one of the factors to improve urinary incontinence after Radical Prostatectomy. Our group previously reported that the reliability of PFM strength assessments for measuring anorectal pressure during PFM contractions in men has been confirmed [1]. To date, there have been several magnetic resonance imaging (MRI) researches on the anatomy and features of the male pelvic floor including levator ani muscle thickness, and membranous urethral length (MUL). A previous study stated that the changes in puborectalis muscle thickness and the position of the bladder neck may contribute to continence after radical prostatectomy [2]. However, the relationships between morphological parameters and PFM strength remain understudied in men. This study aimed to investigate a quantitative evaluation of the morphological features of PFM using MRI and anorectal pressure in men.

STUDY DESIGN, MATERIALS AND METHODS

Forty-nine men with prostate cancer who had undergone Robotic-Assisted Laparoscopic Prostatectomy (RARP) (age: median 70, range 52-82 years old; body mass index: median 23, range 17-32 kg/m2) volunteered for the current study. Pelvic T2-weighted MRI and PFM strength were performed during the preoperative periods. The expert radiologist (K.F.) reviewed MRI blinded to any clinical data, in consensus. The following MRI parameters were obtained: (1) the thickness of the levator ani muscle in coronal (R/L), (2) the distance at the most convex part of the levator ani muscle (R/L): the distance at the most convex part from a straight line connecting the origin and insertion of the levator ani muscle, (3) the thickness of puborectalis muscle, (4) MUL in coronal, (5) MUL in sagittal (6) the position of the bladder neck in relation to the pubic bone, (7) the thickness of obturator internal muscle (R/L) (8) urethra wall thickness. A manometer with an anal sensor (PeritronTM cat 9300A; Laborie, Canada) was used for quantitative PFM strength assessment. All participants were lying on the bed in a lateral position and a pillow was placed under the head. An assessor used standardized instructions to “squeeze and lift or tighten and pull up the PFM as hard as you can” to assess the maximum strength of the PFM. This study was approved by our institutional ethics committee. Statistical analysis was performed using GraphPad Prism 8.4.3 (San Diego, USA). Data distribution was assessed with the Shapiro-Wilk test for continuous variables. We used the Pearson correlation coefficient with normally distributed data and the Spearman's rank correlation coefficient with not normally distributed data for measuring the strength of a linear association between two variables. For between-group comparisons, we used the Mann–Whitney U test with not normally distributed. The significance level was set at $p < 0.05$.

RESULTS

Pelvic MRI parameters and anorectal pressure are listed in Table 1. There was a significant negative correlation between PFM strength and the distance at the most convex part in both right (median 0.88, range -7.96 - 6.88 mm, $r = -0.306$, 95% confidence interval -0.540 to -0.027, $p = 0.033$) in figure 1 and left (median 1.32, range -8.12 - 9.76 mm, $r = -0.297$, 95% CI -0.534 to -0.017, $p = 0.038$) in figure 2. There were no significant differences between PFM strength and other pelvic MRI parameters. The distance at the most convex part on the right side in the aged < 65 years old group was significantly higher than in the aged ≥ 65 years old group (median 3.325, range -3.760 - 6.880 mm and median 0.690, range -7.960 - 5.120 mm, respectively). Also, the distance at the most convex part on the left side in the aged < 65 group was significantly higher than in the aged ≥ 65 group (median 3.350, range -4.860 - 9.760 mm and median 1.120, range -8.120 - 5.310 mm, respectively).

INTERPRETATION OF RESULTS

To our knowledge, this is the first study to investigate the relationships between a quantitative evaluation for the morphological features of PFM using magnetic resonance images (MRI) and anorectal pressure in men. We found that there was a significant negative correlation between PFM strength and the distance at the most convex part in both the right and left sides of the levator ani muscle. The higher PFM strength showed the lower distance at the most convex part from a straight line connecting the origin and insertion of the levator ani muscle. Our findings suggest that the distance at the most convex part of the levator ani muscle can be a surrogate parameter of PFM strength. Moreover, the morphological features of the levator ani muscle are associated with aging. We found levator ani muscle in ≥ 65 years was more downward compared to < 65 years. A previous study also showed the distance at the most convex part in < 65 years was significantly higher than in ≥ 65 years (mean 3.6 range -8.1 – 11.6 mm and mean 0 range -10.5 – 11.9 mm) [3]. The results of the current study agreed with previous studies.

CONCLUDING MESSAGE

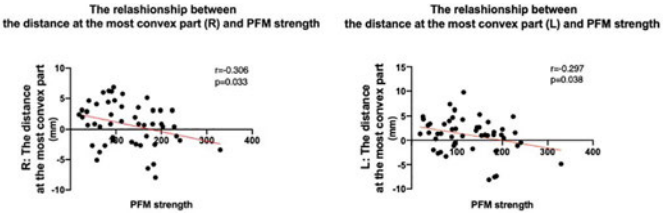
The results of the current study showed that pelvic parameters measured by MRI may be useful to estimate PFM strength in men.

FIGURE 1

n=49	Median	Min	Max
Anorectal pressure (cmH_2O)	112.55	18.70	329.70
R: The thickness of the levator ani muscle coronal (mm)	5.45	2.88	9.12
L: The thickness of the levator ani muscle coronal (mm)	5.20	2.88	9.81
R: The distance at the most convex part (mm)	0.88	-7.96	6.88
L: The distance at the most convex part (mm)	1.32	-8.12	9.76
The thickness of Puborectalis muscle (mm)	7.40	4.77	9.92
Membranous urethral length coronal (mm)	12.18	6.87	24.38
Membranous urethral length sagittal (mm)	12.59	4.94	20.40
The position of the bladder neck in relation to the pubic bone (mm)	25.31	14.58	43.80
R: obturator internal muscle (mm)	20.77	9.50	25.32
L: obturator internal muscle (mm)	20.27	8.88	24.12
Urethra wall thickness (mm)	11.56	5.94	15.94

The anorectal pressure and the pelvic MRI parameters

FIGURE 2



The relationship between the distance at the most convex part of levator ani muscle and PFM strength

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Funding No **Clinical Trial** Yes **Public Registry** No **RCT** No **Subjects** Human **Ethics Committee** Ethical Review Board for Life Science and Medical Research, Hokkaido University Hospital **Helsinki** Yes **Informed Consent** Yes

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CORRELATION OF SHEAR WAVE ELASTOGRAPHY AND TRANSABDOMINAL ULTRASOUND FOR ASSESSMENT OF PELVIC FLOOR MUSCLE FUNCTION

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HYPOTHESIS / AIMS OF STUDY

This study aimed to investigate the association between leavator ani (LA) elasticity using Shear wave elastography (SWE) and bladder base displacement using transabdominal ultrasound (TAUS) for evaluation of Pelvic floor muscle (PFM) function. The secondary objective was to assess the elastic properties of LA muscle and provide a standard reference to evaluate PFM function in nulliparous women.

STUDY DESIGN, MATERIALS AND METHODS

This observational study is in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement. All participants were fully informed about experiment procedures and gave their written informed consent before the beginning of the study. Forty-two nulliparous women (mean age 23.5 ± 3.2 years) with no history of pregnancy were included in the study. All participants were educated on how to contract PFM and asked to practice maximum voluntary contraction (MVC) of PFM three times for familiarization. Another 5 minutes were given to the participants to get relaxed. Then, they were asked to maximally contract PFM and maintain MVC for 5 seconds while SWE and TAUS measurements were obtained simultaneously; 30 seconds was given for relaxation between each contraction to prevent muscle fatigue caused by repeated contraction of PFMs. The elasticity of the LA muscle at rest and during contraction using SWE and the bladder base displacement using TAUS were obtained simultaneously.

RESULTS

The intra-class correlation coefficient for repeat measures of LA elasticity at rest and contraction was 0.906 at rest and 0.687 during contraction. The LA elasticity measured by SWE was 24.7 ± 4.5 kPa at rest and 62.1 ± 10.4 kPa during contraction. There was a significant increase in mean LA elasticity when the muscle was voluntarily contracted compared to rest (95% CI: 34.3 – 40.4, $p < 0.001$). The mean bladder base displacement of the participants was 7.2 ± 2.5 mm, and normalized bladder base displacement by BMI was 0.3 ± 0.1 mm . Analysis of the Pearson's correlation showed that the bladder base displacement was significantly associated with the elasticity of LA differences between contraction and resting when simultaneously performed ($r = 0.486$, $p = 0.001$).

INTERPRETATION OF RESULTS

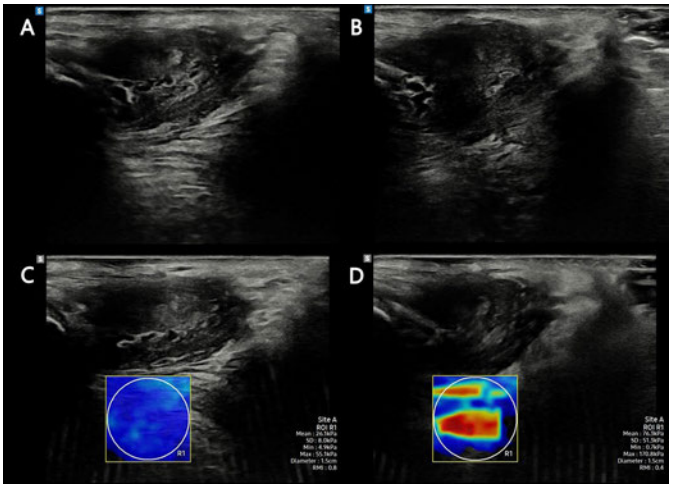
The results of our study assessed non-invasive two different types of PFM function. Our results found a moderate correlation coefficient between the elastic properties of LA measured using a non-invasive method, SWE, and the bladder base displacement measured with TAUS, a gold standard that indirectly measures the function of PFM. An excellent reproducibility (ICC (2,1) =0.906) at rest and a moderate reproducibility (ICC (2,1) =0.687) during contraction were found.

Several studies assessed PFM using direct and indirect methods, but it is difficult to compare with previous studies due to the different metric values. The most direct comparison can be processed with the study of Gachon et al., which assessed elastic properties of LA with similar characteristics of population using SWE . They reported a 21.9 - 22.8 kPa shear modulus at rest and 55.1 - 61.4 kPa during a contraction while our results showed an average 24.7 kPa at rest and average of 62.1 kPa during contraction, indicating that the results are similar [1]. As our study only included nulliparous women with no history of pregnancy, the bladder base displacement is similar to the study of Sherburn et al., which had pre-menopausal nulliparous women as their subjects [2] . In addition, our result showed that the ICC for repeat measures of PFM was stronger when LA was resting than during contraction, which supports the result of a previous study [1]. This can be explained by the lower detection accuracy of SWE measurements due to the generation of high-speed shear waves that are too fast to detect when measuring strongly contracted muscles [3].

CONCLUDING MESSAGE

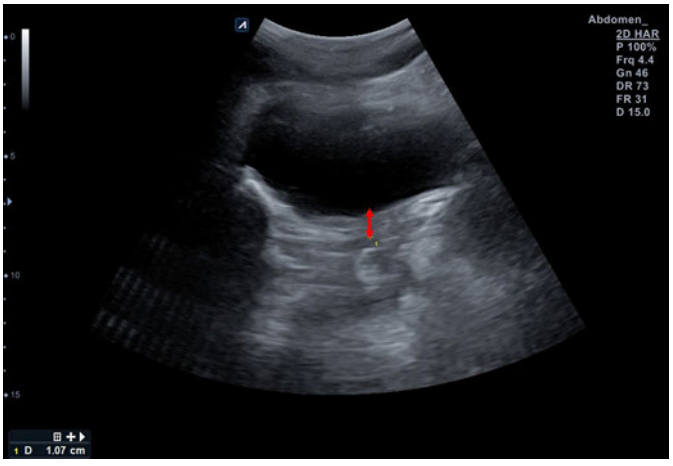
This study showed that SWE is a reliable tool to investigate the elastic properties of PFM in nulliparous women. In addition, this paper adds important findings in terms of establishing the association between the bladder base displacement and elasticity of LA differences between contraction and resting for pelvic floor function. Also, the study findings allow a reference baseline data to have an objective method for a clinical measure and establish an appropriate plan of care.

FIGURE 1



Levator ani muscle assessment in this study. (A) LA at rest using B-mode imaging; (B) LA at contraction using B-mode imaging; (C) LA at rest using shear wave imaging; (D) LA at contraction using shear wave imaging.

FIGURE 2



Bladder base displacement assessment in this study using transabdominal ultrasound

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HOW DOES TRANSPERINEAL ULTRASOUND COMPARE WITH DEFAECATION PROCTOGRAPHY FOR THE ASSESSMENT OF OBSTRUCTED DEFAECATION? A SYSTEMATIC REVIEW

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HYPOTHESIS / AIMS OF STUDY

Transperineal ultrasound may be an alternative to defaecatory imaging for the assessment of obstructive defaecation. The aim was to systematically review the evidence behind the use of transperineal ultrasound for the assessment of obstructed defaecation by analysing studies which compare transperineal ultrasound with defaecatory imaging. The reason was to explore the possibility that transperineal ultrasound may reduce the number of defaecatory investigations needed.

STUDY DESIGN, MATERIALS AND METHODS

Two authors (AH, DS) independently reviewed the abstracts and screened them for their relevance and content. All articles comparing transperineal, translabial or introital ultrasound with defaecation proctography were included. The examination of the anal sphincters was not included, but rather the abnormalities associated with obstructed defaecation (rectocoele, enterocoele, sigmoidocoele, peritoneocoele, intussusception, perineal descent, and dyssynergy). The literature search encompassed all publications to the end of February 2022. Review articles and those which were not published in English were not included.

Due to the heterogeneous nature of the studies reviewed, it was not possible to perform statistical analysis. For studies which provided the number of true and false positives and negatives but did not calculate accuracy, this was calculated using Stats Direct software. Agreement using Cohen's Kappa coefficient was poor (0 - 0.20), fair (0.21 - 0.40), moderate (0.41 - 0.60), good (0.61 - 0.80) and excellent ($>$ 0.81).

There were 570 articles identified during the initial literature search of which 28 were duplicates, and 304 were excluded as irrelevant after review of the abstract. There were 238 articles where the full text was reviewed. There were 14 which compared findings on transperineal (translabial/ introital) ultrasound with defaecation proctography. One study compared transperineal ultrasound with defaecation MRI.

RESULTS

Transperineal or translabial ultrasound was performed with either a curved or linear array probe rested externally. One study performed introital ultrasound using an endocavity transducer placed near the hymeneal ring, on the posterior wall of the vulva. All performed ultrasound scanning during squeezing and maximal straining. There was variation in the use of gel, contrast and patient preparation. Some authors used rectal gel and encouraged evacuation of the gel toward the end of examination and performed ultrasound during rectal evacuation where possible.

Agreement for rectocoele detection between transperineal ultrasound and defaecation proctography was poor to excellent, specificity was 67 to 100% and sensitivity 29 to 88.9%. There was variation in the method for rectocoele measurement and the cut off for a pathological rectocoele on ultrasound. Grasso et al. found 100% of large rectocoeles ($>$4cm on proctography), 12% of moderate (2-4cm on proctography) but no small rectocoeles ($<$2cm on proctography) were visible on introital ultrasound. Steensma et al. showed that 87% of rectocoeles 2cm or greater on proctography but only 25% of those less than 2cm, were seen on ultrasound. Likewise, Beer Gabel et al. showed higher concordance for rectocoeles over 4 cm than those 2 to 4 cm.

A Cul de Sac hernia refers to either an enterocoele, sigmoidocoele or peritineocoele. Agreement for enterocoele (or Cul de Sac hernia) detection was good to excellent, specificity 92 to 96% and sensitivity 64 to 80% (table 3). Steensma et al. showed concordance between the two modalities was higher for grade 2 – 3 enterocoeles only than for all enterocoeles (kappa 0.77 versus kappa 0.65; 14/16 grade 2 – 3 enterocoeles but only 2/9 grade 1 enterocoeles were seen on ultrasound).

The description and grading for intussusception varied. Some calculated accuracy and agreement for internal (i.e. intussusception) and external rectal prolapse as one entity. Concordance for the detection of intussusception/ rectal prolapse was poor to excellent, specificity 84 to 100% and sensitivity 22 to 100%.

INTERPRETATION OF RESULTS

Transperineal ultrasound is cheap, safe and portable. It is non-invasive and therefore avoids the soft tissue distortion associated with endoluminal probes and is well tolerated by patients. It allows the dynamic assessment of the entire pelvic floor including those functional and anatomical elements associated with obstructive defaecation namely rectocoele, enterocoele, sigmoidocoele, peritoneocoele, intussusception, perineal descent and dyssynergy (anismus).

Transperineal ultrasound has a high positive predictive value and specificity for rectocoele, enterocoele and intussusception. Negative predictive value and sensitivity are generally lower. Accuracy for detection of rectal prolapse is less clear. Concordance for all pathologies is variable. Transperineal ultrasound may be a suitable screening tool for obstructive defaecation and may avoid the need for defaecatory imaging in some patients.

CONCLUDING MESSAGE

Transperineal ultrasound more easily detects larger rectocoeles and higher grades of enterocoele or intussusception. Due to concerns that defecation proctography overestimates pathology, this feature of ultrasound may be advantageous in clinical practice to reduce overdiagnosis by avoiding defecation imaging in some patients. Transperineal ultrasound can be an initial screening tool in patients with obstructive defaecation syndrome, while defaecatory proctograghy can potentially be reserved as a second line test if no correspondence between patients' symptoms and sonographic results is detected.

Funding Nil **Clinical Trial** No **Subjects** None

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THERMOGRAPHIC EVALUATION OF PLACENTAL WARMING IN PARTURIENT WOMEN IN NORMAL AND CAESAREAN: OBSERVATIONAL STUDY

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HYPOTHESIS / AIMS OF STUDY

Human body temperature average is 37 ˚C and that of a fetus is higher than the maternal temperature by 0.3 to 0.5 ˚C 2 (1). Heating above this temperature can alter the normal physiological process, causing, for example, changes in metabolic reactions or neuronal migration and even fetal cell death(2). Infectious processes trigger an imbalance in the homeostatic circuit, generating heating of the structures that support intrauterine life and physiological and immunological changes capable of putting the life of the fetus at risk during or after its birth(3). This study aimed to investigate the placental heating of parturient women who had their newborns by vaginal delivery or cesarean section, to verify if placental thermography can serve as a method of classifying the degree of fetal compromise.

STUDY DESIGN, MATERIALS AND METHODS

This is a random observational report. Part of a randomized controlled study involving puerperal women, in which we sought to investigate the effectiveness of a photobiomodulation protocol to modulate the acute inflammatory process and the perception of pain in puerperal women who suffered perineal lacerations in the immediate normal postpartum period, admitted in a Maternity Hospital. The curiosity arose when observing a report of heating increase obtained by a two-finger touch procedure in admitted parturient women and in labor.

'The research was approved by the Ethics Committee for research with human beings and registered in the Brazilian Clinical Trials Registry.

Parturient women aged between 18 and 40 years, with and without reports of infectious diseases, with a clinical history of comorbidities and fetal malformation, literate, admitted to a normal delivery room and operating room were included. Fourteen postpartum women had their newborns by cesarean section, seven normally. Parturient women diagnosed with mental disorders were excluded.

After signing the Free Informed Consent Term, two images of the placenta were captured immediately after delivery by a commercial thermal camera. Both birth places at room temperature. One image from the placenta side closer to the fetus (fetal face) and one from placenta side closet to the uterus m wall (maternal face). Subsequently, the placenta images were analyzed with the Flir tools program and information of the maximum, minimum and average temperature values of the area of interest were extracted. Data were exported and analyzed in Python with the seaborn library. Histogram graphs were also made to verify the thermal distribution of the pixels.

RESULTS

Twenty-one parturient women were admitted to the survey, with a mean age of 26.7 ± 6.2 years. Most were married and had completed high school and declared themselves as mixed race. Seven patients had placental heating with an average of the Maternal Face greater than 36 ˚C. Sixteen patients whose delivery was normal had a placental temperature mean of 37.9 ± 1.7 ˚C, while those who underwent cesarean sections had a mean of 35.4 ± 1.5 ˚C. Two parturient women were induced into labor and had a mean placental heating of the maternal face equal to 38.0 ± 1.2 ˚C, while the mean of those who were not labor-induced was 35.8 ± 1.8 ˚C. Figure 1 shows a graph of the image pixel distribution as a function of the temperature of placentas from normal delivery patients in relation to those who underwent cesarean section. The three patients who were infected with Treponema pallidum had a mean temperature of the placenta's maternal face of 38.7 ± 1.6 ˚C, while the mean of those who did not have the infection was 35.5 ± 1.5 ˚C. Figure 2 shows two thermographic images of patient placentas, one without infection and the other with Treponema pallidum.

INTERPRETATION OF RESULTS

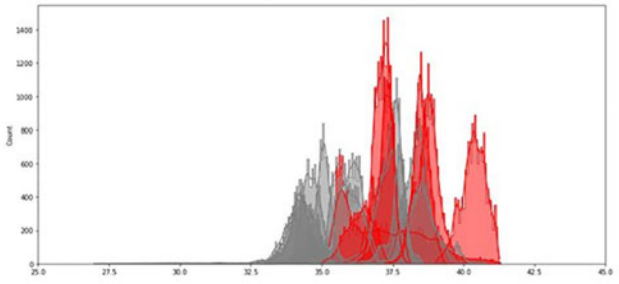
From the histograms It was possible to observe a clear trend of placental heating separation tendency between parturient women with normal delivery and cesarean section. Similar tendency seems to be present when comparing the thermography of the normal and the infected placenta.

CONCLUDING MESSAGE

A survey with a larger sample size needs is being implemented to confirm this finding.

FIGURE 1

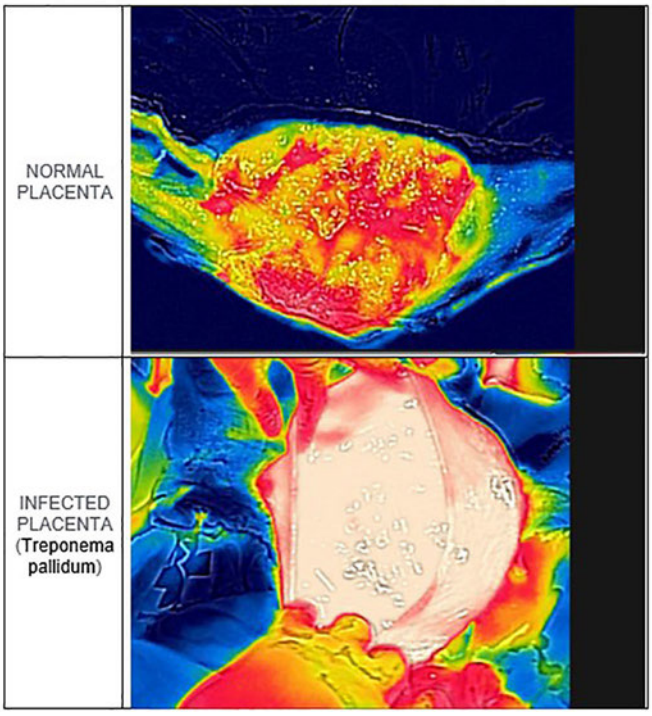
FIGURE 1: Pixels histogram of thermographic images of placentas from normal (red) and cesarean (grey) delivery births.



Gray: Cesarean delivery; Red: normal delivery.

FIGURE 2

FIGURE 2: Color code: White (hottest), red, yellow, green blue (coldest)



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Funding does not exist **Clinical Trial** Yes **Registration Number** UTN: U1111-1273-5518 **RCT** Yes **Subjects** Human **Ethics Committee** CAAE 29787219.0.0000.5010 **Helsinki** Yes **Informed Consent** Yes

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TOTAL PELVIC FLOOR ULTRASOUND CAN RELIABLY PREDICT LONG-TERM TREATMENT OUTCOMES FOR PATIENTS WITH PELVIC FLOOR DEFECATORY DYSFUNCTION

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HYPOTHESIS / AIMS OF STUDY

Integrated total pelvic floor ultrasound (TPFUS) may provide an alternative to defaecation proctography (DP) in decision-making and treatment planning for patients with pelvic floor defaecatory dysfunction (PFDD). This study evaluates the use of TPUS as a screening tool, and its likelihood to predict long-term treatment outcomes.

STUDY DESIGN, MATERIALS AND METHODS

Two blinded clinicians reviewed 100 women who had historically presented to a tertiary referral colorectal unit with PFDD from October 2014 to April 2015. The clinical history of the patients together with TPFUS or DP results were used to decide on main impression, treatment plan, likelihood of surgery and certainty of plan. These were compared to the actual treatment received six months later and again after a median follow-up of 68 months (range 48-84).

RESULTS

82 patients were treated with biofeedback only and 18 also underwent surgery (7 ventral mesh rectopexy, 8 transvaginal rectocoele repair, 1 extended sphincter repair and rectocoele repair, 1 sacral nerve stimulation and 1 injection of sphincter bulking agent).

The accuracy of the decision made with DP or TPFUS when compared to the actual treatment received is outlined in Table 1. A positive decision was the decision for surgery. After review with DP, all women requiring surgery were correctly identified (no false negative). After review with TPFUS alone, there were four women who were deemed suitable for biofeedback but underwent surgery. The decision for three of these four women was 'biofeedback with a proctogram should biofeedback fail' and therefore would have been treated appropriately. One of the four was deemed suitable for biofeedback alone after review of TPFUS, but was actually treated with an extended sphincter repair and rectocoele repair.

On long term follow-up, all 18 patients who underwent surgery did not develop complications. The majority (76/82) of the patients who had biofeedback therapy were eventually discharged from the clinic after significant improvement in symptoms. Two patients were referred again for pelvic floor strengthening exercises, toilet positioning, and lifestyle modifications. Four patients deemed suitable for biofeedback, eventually needed surgery (insertion of gatekeeper implant, Delorme's procedure, transvaginal rectocoele repair, and formation of loop ileostomy).

INTERPRETATION OF RESULTS

When compared with the actual treatment received, TPFUS alone would have ensured the same treatment in 99 out of 100 patients (one deemed suitable for conservative treatment, but actual treatment was surgical). The number of false positives (deemed suitable for surgery where actual treatment was conservative) was lower with TPFUS compared to DP. Both imaging modalities are useful for predicting which patients require surgery, but neither is useful for deciding the type of surgery. These factors support the use of TPFUS as a screening tool for the initial decision-making in symptomatic women with pelvic floor defaecatory dysfunction. However, there are still some discrepancies between the overall impression made using the two assessment tools, and clinician confidence is lower with ultrasound. This is expected as DP is more familiar. Further studies, training and expertise are required before colorectal pelvic floor surgeons can place more confidence in TPFUS.

CONCLUDING MESSAGE

To our knowledge, this is the first study to look at the long-term clinical value of TPFUS in decision-making and treatment planning for patients with PFDD. TPFUS is a reliable assessment tool, has a lower false positive rate for surgical treatment than DP, can highlight those patients who may go straight to biofeedback ,and is just as effective at predicting likelihood of surgery as DP. Neither imaging modality has proven superior for surgical planning, but as our understanding of pelvic floor pathology improves, and the anatomical findings which predict optimal surgical outcomes are identified, we hope to re-evaluate the use of TPUS for surgical planning.

FIGURE 1

Table 1. The accuracy of the decision made for the intended treatment with total pelvic floor ultrasound (TPFUS) only, and defaecation proctography (DP) only, when compared to the actual treatment received.

Intended treatment decision on review with	True positives	False positives	True negatives	False negatives	Positive predictive value	Negative predictive value	Sensitivity	Specificity
DP only	18	32	50	0	50%	100%	100%	73%
TPFUS only	14	26	56	4	35%	93%	78%	68%

The accuracy of the decision made for the intended treatment with total pelvic floor ultrasound (TPFUS) only, and defaecation proctography (DP) only, when compared to the actual treatment received.

Funding Nil **Clinical Trial** No **Subjects** Human **Ethics not Req'd** Audit of routine practice **Helsinki** Yes **Informed Consent** No

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EXPOSURE TO X-RAY RADIATION DURING VIDEO URODYNAMICS FOR PEOPLE WITH ANULTD SECONDARY TO SCI

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HYPOTHESIS / AIMS OF STUDY
Following spinal cord injury (SCI), disruption to neuronal pathways to the bladder can lead to development of neurogenic lower urinary tract dysfunction (NLUTD). The goal of good bladder management is to ensure safe storage pressures and efficient voiding to protect the upper tracts. Videourodynamics (VCMG) is a functional test of the lower urinary tract in which pressure, capacity and flow data are simultaneously combined with real-time fluoroscopic imaging of the upper and lower urinary tract. The NICE guidelines for management of NLUTD state that regular surveillance VCMGs should be performed in patients at high risk of upper tract damage. This may constitute a significant radiation exposure risk over a lifetime for which patients need to be consented. The guiding principle for all examinations requiring ionising radiation is ALARP – 'as low as reasonably practicable'. The aim of this audit was to provide useful information for those requesting and performing VCMGs on exposure levels for people with SCI undergoing VCMG as part of their long-term bladder management.

STUDY DESIGN, MATERIALS AND METHODS
Dose Area Product data for VCMG examinations between March 2021-March 2022 were extracted from the electronic database. Age, sex, level of injury and bladder management technique were recorded. During a standard VCMG investigation, single shots are taken of the bladder at infused volume (IV) of 30 ml and repeated if required during filling. Screening occurs during stress coughs at an IV of 75 ml and at end fill volume (EFV). Screening is also undertaken during the voiding phase if appropriate. Additional screening is undertaken if vesico-ureteric reflux is noted during the test.

RESULTS
270 SCI patients were identified. The mean age was 50 years (range 12-87 years). The mean, SD and range of DAP are shown in the table.

INTERPRETATION OF RESULTS
The greatest DAP were seen in the patients who voided due to the additional screening time during the voiding phase, compared to non-voiders. 16/270 patients had a DAP > 100 cGycm2. 14/16 of these were voiders. The remaining 2 patients had an IDUC, however, one of them had reflux so additional imaging of the kidneys and ureters was undertaken. Other factors affecting absorbed dose which were not analysed include body weight, height, fluoroscopic kV and fluoroscopy time. For comparison, the average DAP for an Abdominal AP x-ray is 260 cGycm2 and for an IVU 1400 cGycm2. The NDRL for Micturating Cystourethrogram is 700 cGycm2

CONCLUDING MESSAGE
Although VCMG is an important tool in the safe bladder management of people with NLUTD following SCI, the absorbed radiation dose should be considered when considering the frequency of the investigation.

FIGURE 1

		Dose Area Product cGycm²	
Bladder Management	**N**	**Mean +/- SD**	**Range**
Voids on urge	93 (34%)	51.78 ± 69.75	1.14 – 547.5
CISC and voiding	14 (5%)	46.88 ± 103.6	3.66 -403.8
IDUC	41 (15%)	26.91 ± 30.45	4.87 – 148.5
Reflex void	5 (2%)	26.55 ± 26.10	7.22 – 59.56
SPC	38 (14%)	13.92 ± 12.61	1.14 – 54.40
CISC	79 (29%)	18.11 ± 13.3	1.11 – 77.87
TOTAL	**270**	**32.10 ± 51.55**	**1.11 – 547.5**

Funding None **Clinical Trial** No **Subjects** Human **Ethics not Req'd** It was a Service Evaluation **Helsinki** not Req'd It was a Service Evaluation **Informed Consent** No

DETRUSOR UNDERACTIVITY (DU) OF FEMALE PATIENTS DIAGNOSED BY VARIOUS UDS CRITERIA

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HYPOTHESIS / AIMS OF STUDY

Detrusor underactivity (DU) is one of the etiologic factors of female LUTS, even though no standardized urodynamics (UDS) criteria for DU have been defined in women. UDS including a pressure flow study is invasive-nature and give discomfort for the patients during UDS. Therefore, UDS is not a routine method for evaluation of LUTS. However, a pressure flow study is still a key procedure because a pressure flow study may be only a method to discriminate BOO and DU from LUTS. Patients with DU or BOO usually have similar voiding symptoms. To establish the refined UDS criterion for DU, we tried to examine the criteria already published for DU. The aim of this study is to investigate and compare the four major UDS criteria for DU.

STUDY DESIGN, MATERIALS AND METHODS

Retrospectively female patients with DU were selected from our pooled UDS database. DU was diagnosed if at least one of the following four criteria for DU was met. The 4 UDS criteria for DU were as follows; A) Pdet@Qmax≦10 and Qmax≦12(Jeong2012), B) Pdet@Qmax ≦ 30 and Qmax≦10 (Abarbanel2007), C) Pdet@Qmax≦20, Qmax≦15, and BVE＜90% (Gammie2016), D) PIP1 (Pdet@Qmax＋Qmax) ＜30 (Griffiths 2004). To investigate the presence of BOO in these DU patients, we used the following UDS criterion for BOO (Pdet@Qmax≧21 and Qmax≦11) (Lemack 2000).

RESULTS

Hundred-five patients (mean age 69.8＋10.7) were selected using 4 UDS criteria from our female UDS database(N＝365). The ages and UDS parameters of DU patients stratified according to the 4 UDS criteria is shown in table 1.The symptoms of these DU patients are as follows; a feeling of pressure in the pelvic area (pelvic organ prolapse) 34, stress urinary incontinence 33, difficulty on urination 14, pollakisuria 10, urgency urinary incontinence 8 and others 2. The Venn diagram (Figure 1) demonstrates the distribution and overlap of DU patients' groups by 4 UDS criteria. No DU patients were selected by only A criterion. Detrusor overactivity was found in 19 patients (18%:19/105) out of 105 DU patients. The number of patients diagnosed by D criterion Griffiths, which is PIP1, was 2 to 4 times as large as those diagnosed with other three criteria. Thirteen (28%, 13/46) out of the DU patients diagnosed using B criterion had BOO based on Lemack's BOO criterion.

INTERPRETATION OF RESULTS

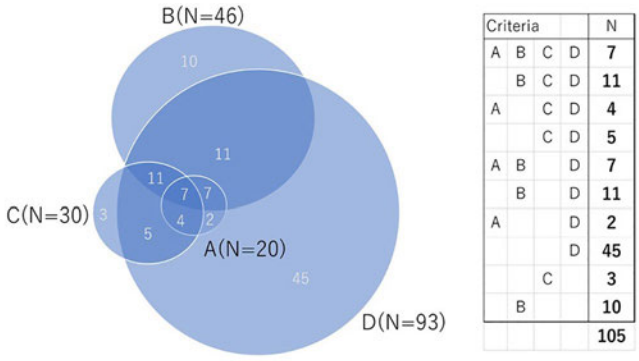
The reason for larger number of DU patients in D criterion, Griffiths' PIP1, may be, not the simple combination of cutoff values of Qmax and Pdet@Qmax, but, different concept, Qmax＋PdetQmax values.

Some (28%) of DU patients diagnosed using B criterion (Abarbanel) had BOO because high Pdet@Qmax value(＝30cmH2O) in B criterion may suggest BOO (low flow and high pressure). B criterion may have weak power to discriminate between DU and BOO.

CONCLUDING MESSAGE

The diagnosis of detrusor underactivity were dependent on the DU criterion used. Some criteria may be difficult to discriminate between DU and BOO. UDS criterion for DU should be carefully used with its limitation. We need more refined UDS criterion for female DU.

FIGURE 1



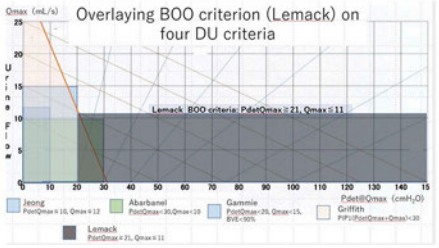
Criteria				N
A	B	C	D	7
	B	C	D	11
A		C	D	4
		C	D	5
A	B		D	7
	B		D	11
A			D	2
			D	45
		C		3
	B			10
				105

Figure 1 Distribution and overlap of DU patients according to 4 UDS criteria

FIGURE 2

Table 1 UDS parameters of female patietns with detrusor underactivity

	Authors	Criteria	N	Age	Qmax	VV	PVR	BVE	P-Qmax	PdetQmax
A/B/C/D	each of them		105	68.7＋12.1	14.1＋8.4	199＋124	63＋114	80＋27	11.8＋5.6	11.4＋7.8
A	Jeong	PdetQmax≦10, Qmax≦12	20	74.9＋13.4	12.4＋6.3	177＋97	97＋121	70＋33	8.0＋3.5	5.0＋3.2
B	Arbabanel	PdetQmax≦30, Qmax≦10	46	68.5＋13.7	11.8＋7.2	187＋114	101＋147	70＋30	6.7＋2.6	15.3＋87
C	Gammie	PdetQmax<20, Qmax<15, BEV<90	30	71.0＋9.5	9.6＋4.5	178＋149	110＋79	59＋26	10.9＋5.8	10.9＋5.8
D	Griffiths	PIP1 (PdetQmax+Qmax)<30	92	69.4＋10.9	14.2＋8.5	195＋124	52＋84	81＋27	12.3＋5.6	9.4＋5.9



Funding None **Clinical Trial** No **Subjects** Human **Ethics Committee** Saitama Medical University Hospital IRB board **Helsinki** Yes **Informed Consent** No

Continence 2S2 (2022) 100302
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COMPARISON OF CERVICAL LENGTH MEASURED BY POP-Q C-D AND ULTRASOUND

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HYPOTHESIS / AIMS OF STUDY
There is a commonly-held opinion that pelvic organ prolapse (POP) is associated with cervical elongation. One study found that about 40% of women with anterior component POP had cervical elongation, with the age of Cervical Elongation (CE), patients relatively younger than POP patients(1). CE is an extension or hypertrophy of the cervix towards the introitus with other uterine supporting tissues still in good condition. CE can occur in both parts of the cervix, supravaginal and vaginal. The presence of CE will affect the management of hysterectomy for POP. Consideration needs to be made to choosing the vaginal or abdominal approach, supravaginal or total hysterectomy, whether or not the uterus is maintained, or the choice of the apical suspension chosen. Undiagnosed CE before surgery will make surgery more complex and at risk of failing to overcome symptoms even with the apical component already supported in patients who have surgery by maintaining the uterus(3). CE is also one factor associated with high prolapse recurrence rates after suspension of the sacrospinous ligament.

This study aimed to compare cervical length based on the Pelvic Organ Prolapse Quantification system (POP-Q) examination as an index test with sonography in patients with POP.

We hypothesized that cervical length measurement using POP-Q, isn't accurate in all patients, and transvaginal sonography examination of the cervix is a reliable and reproducible method(2) to assess the cervical length as it is performed in pregnant women to assess cervical incompetency as usually.

STUDY DESIGN, MATERIALS AND METHODS
A cross-sectional study was performed in the educational hospital's outpatient clinic between January 2020 and December 2021. One hundred women with POP entered in this study. The regional ethical committee approved the proposal. At first, POP staging, was performed according to POP-Q system, and cervical length was determined based on C-D measurements by an urogynecologist. Then, All women were underwent transvaginal ultrasonography to measure cervical length as the distance from the internal to the external os. (for this purpose, the Patient's bladder should be essentially empty). SPSS/Ver24 was used for statistical analysis.

RESULTS
The final analysis included 100 subjects. The mean age of patients was 47.88 ± 8.7 years, the mean BMI was 26.19 ± 1.53 kg/m2, and the mean total vaginal length (TVL) was 9.00 ± 1.20 cm (min 7 cm and max 11 cm). The results of measuring the cervix length by the POP-Q method showed that the mean (SD) was 40.80 ± 22.11 mm (the minimum length of the cervix was 20 mm, and the maximum was 110 mm). The ultrasonography results showed that these amounts were 36.8. ± 6.86 mm (minimum of 28 mm and a maximum of 80 mm.

To assess the agreement between the two measurement methods, Intraclass Correlation Coefficient (ICC) was used, and the results showed that the Intraclass Correlation is 0.476 (95%CI: 0.220-0.648). Given the obtained value for the ICC, there is a relatively weak agreement between the two indicators to measure cervical length. For this purpose, the Bland-Altman method was used, and the results showed that the amount of Bias (mean difference) and SD was 4.00 (19.20), with 95% Limits of Agreement between -33.63 to 41.63.

According to the results of the studies related to the Bland-Altman plot, the most disagreement is related to the following values:

(POPQ = 100, Sono lenght = 34)

(POPQ = 110, Sono lenght = 45)

(POPQ = 110, Sono lenght = 48)

(POPQ = 100, Sono lenght = 40)

(POPQ = 100, Sono lenght = 55)

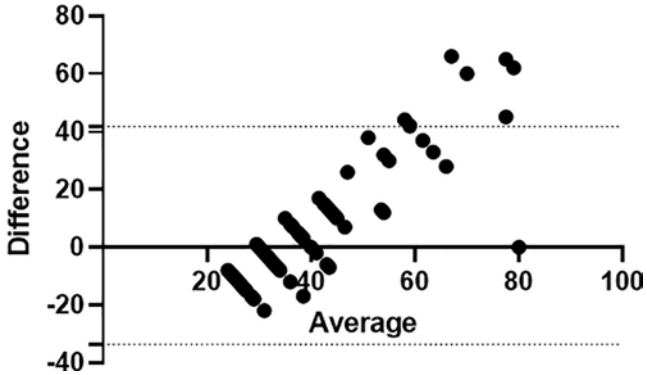
(POPQ = 80, Sono lenght = 36)

INTERPRETATION OF RESULTS
There is a relatively weak agreement between POP-Q and ultrasonography to measure cervical length .When the cervical length is more than 8 cm according to POP-Q, the difference between the two methods is more significant. As in these patients, cervical length in ultrasonography measured approximately half of POP-Q.

CONCLUDING MESSAGE
it is essential to measure the cervical length in POP patients accurately.

Because it affects our plan to choose conservative management or surgery and the kind of surgery. Different measuring techniques (POP-Q, ultrasonography, digital palpation, foley catheter…). have some pros and cons. The POP-Q system is an acceptable method and familiar for pelvic floor specialists worldwide. However, based on this study, it is recommended to repeat measuring by other methods like ultrasonography (that is routinely performed for pregnant women to rollout cervical insufficiency) before choosing therapy in POP patients with doubtful results according to POP-Q measurements.

FIGURE 1
Figure 1. Bland-Altman plot



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Funding no fund no grant **Clinical Trial** Yes **Registration Number** IR.TBZMED.REC.1399.523 **RCT** No **Subjects** Human **Ethics Committee** Ethic committee of tabriz university of medical science **Helsinki** Yes **Informed Consent** Yes

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215 | www.ics.org/2022/abstract/215

UTERINE FIBROIDS AND EFFECT ON PELVIC ORGAN DESCENT: A COMPARATIVE QUANTITATIVE 3D STUDY ON PELVIC ORGAN LOCATION

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HYPOTHESIS / AIMS OF STUDY
Genital descent occurs along gravity and is subject to ageing or birth-related injuries of organ-supporting pelvic floor structures. Injuries of the levator ani muscle (LAM) have a high impact on later pelvic organ disorders. In premenopausal women a reduced function of the pelvic floor was directly correlated with defects in the LAM. However, a factor that has not yet been fully elucidated is the organ-specific weight that acts on the pelvic floor. Elevated organ specific weight of female pelvic organs in premenopausal women is mostly due to pregnancies or fibroids. Uterine fibroids are a common reason for increased uterine volume and are found in up to over 80% of women below the age of 50.

Aim of this MR-imaging study is to assess the impact of uterine volume in premenopausal, nulliparous women with and without uterine fibroids on the organ location of the three pelvic compartments.

STUDY DESIGN, MATERIALS AND METHODS
The study was performed in a cohort study of 2615 MR-scans of the female pelvis in the period of 01.01.2006-31.12.2017. Exclusion criteria were other tumors than uterine fibroids, age <18 or >40 years, endometriosis, MRI slice thickness <7mm, pelvic deformation or POP. The position of the three pelvic compartments, namely the internal urethral meatus or bladder neck for the anterior, the cervix for the apical, and anorectal point for the posterior compartment were measured in the 3D PICS coordinate system where per definition point 0/0/0 is the inferior pubic point. The 3D-PICS is a right-handed coordinate system where the y-axis points along the body axis. Negative y-values are cranially of the 3D PICS plane. X-values point along the anterio-posterior axis and the positive z-axis points towards the right side. The uterine volume in women with and without fibroids was calculated with the Myrian Imaging Layer Software.

RESULTS
108 women met the inclusion criteria: 51 women with fibroids (mean age 34.4 years, median volume 424.0cm3) and 57 women without (27.8 years, 59.3cm3) (both $p<0.001$). In the fibroid group the cervical point was significantly lower above the PICS plane than in the control group (mean y-value -38.6mm vs. -51.1mm, $p<0.001$). The same was true for the position of the anterior (-13.7mm vs. -26.0mm, $p<0.001$) and the posterior compartment (-16.4mm vs. -9.7mm, $p<0.001$). In the high-volume fibroid group (>500 cm3) descent did not differ significantly anymore (-48.2mm vs. -51.1mm, $p=0.385$).

INTERPRETATION OF RESULTS
Our research is the first to compare uterine volume with the position of the three pelvic compartments known to be involved in genital descent measured in a 3D coordinate system (3D PICS).

CONCLUDING MESSAGE
Genital descent differed significantly if uterine fibroids are present and if the uterine volume with fibroids is between 100 and 500cm3. At a volume >500cm3 the uterine fibroids seem to prevent the descending of the three compartments. The significant descent at higher age of the patient is explained by the higher prevalence of uterine fibroids in women above 30 years of age.

Funding None **Clinical Trial** No **Subjects** Human **Ethics Committee** Kantonale Ethikkommission Zürich **Helsinki** Yes **Informed Consent** No

Continence 2S2 (2022) 100304
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SESSION 14 - PRIZE VIDEO, PROLAPSE, URETHROPLASTY, TRANSGENDER

Abstracts 216-225
16:30 - 18:00, Hall G
Chair: Mr Laurence Stewart (United Kingdom)

216 www.ics.org/2022/abstract/216

BEST VIDEO ABSTRACT

SURGICAL REPAIR OF AN OBSTETRIC TRAUMATIC CLOACAL DEFECT

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INTRODUCTION
Obstetric traumatic cloacal defect (TCD) occurs in women that have sustained a third or fourth degree tear during vaginal delivery.The incidence of Obstetric TCD is 0.003% and is characterized by disruption of the anal sphincter complex, loss of the perineal body and distal rectovaginal septum [1]. Risk factors include operative forcep delivery, large fetal weight and median episiotomies. [2, 3] Severe damage to the sphincter and perineal body can cause significant anatomical and functional abnormalities that have a significant impact on women. Common symptoms include fecal incontinence, perineal pain, sexual dysfunction and recurrent urinary infections [2, 3]. This can have serious psychological and social consequences on the affected individual.

DESIGN
We present a case of a 45 year old female with an Obstetric Traumatic Cloacal Defect secondary to a vaginal delivery with a fourth degree tear. She presented with several episodes of postcoital bleeding. On examination, it became clear that she had sustained an Obstetric TCD. She had no other complaints and denied Fecal incontinence. Her Wexner Score was 2.

The aim of this case is to describe the repair of an obstetric traumatic cloacal defect remote from delivery.

RESULTS
The procedure started with an inverted U incision in order to facilitate access to the sphincter complex. The sphincter complex was carefully dissected. It was noted that the right sphincter complex was more retracted and atrophied than the left. Therefore the left sphincter complex had to be mobilized to compensate for this. The distal vagina was divided above the thinnest area on the posterior vaginal wall and continued apically in order to adequately mobilize the posterior vaginal mucosa in order to sufficiently cover the reconstructed posterior vaginal wall and perineal body. A standard overlapping sphincteroplasty was done. Care was taken to maintain a normal anal calibre. The rectal muscularis layer was reinforced. The noted rectocele was repaired and a levatorplasty was done. Care was taken not to narrow the vaginal introitus. The perineal body reconstruction was continued with the approximation of the bulbocavernosus muscle and perineal fascia. The skin was then closed. The immediate postoperative course was uncomplicated. The patient was not experiencing any fecal incontinence at the 6 week postoperative visit.

CONCLUSION
Obstetric traumatic cloacal defect repair is challenging, particularly when remote from delivery. The anatomic deformities and atrophy of the sphincter muscles can make it difficult to identify and repair the structural defects. Our video demonstrates this rare presentation and the surgical approach to its repair.

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Funding None **Clinical Trial** No **Subjects** Human **Ethics not Req'd** patient consent was obtained for a video of the surgical steps **Helsinki** Yes **Informed Consent** Yes

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217 | www.ics.org/2022/abstract/217

REVISION CLITOROLABIAPLASTY AND URETHROPLASTY AFTER GENDER-AFFIRMING VAGINOPLASTY

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INTRODUCTION
Gender-affirming vaginoplasty was historically a two-stage procedure with secondary labiaplasty after the initial vaginoplasty. Techniques have evolved into what is now generally a single stage procedure, however some patients may still require revision surgery for cosmetic or functional reasons. Additionally, as with any urethral procedure, patients may develop issues with their urinary stream requiring repeat surgery.

DESIGN
The patient is a 51-year-old transgender woman. She underwent robotic-assisted peritoneal flap vaginoplasty in the summer of 2020. Her post-operative course was complicated by recurrent infections. Once the infections had settled and the surgical site was well healed, she had persistent complaints of flat labia majora, overly exposed clitoris causing hypersensitivity, as well as spraying of her urinary stream. We aimed to demonstrate that minor revisions with urethroplasty to relocate the urethral meatus inferiorly as well as securing the clitoris in a more inferior position and bringing the labia together in the midline can provide coverage for the clitoris, more aesthetic appearance of the vulva, and an excellent functional outcome.

We first performed the urethroplasty. We began with cystoscopy to identify the level of the external sphincter which was marked externally on the skin. We then incised the skin in the midline starting at the level of the current urethral meatus and extending inferiorly for approximately 2cm. Skin flaps were mobilized off of the urethra bilaterally. The urethra was spatulated ventrally for approximately 1.5cm. The edges were oversewn with 3-0 Vicryl for hemostasis. The superior part of the spatulated urethra was sutured to the surrounding skin to form the lower edge of the vestibulum and provide further definition to the labia minora. The lower edge of the spatulation was sutured to the surrounding skin to become the new urethral meatus.

We then turned our attention to the clitoroplasty and labiaplasty. The patient's clitoris was sitting high, over-exposed, and somewhat prolapsed after her initial vaginoplasty and post-operative infections. We started by making a circumferential degloving incision at the level of the glans clitoris. The skin was then carefully mobilized off of the clitoris. A midline incision was made inferior to the clitoris and the clitoris was secured to the vestibulum. A double Z-plasty was performed, in order to bring the labia majora together in the midline to provide better coverage for the clitoris.

RESULTS
The procedure lasted 4 hours. There was minimal bleeding and no intra- / post-operative complications were encountered. She was discharged home on post-operative day one in good condition. The Foley catheter was left in place until post-operative day five. One month post-operatively, the patient reported resolution of urinary spraying, improved cosmesis, and better coverage for the clitoris.

CONCLUSION
Patients may not be satisfied with the cosmetic and functional results following gender-affirming vaginoplasty even if the vaginal canal itself is of adequate dimensions. Minor revisions can provide significant rewards in terms of improvements to the cosmetic appearance of vulva and lower urinary tract symptoms.

Funding None **Clinical Trial** No **Subjects** Human **Ethics not Req'd** It is a video of a surgery. **Helsinki** Yes **Informed Consent** Yes

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218 | www.ics.org/2022/abstract/218

REVISION VAGINOPLASTY WITH ABDOMINAL FULL-THICKNESS SKIN GRAFT

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INTRODUCTION
Graft nonadherence can complicate the postoperative course of gender-affirming vaginoplasty with penile skin inversion. Some of the patients might be amenable to management with neovaginal packing. However, those with nonadherence involving the whole canal that persists despite prolonged packing would benefit from a corrective surgery. Herein, we report a case with poor graft take after penile inversion vaginoplasty (PIV) who was salvaged with a redo procedure using a full-thickness abdominal skin graft to resurface the neovaginal cavity

DESIGN
This is a 53-year-old trans female who underwent PIV. Her postoperative course was complicated with complete graft nonadherence and neovaginal prolapse which persisted despite numerous packing/depacking sessions. Additionally, she developed urethro-neovaginal fistula due to packing-induced pressure necrosis. Urethral fistula was repaired primarily over a Foley catheter. At the last packing exchange session, her cavity was found to be patent with preserved dimensions. However, poor graft take did not resolve with conservative measures. The shared decision was to proceed with a redo procedure using abdominal skin to line the vaginal cavity.

RESULTS
Vaginal packing and the previous skin graft were removed at the beginning of the procedure. Vaginal canal was copiously irrigated with 3 liters of saline. Cystoscopy confirmed urethral patency. There were no signs of fistula or stricture. Foley catheter was exchanged.

A full-thickness skin graft, measuring 16 cm in length and 14 cm in diameter, was harvested from the abdomen. Graft was defatted and tubularized around a dilator (17/16 inch width, 5½ inch length). The abdominal skin was elevated and midline was plicated with 2 sutures placed lateral to the umblicus. Abdomen was closed in a layered fashion over 2 15 Fr. drains.

The skin graft was sutured to the apex of the vaginal canal as well as the side walls and introitus. Vault was suture fixated (with Prolene) to the levator side wall via anchoring device (Anchorsure system, Neomedic International). Graft was then quilted to the side walls by way of interrupted 2/0 Vicryl stitches, starting at the apex advancing towards introitus.

A 15 Fr. drain was placed in the vaginal cavity beneath the skin graft and brought out through a seperate incision. Cavity was packed with vaginal pack soaked in Sulfamylon and lubricating gel. Procedure lasted 3 hours with an estimated blood loss amount of 250 ml. Packing was exchanged on day 7 and removed on day 14. She did well in the long run with no further problems with graft take and no recurrence of neovaginal prolapse. She was put on anticholinergics due to de-novo OAB symptoms.

CONCLUSION
Graft nonadherence after PIV can be initially managed with neovaginal packing. In patients with complete graft nonadherence refractory to packing and preserved neovaginal patency and dimensions, resurfacing the cavity with full-thickness abdominal skin graft can be considered as a viable salvage option. Fixating the apical part of the cavity to the levator side walls with an anchoring device will aid in preventing recurrence of neovaginal prolapse.

Funding None **Clinical Trial** No **Subjects** Human **Ethics not Req'd** It's a surgical video **Helsinki** Yes **Informed Consent** Yes

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LAPAROSCOPIC COLPOSACROPEXY IN TRANSGENDER PATIENT (M/F) WITH A NEO-VAGINA PROLAPSE

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INTRODUCTION
In the male-to-female transgendered patient, the creation of esthetic and functional external female genitalia with a functional neovagina represent the main objective. The most used M/F surgery is represented by peno-scrotal inversion vaginoplasty, while other techniques are represented by colon-vaginoplasty or peritoneal flap vaginoplasty. This fascinating and challenging surgery is not without complications. The prevalence of complications is extimated to be about 32.5%. The most common complication is stenosis or stricture of the neo-meatus/ urethral complex and stenosis of the neovagina. Other relatively rare complications are represented by wound infection rectal injury, hematoma, tissue necrosis, rectovaginal fistula and transfusions. The prolapse of the neovagina is a relatively rare event and it is estimated to be approximately between 1.6- 7.5% . The pathophysiology of a neovaginal prolapse is still unclear. It is probably explainable with the missing integration into the pelvic floor in comparison to a natural vagina with its anterior and apical support to the pelvic side walls. Prolapse of the neovagina after vaginoplasty in M/F patients represent a poor aesthetic appearance as well can lead to possible difficulties with or obstacle to sexual intercourses. The management of vaginal prolapse after sex reassignment surgery represent a great challenge in the field of pelvic reconstructive surgery. To date there are no standardized techniques established to re-suspend the prolapse. Various surgical approaches ranging from vaginal mesh repair, to open or laparoscopic fixation of the neovagina with or without mesh inlay have been described.

The purpose of this video is to show a laparoscopic approach to repair a neovaginal prolapse in a male to female patient who underwent sex reassignment surgery and a neovagina creation with peno-scrotal inversion.

DESIGN
She was 42 years old. The preoperative evaluation including history, urogynaecological examination, urodynamic test.She reported bulging symptoms, pain during sexual intercourse enough to interrupt sexual relations with the partner.She had a vaginal vault prolapse III stage in according to POPQ, no urinary incontinence,and urinary symptoms. The surgery was performed by two experienced surgeons.Laparoscopic repair of the neovaginal prolapse followed the principles used for the native female patients with pelvic organs prolapse

The patient is positioned in a forced Trendelemburg position under general anaesthesia; the laparoscopic ports were placed in a standard position (10 mm optic port above the umbilicus and other two 10 mm and 5 mm for the surgeon and another one on right side for the assistance). The first step is represented by a bluntly dissection of sacral promontory in order to get space enough to put a 2/0 not adsorbable suture in the periostium. Peritoneum is than prepared in the douglas space and the neo-vaginal dome is visualized; the neo-vaginal dome is than bluntly prepared using a retractor that pushes it into the abdominal cavity. A polypropylene mesh is positioned, shaping dimensions of the vagina and it is fixed on vaginal dome using three reabsorbable 3/0 sutures. Retro-peritoneum is than opened in the space between vagina and sacrum, in order to create a retroperitoneal passage of the mesh. The mesh is than fixed on the sacrum using previously apposed suture. Closure of retroperitoneum with a running suture.

RESULTS
The operation was completed successfully, without blood loss or complications and the patient was discharged on the 3 rd postoperative day. After one month from the surgical treatment, the patient presented the complete correction of the prolapse, the absence of vaginal exposure of the mesh, the absence of urinary symptoms. After 8 weeks she resumed sexual intercourse without reporting any discomfort either her or her partner

CONCLUSION
Our case showed that laparoscopic sacropexy could be used to treat a neo-vagina prolapse with a good anatomic outcome

Funding None **Clinical Trial** No **Subjects** Human **Ethics Committee** Local Ethic Commitee of Pisa **Helsinki** Yes **Informed Consent** Yes

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OPEN SACROHYSTEROPEXY FOR PELVIC ORGAN. PROLAPSE IN A CONGENITAL BLADDER EXSTROPHY PATIENT

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INTRODUCTION

Pelvic organ prolapse is uncommon in pediatric patients, but can occur in patients with congenital urologic disorders such as classic bladder exstrophy (CBE). Following interventions including vaginoplasty or introitoplasty these patients may experience prolapse as an unintended consequence. Due to the paucity of pelvic floor musculature in classic bladder exstrophy prolapse repair can be challenging.

DESIGN

We present the case of a 15-year-old female with a history of (CBE). She had previously undergone two failed attempts at bladder exstrophy closure, ultimately undergoing cystectomy and creation of Mainz II pouch. She underwent vaginoplasty and clitoroplasty at age 11. At follow up, she had stage 2 apical prolapse that was not bothersome. However, at 14 she complained of bothersome pelvic pressure and bulging and was noted to have worsening stage 3 apical prolapse. MRI of the pelvis showed descent of the uterus 4cm below the pubococcygeus line and the Mainz II pouch to be anterior and superior to the uterine fundus. She wished to proceed with reconstructive repair of her prolapse with preservation of fertility. The aim of this video was to describe the procedure for open sacrohysteropexy in a pediatric patient with bladder exstrophy.

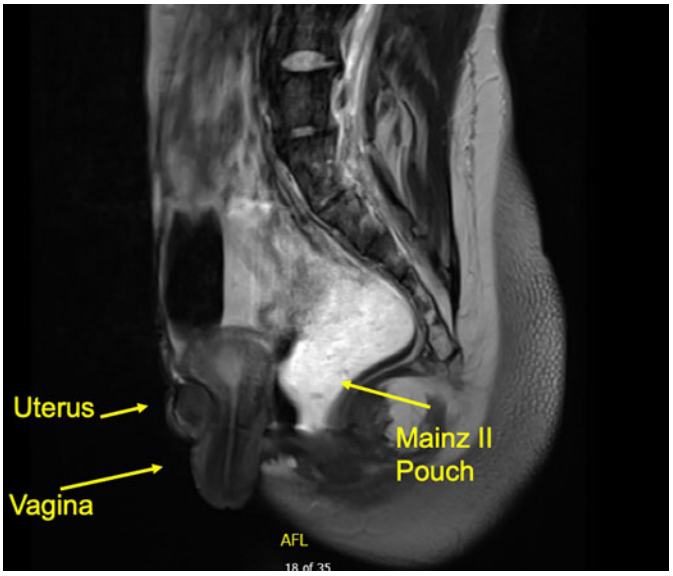
RESULTS

The patient was positioned supine with slight frog leg with the vagina prepped into the field. A 10Fr foley catheter was placed into the rectum. A low midline incision was made and upon entering the abdomen, the Mainz II pouch was immediately identified and confirmed with palpation of the foley catheter. The pouch was mobilized circumferentially and lifted superiorly. This allowed for identification of the right ureter and uterus. It was then retracted laterally to expose the sacral promontory, which was incised, and a space cleared for pre-placement of of two 2-0 gore tex sutures. The peritoneum was then dissected from the vagina as distally as possible until a 4cm area was identified along the posterior vagina and uterus for mesh placement. The anterior arm of a Vertessa light Y mesh was truncated due to the patient's desire for future fertility. Two 3-0 PDS sutures were placed on the proximal portion of the vagina to fix the distal extent of the posterior limb of the mesh to the vagina. Additional interrupted 3-0 PDS sutures were used to anchor the mesh to the posterior uterus. The distance required for reduction of the prolapse was measured and the Goretex sutures were passed through the sacral limb of the mesh and tied down to complete the hysteropexy. Excess mesh was removed. The posterior peritoneum was then closed with running 2-0 vicryl suture.

CONCLUSION

Bladder exstrophy is rare, but these patients are at risk for pelvic organ prolapse due to absence of the anterior portion of the levator ani muscles, flattening of the normal conical shape of the pelvis, and anterior displacement of a shortened and stenotic vagina. Due to the paucity of pelvic floor musculature, transvaginal attempts at repair are generally unsuccessful. Trans abdominal suspension is therefore a feasible and safe option. In our case, placement of a rectal catheter assisted in the identification of the Mainz pouch. Additionally, pelvic MRI was used for quantification of the extent of prolapse and the reconstructed anatomy. Lastly, incorporation of a multidisciplinary approach to pediatric prolapse is important given the knowledge of pediatric urologists regarding congenital anomalies and FPMRS Urologists expertise with reconstructive techniques for prolapse.

FIGURE 1



MRI Pelvis demonstrating the location of the Mainz II pouch and extent of uterine prolapse

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Funding None **Clinical Trial** No **Subjects** Human **Ethics not Req'd** IRB Exemption - informed consent was obtained from patient's family **Helsinki** Yes **Informed Consent** Yes

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LAPAROSCOPIC PECTOPEXY FOR APICAL PROLAPSE

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INTRODUCTION

Sacrocolpopexy can be considered the “gold standard” in the correction of vaginal vault prolapse, however it depends on the experience of the surgeon.

During sacrocolpopexy, sigmoid colon and sacral promontorium should be identified and care should be taken to avoid damaging the right ureter, presacral veins, hypogastric nerve and sigmoid colon in the sacral area. Some well-known disadvantages of the technique are : extended surgical time, long learning curves, postoperative defecation disorders and pelvic pain.

Laparoscopic pectopexy is a novel method of vaginal prolapse repair that offers clear practical advantages compared with laparoscopic sacropexy. This technique uses the iliopectineal ligament on both sides for the mesh fixation, so there is no restriction caused by the mesh. The mesh follows natural structures (round and broad ligaments) without crossing sensitive spots, such as the ureter or bowel. This surgical modifications help reduce the complications of the sacrocolpopexy, operation time and learning curve.

DESIGN

59 years-old female patient with Steinert disease and previous hysterectomy plus double adnexectomy, complaining of voiding dysfunction due to vaginal vault prolapse requiring CIC (Clean Intermittent Catheterization) for bladder emptying.

The physical examination showed vaginal vault prolapse stage 3. The Pelvic Organ Prolapse Quantification System (POP-Q) is shown above

Urodynamics Study: Bladder Outlet Obstruction due to vaginal vault prolapse.

Due to high anesthetic risk involving her muscular dystrophy and her altered anatomical condition, laparoscopic pectopexy was proposed.

RESULTS

The surgery was performed using standard laparoscopic equipment with 4 trocars of 10-mm and 5-mm. The optical access was placed via infraumbilical trocar, and the working devices were introduced through a pararectal, left, and right incisions as usual.

In this particular case with the uterus missing, we opened the peritoneal layer along the theoretical direction of both round ligaments towards the pelvic wall. The dissection begins at the right external iliac vein. We exposed an approximately 3-cm segment of the right iliopectineal ligament (Cooper ligament) adjacent to the insertion of the ileopsoas muscle.

We must take care of the obturator nerve, situated caudal to our dissection field. Vaginal apex was prepared for mesh placement and the anterior and posterior wall of the vaginal peritoneum were dissected.

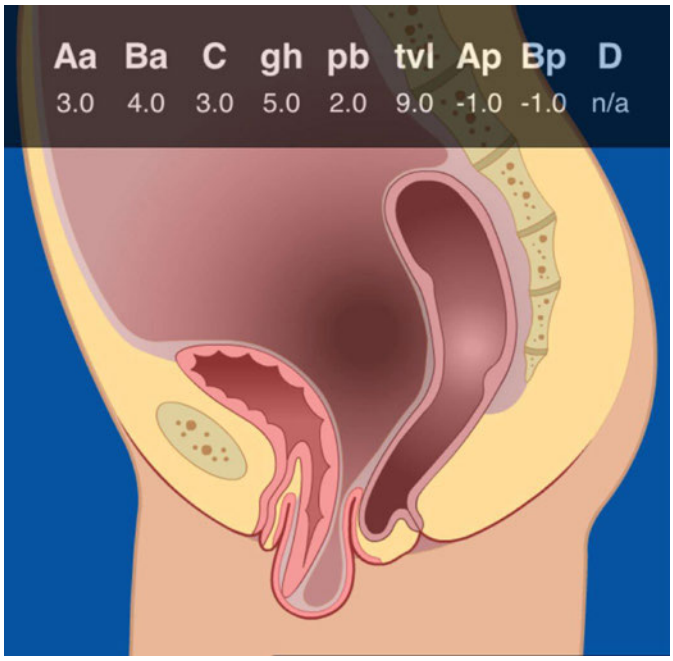
The vaginal apex was fixed with absorbable suture material. The mesh ends were attached to both iliopectineal ligaments using nonabsorbable suture material of polyvinylidene fluoride (PVDF) pulled up to the intended tension-free position. A hammock-like fixation of the vaginal apex was performed. Finally, we covered the mesh with peritoneum using absorbable suture material in a continuous suturing technique.

Total surgical time was 120 minutes, with no subsequent surgical or anesthetic complications. The patient was discharged at 48h. The anterior and middle prolapse was minimally invasively resolved. Voiding dysfunction disappeared and no constipation was observed in the follow up.

CONCLUSION

According to our experience, laparoscopic pectopexy offers a feasible, safe, and comfortable alternative for apical prolapse surgery with shorter surgical time.

FIGURE 1



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Funding None **Clinical Trial** No **Subjects** None

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COMPARISON OF OUTCOMES OF RECTAL AND PELVIC ORGAN PROLAPSE TREATMENT BY MEANS OF ONE- AND TWO- STAGE SURGERIES

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INTRODUCTION
Full-thickness rectal prolapse frequently co-exists with pelvic organ prolapse in elderly women. These patients are mostly qualified for two separate procedures: a perineal defect repair performed by gynecologists and then a rectal prolapse surgery carried out by surgeons. An alternative is a one-stage repair of both abnormalities.

The aim of the study was to compare the outcomes of one-stage rectal and pelvic organ prolapse surgery (Group A) with a two-stage procedure (Group B). The video shows the one stage operation technique.

DESIGN
23 female patients qualified for rectal prolapse treatment using the perineal approach were the subjects of the analysis over the period from 2012 to 2020. They also experienced pelvic organ prolapse and had been operated on previously or at the time of the rectal prolapse surgery. The patients were classified into two groups:

Group A – patients who underwent one-stage surgery for full-thickness rectal and pelvic organ surgery (RP + POP).

Group B – patients who underwent full-thickness rectal prolapse surgery and presented a history of pelvic organ prolapse repair (RP-POP).

The treatment outcomes were assessed based on the number of recurrent rectal and/or pelvic organ prolapse cases, complications and the patients' quality of life before and after the procedure. Standard quality of life assessment scales (EQ5D and QoL) and the Wexner Score (for the assessment of gas and fecal incontinence) were applied. Concurrent constipation and urinary incontinence were assessed during the physical exam. In addition, an obstetric history was collected. Both groups were evaluated before the surgery and at 6 months (half a year) after the procedure. The follow-up period was 6 months to 62 months (mean value: 36 months). Both groups were comparable in terms of the age, gender and significance of the obstetric history. In the statistical analysis, the Wilcoxon test and descriptive statistics for the parameters with insufficient values were used.

RESULTS
The numbers of recurrence cases were 1 (A - 11%) and 2 (B - 14%), respectively. No complications were observed in either of the groups. The mean surgery time was longer in the one-stage surgery group (A - 124 min / B - 110 min). Improved quality of life (A - EQ5D - 15%, QoL - 13%; B - EQ5D - 22%, QoL - 23%) and functional parameters (decreased rates of constipation and incontinence: A - 63%, 51%; B - 46%, 40%) were observed in both groups following the surgeries. Too small group sizes do not allow for confirmation of the statistical significance of this difference.

CONCLUSION
1. The treatment outcomes of one-stage pelvic organ and rectal prolapse surgery are comparable to those achieved by means of a two-stage procedure. The one-stage approach allows for a significant reduction of costs and risks related to double hospitalization, anesthesia and surgery.

2. The small number of patients limits the potential for a comprehensive assessment of the statistical significance of differences at this stage of the research.

Funding I declar no financial conflict of interest **Clinical Trial** No **Subjects** Human **Ethics Committee** Warsaw Medical Chamber Ethics Commeetee **Helsinki** Yes **Informed Consent** Yes

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LAPAROSCOPIC BILATERAL UTEROSACROPEXY - ADVANCEMENT OF A NEW SURGICAL TECHNIQUE WITH UTERINE PRESERVATION AND APICAL RESTORATION IN WOMEN WITH SYMPTOMATIC PELVIC ORGAN PROLAPSE

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INTRODUCTION

Symptomatic pelvic organ prolapse (POP) affects many women. If conservative therapies fail, reconstructive surgical therapies come into question, which depends on a number of factors. In addition to the correction of the affected anatomical structures, the patient's desire or preference with regard to uterine preservation and desire for fertility preservation must also be taken into account.

In the last 2 decades, attitudes toward and interest in uterus-preserving POP surgery have increasingly changed. There are a variety of uterus-preserving surgical options, but few publications on subsequent pregnancy. Uterus-preserving procedures have the advantage of significantly shorter operative time, less blood loss, as well as faster recovery and the possibility of fertility preservation. So far, there is also no clear consensus on a uniform surgical procedure in terms of standardization of individual surgical steps for better comparability of clinical outcomes.

For the first time, we present a uterus-preserving surgical technique with a bilateral apical suspension (replacement of both uterosacral ligaments, USL) in a step-by-step standardized surgical technique called laparoscopic uterosacropexie with a minimum amount of synthetic material.

DESIGN

Women with symptomatic uterine prolapse were referred to our tertiary unit and were included in this pilot study. These patients have failed or declined conservative management; none of them had undergone previous urogynecological surgery.

For the laparoscopic uterosacropexy, both USLs were replaced with a tape-like synthetic structure made of polyvinylindene-fluoride (PVDF) (Fig. 1). These tapes of defined length (9 cm) and width (0.4 cm) were retroperitoneally implanted within the run of both USL under preservation of the integrity of the peritoneum by using a semi-circular tunneler.

RESULTS

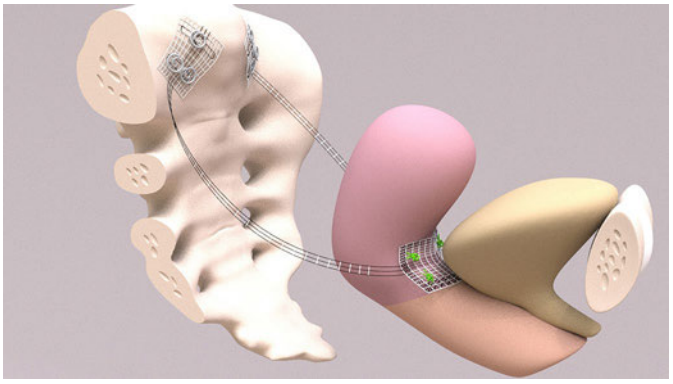
Apical support was restored in all 15 patients (mean age: 41 years), as well as urinary continence (in all 6 patients with prior mixed urinary incontinence). No intraoperative complications occurred (vessel or ureter injury and bowel or bladder lesions). Blood loss was less than 30 mL per patient, and the mean operation time was 56 minutes. Over a mean follow-up period of 20 months, no mesh erosions or relapse of prolapse was detected. One patient became pregnant and was delivered by cesarean section in the 39th week without complications.

CONCLUSION

This laparoscopic bilateral uterosacropexy represents one alternative treatment option for uterus-preserving standardized apical reconstruction in premenopausal patients. This uterosacropexy also offers the advantage of fertility preservation in addition to shorter surgical time, low blood loss, and faster convalescence. This clearly defined surgical technique leads to a better comparability of clinical outcomes.

To date, there are only 8 case series in the literature of reported pregnancies after unilateral hysteropexy. However, to date, there is no described case of bilateral uterosacropexy with subsequent successful pregnancy. Nevertheless, further studies need to provide long-term data on anatomic recurrence, and in the case of subsequent pregnancy, especially on the risk of intrapartum complications as well as postpartum anatomic recurrence.

FIGURE 1



Funding N/A **Clinical Trial** No **Subjects** Human **Ethics Committee** 18-217 **Helsinki** Yes **Informed Consent** Yes

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AUGMENTATION URETHROPLASTY FOR FEMALE URETHRAL STRICTURE. TECHNIQUE & SHORT TERM OUTCOME

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INTRODUCTION
Female urethral strictures are frequently misdiagnosed. There is a paucity in literature regarding the ideal technique of urethroplasty in female urethral strictures.

DESIGN
This is a prospective study of female patients with urethral stricture who underwent urethroplasty at our institute from January 2018 to February 2022. Patients with minimum follow-up of 6 months were included in the study. Female stricture disease was diagnosed based on the obstructive voiding symptoms, voiding cystourethrogram and urethroscopy. Female urethral stricture was defined as a urethral caliber <12 Fr on urethroscopy. We performed Anterior onlay buccal mucosal graft urethroplasty in all patients as described in the video. Patients were followed up with symptom scores, uroflometry and ultrasound for postvoid residual urine at 3rd month and 6th monthly thereafter. A successful outcome was defined as normal voiding without the need for any instrumentation to improve urinary flow rate.

RESULTS
A total 24 female patients underwent urethroplasty with a mean age of 45 ± 2.5 years. The mean stricture length was 2.5 ± 0.5 cm. The mean operative time was 48 ± 5 minutes. There were no peri-operative complications. Overall success rate was 91.6% with a median follow-up of 22.5 months One patient developed recurrent stricture. One patient had poor urinary flow due to hypotonic bladder with no anatomical obstruction in urethra.

CONCLUSION
Anterior onlay augmentation urethroplasty technique for female urethral strictures is feasible safe, with excellent short-term outcomes.

Funding None **Clinical Trial** No **Subjects** Human **Ethics not Req'd** it is aretrospective study. **Helsinki** Yes **Informed Consent** Yes

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URETHROPLASTY IN COMPLEX INFANTILE STRICTURE

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INTRODUCTION
Anatomic lower urinary tract obstructions in boys are not a common problem in pediatric urology.

Although there have been many studies reporting cases of posterior urethral valves, there have been relatively few regarding strictures in children despite the fact that strictures are actually seen more commonly than cases of posterior urethral valves.

However, urethral instrumentation is the main factor for urethral stricture.

DESIGN
We present the case of a 4 years old boy diagnosed of posterior urethral valves at birth. The urethral obstruction was managed with multiple surgeries including internal urethrotomy, holmium laser ablation of PUV, and urethroplasty with buccal mucosa. The patient was referred to our centre with an obliterative stenosis in the bulbar urethra, requiring a vesicostomy to void.

We evaluated anterograde and retrograde the urethra the a total obliterative stenosis in bulbar urethra was confirmed. Open urethroplasty was indicated and the video shows the surgery.

RESULTS
Perineal incision was made in order to dissect both end of the urethral. Endourological approach was used to indicate the stop in the urethra. A tension-free end-to-end anastomosis with interrupted suture 6/0 Monocryl was successful performed. 12ch catheter was inserted when the anastomosis was completed. Vesicostomy was maintain till urethrography demonstrated the absence of urethral fistula.

CONCLUSION
- Open urethroplasty is the procedure of choice in complex and recurrent strictures.

- The combined approach can help locate both ends in obliterated strictures.

- End-to-end anastomosis is successful in short strictures with tension-free anastomosis.

Funding No **Clinical Trial** No **Subjects** None

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FRIDAY 9TH SEPTEMBER

SESSION 15 - BEST BASIC SCIENCE

Abstracts 226-231
09:35 - 11:05, Hall D
Chair: Dr Lori A Birder (United States)

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BEST IN CATEGORY PRIZE: PELVIC PAIN SYNDROMES

INTEGRATING SINGLE-CELL RNA SEQUENCING WITH SPATIAL TRANSCRIPTOMICS REVEALS IMMUNE LANDSCAPE FOR INTERSTITIAL CYSTITIS

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HYPOTHESIS / AIMS OF STUDY

Interstitial cystitis (IC), referred to bladder pain syndrome, characterized by intense pelvic pain and urinary symptoms, is a severely debilitating and chronic disorder. The etiology and pathophysiology of IC still remain an enigma, which makes the diagnosis difficult and treatment challenging. The current therapies of IC showed limited effects and relatively high recurrence rates in the long-term follow-up. About 10% of the diagnosed patients have to receive destructive surgeries (augmentation ileocystoplasty, urinary diversion, etc.) followed by stepwise therapeutic approaches, and 20% of whom have to face the failures (reference 1). Therefore, there is a pressing need to understand the molecular mechanisms underlying the IC development and to identify more efficient targets for therapeutic treatments.

There have been several theories suggesting the causes of IC, including inflammation, neural changes, defects in the wall of bladder and activated mast cells, but none of which has fully explained the manifestations of this disease. Although no one could determine whether IC is an autoimmune disease, the current evidence shows that immunity might play an important role in the progress of IC (reference 2). Thus, we aimed to investigate the immune landscape (the distribution of immune cell subsets) in IC bladders and the specific stage in which the immunity might involve in the progress of IC. Single-cell RNA sequencing (scRNA-Seq), with the ability to reveal distinct subpopulations among cell types, has emerged as a powerful tool to capture the complex profiles of immune infiltrations in diseases. Integrating scRNA-seq with spatial transcriptomic (ST) has been applied to uncover the tissue architecture in pancreatic ductal adenocarcinomas (reference 3). To better understand the role of immunity in IC bladders, we firstly conducted a comprehensive phenotypic and functional investigation of immune parameters (using only CD45+ single cells) through scRNA-Seq combining mass cytometry (CyTOF). Then, the immune views resulted from scRNA-Seq were integrated with the results of ST through multimodal intersection analysis. The findings of this study reveal the immune landscape of bladder in IC patients and may pave the way for future studies of pathophysiology and therapy.

STUDY DESIGN, MATERIALS AND METHODS

This prospective study was designed to investigate the immune atlas of human bladder of female patients with IC. Human research was approved by our Medical Ethics Committee. The study was performed after obtaining informed consent from all participants. The diagnosis of IC was in line with the National Institute of Diabetes, Digestive and Kidney Diseases guidelines. The characteristic pathological findings in the bladder wall were identified by cystoscopy. The inclusion criteria and exclusion criteria for IC patients were shown as follow.

Inclusion criteria

1) Patients of 18 years of age or older at the time of informed consent;

2) Previously diagnosed with interstitial cystitis/bladder pain syndrome (IC/BPS) for a duration of >6 months;

3) Currently diagnosed with Hunner type interstitial cystitis by cystoscopy;

4) O'Leary-Sant Interstitial Cystitis Symptom and Problem Index score over 18;

5) Understands the purpose of this study as explained by the investigator, and that their participation is voluntary and they are free to withhold consent or withdraw from the study at any time, and the investigators determined that the patient is suitable for participation in the study.

Exclusion criteria

1. General conditions

1) The investigators determined she was not suitable for the study;

2) Currently diagnosed with cancer, or have previous history of cancer within the preceding 5 years;

3) Currently diagnosed with severe heart, lung, liver, kidney, or blood disorder;

4) Patients who are pregnant, pregnant women or lactating women or women who desire to become pregnant.

2. Urological problems

1) Have previous history of urinary infection (e.g., bacterial cystitis, bladder tuberculosis, urethritis, genital chlamydia infection, and genital herpes) within 12 weeks;

2) Currently diagnosed with any of following diseases, and/or current urinary symptoms (i.e., bladder pain, bladder discomfort, urinary frequency, persistent urge to urinate, and/or urinary urgency) are caused primarily by these diseases:

a. Bladder diseases (overactive bladder, neurogenic bladder, bladder stone, radiation cystitis)

b. Urethral diseases (urethral diverticulum, urethral stricture, urethral stone)

c. Gynaecological diseases (endometriosis, uterine fibroids, vaginitis, menopausal syndrome, pelvic organ prolapse)

d. Others (neurogenic urinary frequency, polyuria)

3) Have previous history of augmentation cystoplasty or cystectomy;

4) Have previous history of chemical compound (such as cyclophosphamide) derived cystitis.

3. Treatment related

1) Have history of the following therapies within 24 weeks: Hydrodistension, intravesical laser therapy, intravesical electrical coagulation, transurethral resection, pelvic reconstructive surgery, nerve block or spinal cord stimulation for pain relief;

2) Received intravesical instillation of any drugs within 12 weeks.

Female patients with pure stress urinary incontinence (SUI) but stable bladder function admitted for anti-incontinence surgery were offered enrolment as controls.

135,091 CD45+ immune cells from bladders of 15 female patients with IC and 9 controls were captured to perform scRNA-seq to identify the specific immune cell types. Mass cytometry was performed to confirm the identified cell subsets. Then, immunofluorescence, ELISA tests, and the virus detection were performed to validate the possible biomarkers. Lastly, by integrating the results of scRNA-seq with ST, the identified immune subpopulations were re-located in the anatomical structure of IC bladders.

RESULTS

22 immune subpopulations were identified in the constructed landscape. Among them, macrophages, conventional dendritic cells, and effector memory CD4+ T cells had the most communications with other immune cells. Then, a significant increase of central memory CD4+ T cells, regulatory T cells, GZMK+CD8+ T cells, activated B cells, un-switched memory B cells, and neutrophils, and a significant decrease of CD8+ effector T cells, Th17 cells, follicular helper T cells, switched memory B cells, transitional B cells, and macrophages were noted in IC bladders. The enrichment analysis identified a virus-related response during the dynamic change of cell proportion, furthermore, the human polyomavirus-2 was detected with a positive rate of 95% in urine of patients with IC. By integrating the results of scRNA-seq with spatial transcriptomics, we found nearly all immune subpopulations were enriched in the urothelial region or located close to fibroblasts in IC bladders, but they were discovered around urothelium and smooth muscle cells in control bladders.

INTERPRETATION OF RESULTS

1. An immune landscape in IC bladders was constructed.

2. The interactions within immnue cells were investigated.

3. Although this study evidenced that inflammation or immunity had an important role in IC progress, it seemed that it was more likely to be a downstream manifestation after the destruction of epithelial barrier.

CONCLUDING MESSAGE

We constructed the immune landscape of bladder in women with IC, and then confirmed the characteristics of these immune cell subsets and elaborated the relation and interaction within them. This study sets a precedent for investigating the immune atlas for IC. The immune landscape may provide profound insight into the pathophysiology of IC and work as the foundation for the diagnosis and treatment of this disease in the future.

FIGURE 1

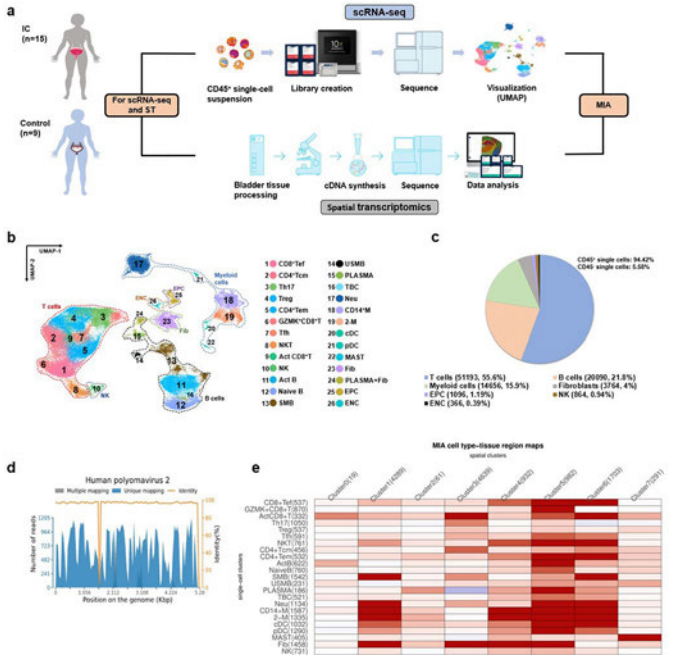

Figure 1 a. Overview of workflow for scRNA-seq and ST. b. The immune landscape of IC bladders. c. The proportion of each cell type. d. Human polyomavirus-2 was detected in IC urine. e. Distribution of immnue cells in IC bladders.

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REVISITING THE LOW BLADDER CAPACITY PHENOTYPIC SUBGROUP IN INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME

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HYPOTHESIS / AIMS OF STUDY

Efforts to research and treat interstitial cystitis/bladder pain syndrome (IC/BPS) are complicated by the broad heterogeneity within the disorder. Efforts to identify clinically meaningful IC/BPS subgroups have found that molecular profiling of bladder mucosal tissue from a modest number of IC/BPS patients and controls shows a separation of profiles based on anesthetic bladder capacity (BC) [1]. Patients with a low BC (which was defined empirically as BC $\leq$ 400cc) had a characteristic gene expression profile that was distinct from patients with a non-low BC ($>$ 400cc), and controls. Further examination of clinical and demographic information utilizing a patient registry, using low BC as the benchmark, revealed a bladder-centric IC/BPS patient subgroup characterized by older age, higher symptom scores on validated questionnaires, higher prevalence of Hunner's lesions (HL), and fewer non-urologic associated symptoms and syndromes [2]. With the understanding that the cutoff of BC $\leq$ 400cc to identify as 'low BC' was truly an estimate, we have undertaken an analysis of our large patient registry utilizing genetic expression data as well as demographic and clinical data to determine if an adjustment in this cutoff estimate is warranted.

STUDY DESIGN, MATERIALS AND METHODS

IC/BPS patients scheduled to undergo therapeutic hydrodistention (HOD) were recruited to participate in our IRB-approved study. Following written informed consent, mucosal biopsies were collected at the time of HOD and stored for genomic analysis in our biobank. Clinical and demographic information, including BC, HL status, scores on validated IC/BPS symptom scores (O'Leary Sant Interstitial Cystitis Symptom & Problem Indices [ICSI/ICPI], and Pain & Urgency/Frequency [PUF] patient symptom scale), were collected for each patient. In addition, questionnaire data to determine the presence/absence of several common non-urologic associated symptoms (NUAS), subdivided into localized pelvic pain syndromes (PPS) and widespread neurologic, allergic, and systemic pain syndromes (NASP), were also prospectively collected. For this study, we initially analyzed whole genome gene expression array data from 48 mucosal biopsy samples (41 from IC/BPS patients; 7 from controls) to provide an updated assessment of patient stratification based on anesthetic BC. Next, we identified 491 individual recruited patients with complete demographic, clinical, and questionnaire data that were available for analysis. Characteristics of these 491 patients were compared between those having the current low BC cutoff ($\leq$ 400cc) and the proposed new cutoff ($\leq$ 500cc) utilizing independent samples t-test (continuous variables) and chi square tests (categorical variables), with a $p < 0.05$ being considered significant.

RESULTS

Unsupervised clustering and principal component analysis (PCA) of 48 whole genome data profiles identified three primary individual clusters: (1) IC/BPS patients with a BC between 200-500cc, (2) IC/BPS patients with a BC of 500-1500cc, and (3) controls (Figure 1). A statistical comparison of the demographic and clinical characteristics of these IC/BPS patient subgroups showed that those with a bladder capacity $\leq$500cc were older, more likely to have Hunner's lesions, had higher ICSI and ICPI scores, as well as frequency and nocturia sub scores (PUF) ($p < 0.05$), were less likely to be female, and had a shorter length of diagnosis than those with a BC $>$500mL ($p < 0.05$). This group also had a lower average number of NUAS, pelvic pain syndromes (PPS), and neurologic, immune, or systemic pain syndromes (NASP), including lower rates of endometriosis, pelvic floor muscle dysfunction, irritable bowel syndrome (IBS), chronic fatigue syndrome (CFS), fibromyalgia, migraines, depression, panic disorder, insomnia, and asthma. These findings, based on a low BC designation of $\leq$500cc, were closely aligned with the former low BC designation ($\leq$400cc) findings (Table 1).

INTERPRETATION OF RESULTS

Molecular (gene expression) analysis can be used to highlight a statistically meaningful difference between IC/BPS patients that is based on anesthetic bladder capacity. Using this molecular information together with demographic and clinical data from a large cohort of IC/BPS patients, we have identified significant differences between these subgroups, with a low bladder capacity (i.e., bladder centric) phenotype having a high prevalence of Hunner's lesions, as well as higher symptom scores and fewer non-urologic associated syndromes. Comparatively, the non-bladder centric phenotype has a low prevalence of Hunner's lesions, moderately lower validated symptom scores, and higher numbers of combined non-urologic associated syndromes, including higher prevalence rates of many syndromes individually. These findings expand upon earlier data that posited a 400cc cut-off for low BC and supports that idea that the 400mL cutoff may be too low and may exclude patients with a true bladder-centric phenotype.

CONCLUDING MESSAGE

In the context of IC/BPS, low anesthetic bladder capacity is a relative, rather than absolute, categorization. By combining newly acquired molecular data with clinical and demographic characteristics in a large cohort of IC/BPS patients, we consider a shift in the definition of bladder-centric disease to encompass patients with an anesthetic BC $\leq$ 500cc.

FIGURE 1

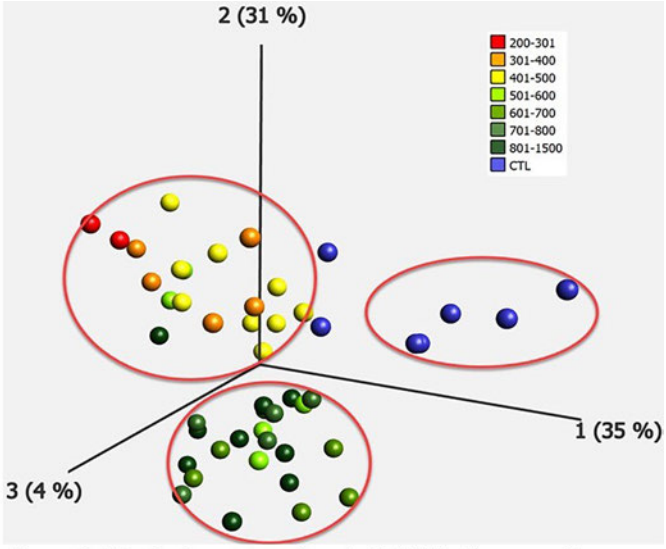

Figure 1. Principal component analysis (PCA) of comparative gene expression in mucosal tissue from IC/BPS patients and controls. Each small colored circle represents the comprehensive gene expression profile from a single individual biopsy. Samples are color-coded to identify membership in a specific bladder capacity 'bin' (e.g., yellow: BC = 401-500 cc).

FIGURE 2

Variable	BC ≤ 400cc N=78 Mean (SD) Number (%)	BC > 400cc N =413 Mean (SD) Number (%)	p-value	BC ≤ 500cc N=111 Mean (SD) Number (%)	BC > 500cc N=380 Mean (SD) Number (%)	p-value
Race (white)	71 (91.0%)	366 (88.6%)	0.098	101 (91.0%)	336 (88.4%)	0.247
Gender (female)	61 (78.2%)	393 (95.2%)	**<0.001**	87 (78.4%)	367 (96.6%)	**<0.001**
Age (years)	58.78 (13.95)	44.94 (13.92)	**<0.001**	56.19 (15.89)	44.49 (13.38)	**<0.001**
BMI	30.19 (6.62)	29.11 (8.15)	0.235	30.07 (6.89)	29.05 (8.20)	0.157
IC diagnosis (months)	68.40 (87.27)	91.5 (92.52)	0.052	70.78 (83.40)	92.64 (93.85)	**0.033**
Hunner's lesion	35 (45.5%)	19 (4.8%)	**<0.001**	41 (37.3%)	13 (3.5%)	**<0.001**
PUF (0-35)	19.75 (10.97)	19.49 (10.30)	0.858	19.48 (11.35)	19.55 (10.10)	0.957
Frequency (0-4)	2.61 (1.33)	1.93 (1.30)	**<0.001**	2.33 (1.36)	1.95 (1.31)	**0.013**
Nocturia (0-4)	3.59 (0.76)	2.60 (1.22)	**<0.001**	3.40 (0.99)	2.57 (1.21)	**<0.001**
ICSI (0-21)	14.84 (3.76)	13.18 (3.88)	**0.001**	14.81 (3.72)	13.04 (3.87)	**<0.001**
ICPI (0-16)	13.60 (2.56)	12.47 (3.07)	**0.006**	13.46 (2.66)	12.41 (3.08)	**0.003**
Number of PPS	0.64 (0.82)	1.04 (0.97)	**<0.001**	0.68 (0.81)	1.06 (0.98)	**<0.001**
Endometriosis*	5 (8.2%)	89 (22.6%)	0.01	9 (10.3%)	85 (23.2%)	**0.008**
Dyspareunia*	18 (29.5%)	144 (36.6%)	0.279	26 (29.9%)	136 (37.1%)	0.209
Vulvodynia*	11 (18.0%)	66 (16.8%)	0.81	16 (18.4%)	61 (16.6%)	0.693
PFMD	16 (20.5%)	130 (31.5%)	0.052	24 (21.6%)	122 (32.1%)	**0.034**
Number of NASP	1.81 (1.56)	3.00 (1.99)	**<0.001**	1.98 ± 1.66	3.05 ± 2.00	**<0.001**
IBS	21 (26.9%)	169 (40.9%)	**0.02**	29 (26.1%)	161 (42.4%)	**0.002**
CFS	6 (7.7%)	64 (15.5%)	0.071	12 (10.8%)	58 (15.3%)	0.238
Fibromyalgia	10 (12.8%)	118 (28.6%)	**0.004**	20 (18.0%)	108 (28.4%)	**0.028**
Migraines	10 (12.8%)	136 (32.9%)	**<0.001**	14 (12.6%)	132 (34.7%)	**<0.001**
Depression	17 (21.8%)	152 (36.8%)	**0.011**	28 (25.2%)	141 (37.1%)	**0.02**
Panic disorder	15 (19.2%)	157 (38.0%)	**0.001**	23 (20.7%)	149 (39.2%)	**<0.001**
Sleep disorder	5 (6.4%)	45 (10.9%)	0.230	8 (7.2%)	42 (11.1%)	0.239
Allergies	49 (62.8%)	309 (74.8%)	**0.029**	73 (65.8%)	285 (75.0%)	0.054
Asthma	5 (6.4%)	76 (18.4%)	**0.009**	9 (8.1%)	72 (18.9%)	**0.007**
Number of NUAS	2.78 (2.07)	4.61 (2.72)	**<0.001**	3.11 (2.25)	4.67 (2.74)	**<0.001**

*N= 454 as men excluded from analysis; PPS = pelvic pain syndrome, PFD = pelvic floor muscle dysfunction, NASP = neurologic, autoimmune, or systemic pain syndrome, IBS = irritable bowel syndrome, CFS = chronic fatigue syndrome, NUAS = non-urologic associated syndromes

Table 1. Statistical comparison of patient demographic and clinical data when considering low bladder capacity at ≤ 400cc versus ≤ 500cc.

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SAFETY OF HUMAN EMBRYONIC STEM CELL DERIVED MESENCHYMAL STEM CELLS FOR TREATING INTERSTITIAL CYSTITIS: A PHASE 1 STUDY

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HYPOTHESIS / AIMS OF STUDY
Interstitial cystitis (IC) is a chronic inflammatory disease with characteristic pelvic pain with varying degrees of accompanied lower urinary tract symptoms. Tiered therapy are recommended in guidelines but most them result in temporary alleviation of pain and have limited evidence strength, in other words, there is no definite cure for IC. Stem cell therapy is emerging as potent alternatives in chronic diseases and IC is one of the possible candidates considering its intractable nature. Here we report the first clinical application of human embryonic stem cell (ESC) derived mesenchymal stem cells (MSCs) on IC.

The therapeutic efficacy of autologous MSCs in stress urinary incontinence and detrusor underactivity patients have been introduced in the literature, but none in IC. Previously, we have reported the beneficial effects and non-tumorigenicity of multipotent-MSC (M-MSCs) derived from human ESCs in various preclinical voiding dysfunction models. In this regard, we developed clinical grade MSCs derived from hESCs into cell-type product with code name MR-MC-01, and investigated its potential in treating IC patients. The primary outcome was safety and tolerability of MR-MC-01 in human subjects and the secondary outcomes were efficacy of MR-MC-01 in clinical symptoms including pain, voiding profiles and characteristic of Hunner lesions on cystoscopy.

STUDY DESIGN, MATERIALS AND METHODS
Three female patients with 1) symptom duration $>$ 6 months, 2) visual pain analog scale (VAS) $\geq$ 4, and 3) 1–2 Hunner lesions $<$ 2 cm on cystoscopy within 1 month were included. Patients unsuitable for participation based on criteria and investigators' consideration were excluded. Under general anesthesia, participants received a cystoscopic submucosal injection of MR-MC-01 (2.0 $\times$ 107 /5 mL) at the center or margin of Hunner lesions and another part of the bladder wall (except trigone), at a volume of 1 mL. Follow-up was performed 1, 3, 6, 9, and 12 months post-procedure. Patients underwent scheduled work-ups, and symptoms were evaluated with validated questionnaires at each visit.

RESULTS
The median age of patients were 71 years (range 68 – 77) with symptom duration more than one year. All patients had refractory symptom to oral medication including pentosan polysulfate. Two patients had previous history of intravesical instillation and endoscopic operation but had recurrent symptoms. All patients had negative urine cytology or bladder biopsy to rule out combined malignancy before screening. First two participants completed 12-month follow-up and third participant finished 6-month follow-up.

No MR-MC-01 related adverse events including immune reaction and abnormalities on laboratory tests and imaging work-ups were reported. Patient 1 reported temporary right-side suprapubic pain after stem cell injection but it was tolerable and did not require opioid analgesics, additional intervention or admission. Pain improved significantly at post-procedure 1 month, but changes differed afterwards. However, none of the patients required gabapentin or opioid analgesics and unexpected transiently aggravated pain was well-controlled with prn NSAIDs. There was no significant aggravation in subjective symptom questionnaires and voiding diaries. None of the patients presented de novo Hunner lesions or any abnormalities in the bladder. Except one Hunner lesion of Patient 1, which was not identifiable on 12-month cystoscopy, the extent of other lesions were similar or slightly decreased.

INTERPRETATION OF RESULTS
Main difference between previous clinical trials using hESC-derived cells and this study is the use of immunosuppressant. In clinical trials using hESC-RPE cells or patch, patients were prescribed a temporary systemic immunosuppression regimen such as oral tacrolimus, mycophenolate mofetil, or oral prednisolone to prevent rejection. These regimens led to a wide range of side effects including fatigue, diarrhea, stomach ache, uncontrolled diabetes, infection, and shortness of breath. We did not use a systemic immunosuppressant due to following reasons; First, injection site was submucosa of the bladder that transplanted cells were highly likely to be localized between submucosa and detrusor which might result in limited systemic response. Second, IC bladder present changes in immune responses like B-cell abnormalities that cyclosporine A which modulate immunity is recommended as fifth-line treatment for IC in American Urological Association (AUA) guidelines. Concurrent prescription of an immunosuppressant is most likely to overestimate the therapeutic efficacy of MR-MC-01 in future studies. Third, actual injected number of cells might be less than expected as needle injection result in a tiny defect of urothelium which could be route for cell spillage. In addition, human urinates regularly that spilled cells into the urinary bladder are immediately diluted by urine and get washed out during voiding.

The therapeutic efficacy of MR-MC-01 varied among study participants but VAS pain improved significantly (VAS $\leq$ 4) at post-procedure 1 month in all subjects. Size of Hunner lesion is not always proportional to the degree of pain, but initially large (nearly 2cm) Hunner lesions were more likely to persist throughout the follow-up. Meanwhile, extent of small Hunner lesions ($<$1cm) tended to decrease that one Hunner lesion of Patient 1 was not identifiable at 12-month follow-up. This trend was not applicable to Patient 3 who had initially smallest Hunner lesions. However, the subject had longest symptom duration (11 years), previous history of TURC four times and relatively decreased functional bladder capacity than other subjects. Disease duration of IC and extent of previous therapy might play a key role in variation of therapeutic efficacy.

CONCLUDING MESSAGE
This study presents the preliminary investigation on safety of M-MSC in IC patients but is limited by a small number of patients. A long-term safety monitoring is scheduled up to 5 years for these subjects and follow-up clinical trial which investigates the safety of a higher-dose MR-MC-01 to decide the optimal therapeutic dosage in more number of patients is about to be launched. Further investigations should focus on an optimal dosage and injection schedule of MR-MC-01 to maximize the efficacy with continuous monitoring on safety, in order to suggest stem cell injection as one possible therapeutic modality for treating IC patients.

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EFFECTS OF ORAL ADMINISTRATION OF NON-SELECTIVE TRK INHIBITOR ON BLADDER OVERACTIVITY IN A RAT MODEL OF PROSTATIC INFLAMMATION

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HYPOTHESIS / AIMS OF STUDY

Prostatitis is one of the most common urinary tract problems for men at any age with an estimated prevalence in the community of about 9%. In addition, more than 90% of patients with prostatitis are classified into chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS), which is the category IIIA and IIIB without bacterial infection in National Institutes of Health (NIH) classification of prostatitis. Although CP/CPPS often reduces quality of life, the underlying mechanism is still not fully clarified. Also, the currently available treatments such as alpha-blockers, anti-inflammatory drugs and phytotherapeutic agents are often ineffective to improve CP/CPPS symptoms including pain, pressure and discomfort related to the lower urinary tract as well as overactive bladder (OAB)-like storage symptoms. Our previous studies reported that a rat model of prostatic inflammation (PI) showed bladder overactivity, afferent hyperexcitability due to prostatic-to-bladder cross-organ sensitization, and nerve growth factor (NGF) upregulation in the bladder epithelium and that intravesical instillation of liposome conjugated with NGF antisense oligonucleotide, which normalized local NGF overexpression, significantly reduced bladder overactivity [1]. Therefore, local blockade of NGF in the bladder could be a therapeutic modality for male lower urinary tract symptoms (LUTS) due to PI. Neurotrophic factors including NGF and brain derived neurotrophic factor (BDNF) are known to bind to high-affinity tropomyosin receptor kinase (Trk) receptors such TrkA and TrkB, respectively. Because increased expression of TrkA and TrkB receptors has been reported in inflamed urinary bladders [2], we hypothesized that blockade of Trk receptors such as TrkA and TrkB is effective for the treatment of male LUTS in patients with PI. Thus, in the present study, we examined the effects of systemic non-selective Trk receptor inhibition on bladder hypersensitivity using a rat model of PI.

STUDY DESIGN, MATERIALS AND METHODS

Male Sprague-Dawley rats at 8 to 9 weeks of age were used and they were divided into three groups (n = 6 in each group): (1) Control group; rats without intraprostatic instillation and with oral administration of vehicle. (2) Untreated groups; PI rats with oral administration of vehicle (3) Treated group; PI rats with oral administration of non-selective Trk inhibitor (GNF 5837). PI was induced by intraprostatic 5% formalin injection (50 µl per each ventral lobe) in Untreated and Treated groups. Then, GNF 5837 at a dose of 40 mg/kg dissolved in methyl cellulose (0.5w/v %, 0.1 ml) and TWEEN 80 (0.5w/v %, 0.1 ml) [3], or vehicle was given to each group daily by oral gavage for 10 days from day 18 after inducing PI. On day 28, conscious cystometry (CMG) was performed. Tissues were then harvested for histological analysis as well as for evaluation of protein expression levels of NGF and BDNF in the bladder mucosa and the ventral lobes of prostate by ELISA, mRNA expression levels of Trk receptors (TrkA, B and C), a C-fiber afferent marker (TRPV1) in L6-S1 dorsal root ganglia (DRG), and inflammation markers (IL-1β, IL-18) in the ventral lobes of prostate by RT-PCR.

RESULTS

In CMG, Treated group demonstrated a significant decrease in non-voiding contractions (Fig. 1A; NVC) compared to Untreated group in association with reductions of NGF and BDNF protein expression levels in both bladder mucosa and prostate, whereas there were no significant differences between Treated and Control groups (Fig. 2A). In other CMG parameters including intercontraction intervals (ICI), there were no significant differences among three groups. In Untreated group, mRNA expression levels of all Trk receptor subtypes (Trk A, B and C) and TRPV1 in L6-S1 DRG were significantly increased, compared to Control group; however, these changes were normalized in Treated group (Fig. 2B and 2C). In Untreated group, mRNA expression levels of IL-1β and IL-18 in the prostate were significantly greater than those of Control group whereas there were no significant differences between Treated and Control groups (Fig. 2D). In addition, although there were inflammatory cells infiltration in the prostatic stroma of Untreated group compared to Control group, these changes in Treated group were lesser than in Untreated group (Fig. 1B).

INTERPRETATION OF RESULTS

Systemic blockade of Trk receptors reduced NGF and BDNF expression in both bladder and prostate, which was increased after PI. Also, oral administration of non-selective Trk inhibitor reduced PI as well as PI-induced bladder overactivity shown by increased NVC and C-fiber afferent marker (TRPV1) overexpression in L6-S1 DRG that contain bladder and prostate afferent neurons. Thus, it is assumed that Trk receptors plays a significant role in prostate-to-bladder cross-organ sensitization, which induces bladder overactivity due to enhanced bladder afferent activity after PI.

CONCLUDING MESSAGE

Systemic blockade of Trk receptors improved not only PI, but also bladder overactivity shown by increased NVC in a rat model of PI. Also, improvement of bladder overactivity is associated with reductions of Trk A, B and C receptors, TRPV1 in L6-S1 DRG as well as NGF and BDNF in the bladder mucosa and the prostate. Thus, the NGF/BDNF-Trk receptor mechanism would be a potential target for the treatment of irritative bladder symptoms in patients with chronic prostatitis.

FIGURE 1

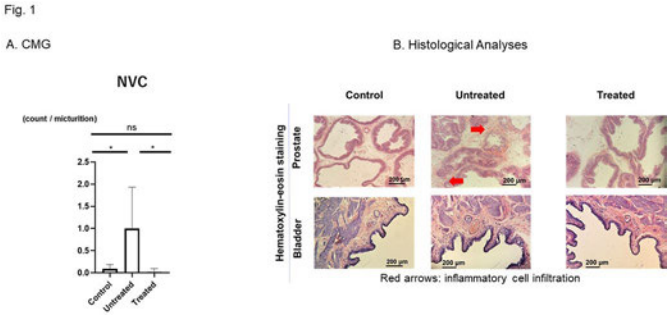
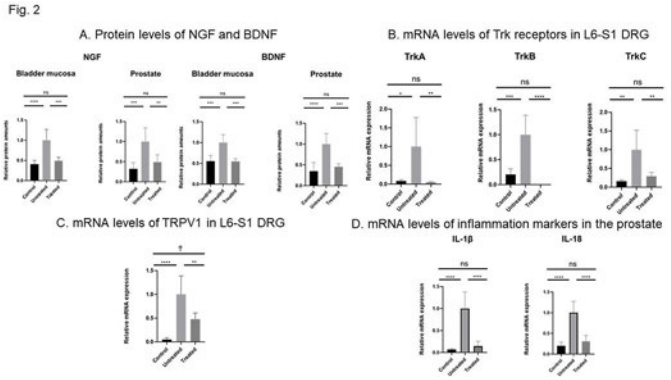


FIGURE 2



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BEST IN CATEGORY PRIZE: PHARMACOLOGY

A STRESS-RELATED NEUROPEPTIDE CORTICOTROPIN-RELEASING FACTOR INDUCES FACILITATION OF THE RAT MICTURITION THROUGH BRAIN GLUTAMATERGIC RECEPTORS

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HYPOTHESIS / AIMS OF STUDY

Psychological/mental stress can influence on urinary function as evidenced by studies in humans and animal models [1]. In addition, a strong correlation has been reported between psychological/mental stressors and symptoms in patients with lower urinary tract dysfunction (LUTD) including overactive bladder (OAB) and bladder pain syndrome/interstitial cystitis (BPS/IC) [1]. Stress-related information is conveyed to the central nervous system (CNS), thereby inducing physical and behavioral responses for adaptation to stress (stress responses), such as the hypothalamus-pituitary-adrenocortical (HPA) axis and the sympatho-adrenomedullary (SA) system. The HPA axis is more reactive in patients with OAB than in healthy controls, and psychological stress-induced frequent urination is mediated at least by the activation of the SA system in rats. Therefore, stress responses can provide a link to LUTD. However, the central mechanisms underlying psychological/mental stress-induced effects on urinary function and LUTD are not fully elucidated

Corticotropin-releasing factor (CRF) and its receptors [type 1 (CRFR1) and type 2 (CRFR2)] have been recognized as central components to stress. In fact, central CRF is identified as the master regulator of the HPA axis and induces activation of the SA system. However, roles of central CRF in regulation of the micturition are still controversial, both facilitatory and inhibitory roles are reported [2,3]. In this study, we investigated the effects of centrally administered CRF on the rat micturition and central mechanisms for the CRF-induced responses, focusing on brain CRFR1 and CRFR2 and glutamatergic receptors.

STUDY DESIGN, MATERIALS AND METHODS

Urethane anesthetized (0.8 g/kg, ip) male Wistar rats (300-450 g) were used.

(1) A catheter was inserted into the bladder from the dome to perform cystometry (12 ml/h saline infusion). Two hours after the surgery, continuous cystometry was started to evaluate intercontraction interval (ICI) and maximal voiding pressure (MVP). One hour after the start, CRF (1 or 3 nmol/rat) or vehicle-1 (10 µl 0.08% AcOH in saline/rat) was intracerebroventricularly (icv) administered. Evaluations of ICI and MVP were continued 3 h after the administration.

(2) Three hours after the surgery described in (1), single cystometry (12 ml/h saline infusion) was performed. After 4-5 times of single cystometry, CRF (3 nmol/rat) or vehicle-1 (10 µl 0.08% AcOH in saline/rat) was icv administered, then single cystometry was performed during 60-120 min after the administration.

(3) Effects of central pretreatment with CP154526 [CP, CRFR1 antagonist, 30 or 100 nmol in 3 ul N,N-dimethylformamide (DMF)/rat, icv], K41498 (K, CRFR2 antagonist, 30 nmol in 10 µl in saline/rat, icv), MK-801 [MK, an antagonist of N-methyl-D-aspartate type glutamatergic receptors (NMDA receptors), 3 or 10 nmol in 5 µl saline/rat, icv] or DNQX [an antagonist of alpha-amino-3-hydroxy-5-methyl-4-isoxazole propionate type glutamatergic receptors (AMPA receptors), 1 or 3 nmol in 5 µl saline/rat, icv] on the CRF (3 nmol/rat, icv)-induced responses were also investigated.

RESULTS

(1) Centrally administered CRF dose-dependently shortened ICI without changing MVP (Fig. 1).

(2) Centrally administered CRF significantly reduced single-voided volume (Vv) and bladder capacity (BC) without affecting post-voiding residual volume (Rv) or voiding efficiency (VE) compared to the vehicle-1-treated group (Table 1).

(3) Central pretreatment with CP, MK, and DNQX significantly attenuated the CRF-induced ICI shortening (Fig. 2), while K showed no significant effect on the CRF-induced response (data not shown). Central administration of each antagonist alone showed no significant effect on ICI or MVP (data not shown).

INTERPRETATION OF RESULTS

Our present data indicate that CRF centrally induces facilitation of the micturition as shown by centrally administered CRF-induced ICI shortening and reduction in Vv and BC without changing MVP, Rv or VE. The CRF-induced ICI shortening was attenuated by centrally pretreated CP, but not by K, indicating that CRF induced facilitation of the micturition via brain CRFR1. Because in response to centrally administered CRF, urodynamic parameters of bladder efferent activity such as MVP, Rv or VE were not changed, CRF in the brain might induce facilitation of the micturition reflex through facilitation of sensory inputs to the micturition center. We also investigated central mechanisms for the CRF-induced facilitation of the micturition in relation to the glutamatergic receptors because an interaction between CRFergic and glutamatergic neurotransmission is reported, and glutamatergic nervous system in the CNS is a central component for regulation of the micturition. In this study, the CRF-induced ICI shortening was attenuated by centrally pretreated MK and DNQX, suggesting that CRF induced facilitation of the micturition via brain NMDA and AMPA receptors. Each antagonist (MK or DNQX) alone showed no effect on ICI or MVP, indicating that basal activity of the glutamatergic nervous system was partially suppressed by the pretreatment at least under our conditions. Therefore, stimulation of brain CRFR1 might facilitate the micturition through brain NMDA and AMPA glutamatergic receptors.

CONCLUDING MESSAGE

Brain CRF induces facilitation of the rat micturition through brain CRFR1 and NMDA and AMPA glutamatergic receptors. These findings would be useful for understanding the underlying mechanisms of psychological/mental stress-induced effects on LUTD, and CRFR1 might be new therapeutic target for neurogenic bladder overactivity.

FIGURE 1

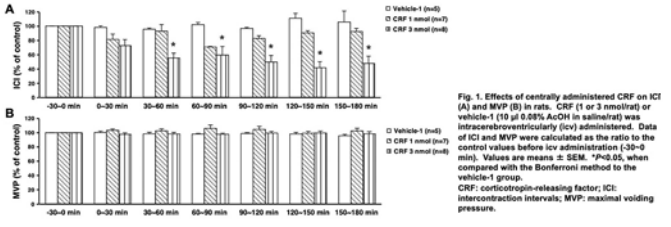

Fig. 1. Effects of centrally administered CRF on ICI (A) and MVP (B) in rats. CRF (1 or 3 nmol/rat) or vehicle-1 (10 µl 0.08% AcOH in saline/rat) was intracerebroventricularly (icv) administered. Data of ICI and MVP were calculated as the ratio to the control values before icv administration (-30–0 min). Values are means ± SEM. *P<0.05, when compared with the Bonferroni method to the vehicle-1 group.
CRF: corticotropin-releasing factor; ICI: intercontraction intervals; MVP: maximal voiding pressure.

Table 1. Effects of centrally administered CRF on urodynamic parameters in single cystometry

	% of Before icv							
	Vv		Rv		BC		VE	
	Vehicle-1 (n=6)	CRF (n=6)	Vehicle-1 (n=6)	CRF (n=6)	Vehicle-1 (n=6)	CRF (n=6)	Vehicle-1 (n=6)	CRF (n=6)
Before icv	100.0 ± 0.0	100.0 ± 0.0	100.0 ± 0.0	100.0 ± 0.0	100.0 ± 0.0	100.0 ± 0.0	100.0 ± 0.0	100.0 ± 0.0
After icv (60–120 min)	104.5 ± 9.8	55.9 ± 6.4*	104.5 ± 10.0	97.6 ± 3.7	99.1 ± 4.1	73.6 ± 4.5*	106.0 ± 6.7	90.1 ± 4.0

CRF (3 nmol/rat) or vehicle-1 (10 µl 0.08% AcOH in saline/rat) was icv administered. Data calculated as the ratio to the pretreatment (Before icv) control values present means ± SEM. *P<0.05, when compared with unpaired Student *t*-test to the vehicle-1 group. BC: bladder capacity; CRF: corticotropin-releasing factor; Rv: post-voiding residual volume; VE: voiding efficiency; Vv: single-voided volume.

FIGURE 2

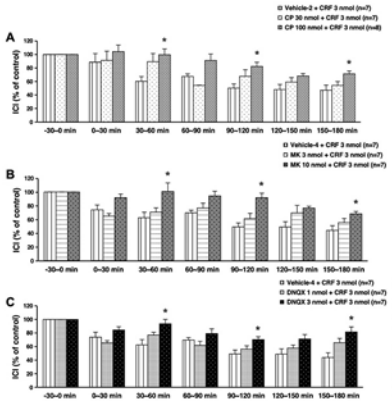

Fig. 2. Effects of centrally pretreated CP154526 (CP, CRFR1 antagonist) (A), MK-801 (MK, NMDA receptor antagonist) (B), or DNQX (AMPA receptor antagonist) (C) on CRF-induced ICI shortening. CP (30 or 100 nmol/rat, icv), vehicle-2 (3 μl DMF/rat, icv), MK (3 or 10 nmol/rat, icv), DNQX (1 or 3 nmol/rat, icv) or vehicle-4 (5 μl saline/rat, icv) was administered 30 min before CRF administration (3 nmol/rat, icv). Data of ICI were calculated as described in Fig. 1A. Values are means ± SEM. *P<0.05, when compared with the Bonferroni method to the vehicle-2 + CRF group (A) or to the vehicle-4 + CRF group (B, C). AMPA: alpha-amino-3-hydroxy-5-methyl-4-isoxazole propionate; CRF: corticotropin-releasing factor; DMF: *N,N*-dimethylformamide; ICI: intercontraction intervals; NMDA: *N*-methyl-D-aspartate.

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IDENTIFICATION OF THE MAJOR NADPH OXIDASE SUBTYPE AND SUPEROXIDE PRODUCTION IN THE MICTURITION CENTRE – PATHOLOGICAL IMPLICATIONS

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HYPOTHESIS / AIMS OF STUDY

Oxidative inflammatory damage to the specialised brain centres may lead to aging and the dysfunction of their associated peripheral organs such as bladder disorders (1). However, the source of reactive oxygen species (ROS) in specific brain regions that regulate bladder function is poorly understood. Of all ROS-generating enzymes, NADPH oxidase (Nox) family produces ROS as its sole function and offers advantage over other enzymes as a drug targetable molecule to selectively control excessive ROS generation without compromising physiological oxidation. Our pilot studies have identified the Nox system in the bladder tissue and demonstrated its functional and pathological significance (2). However whether Nox system exists in the brain micturition centre and hence affects the micturition process has not been examined. We have investigated whether the major pathological Nox subtype, Nox 2, is expressed in micturition regulatory Periaqueductal gray (PAG) and Barrington's nucleus (pontine micturition centre, PMC) and examined the Nox-derived ROS production in these structures.

STUDY DESIGN, MATERIALS AND METHODS

C57BL/6J mice (male, 2-5 months) were used as the experimental model in compliance with the UK regulations. PAG and PMC were obtained by stereotaxic dissection using a rodent brain slicer. Cardiac tissue, bladder tissue and aorta were micro-dissected under the microscopic guidance. The Nox 2 expression was determined by Western blot with primary antibodies for NOX2/gp91phox and the reference protein beta-actin, and Infra-red dye conjugated secondary antibodies. Lucigenin enhanced chemiluminescence quantified real-time superoxide production in live tissues, incubated with an artificial cerebral spinal fluid (ACSF). ACSF contained 128 mM NaCl, 3 mM KCl, 1 mM MgCl2.6H2O, 24 mM NaHCO3, 0.5 mM NaH2PO4.2 H2O, 30 mM glucose, and 1.5 mM CaCl2. The NADPH-dependent superoxide production was stimulated by 100μM NADPH. The specificity was verified by superoxide scavenger Tiron. The quantity of photons collected was expressed as relative light units (RLU) per unit tissue weight (RLU/mg). Data are expressed as mean ± SEM. For data with a normal distribution, the difference between two group means was tested with Student's t-test, paired or unpaired as appropriate. For data which did not follow a normal distribution or had an unknown distribution, the difference between two group means was tested with equivalent non-parametric tests. The difference among multiple means was tested with ANOVA followed by pair-wise comparisons or non-parametric equivalents. The null hypothesis was rejected at $p < 0.05$.

RESULTS

Western blot results show a clear protein band with the expected molecular weight of Nox 2 from PAG and PMC extracts ($N = 6$). This was validated by Nox 2 positive HEK 293 cells with the same molecular weight and comparable intensity confirming significant expression of Nox 2 in the PAG and PMC. There was a significant level of NADPH dependent superoxide production in both brain tissues (RLU/mg, PMC: 127 ± 17; PAG102 ± 13, $N = 110$). The magnitude was higher than that from cardiac tissue (32 ± 3, $P < 0.01$), similar to that from bladder smooth muscle (91 ± 19, $p > 0.05$) and lower than that in bladder mucosa (262 ± 55, $p < 0.01$). The time course analysis shows that the rise of superoxide production in these two brain tissues was more sustained than that in bladder mucosa and smooth muscle (half peak duration PD50, minutes: PMC, 101 ± 2; PAG, 99 ± 2; bladder mucosa, 48 ± 3, $p < 0.01$; smooth muscle, 67 ± 9, $p < 0.01$). The superoxide generation from these brain tissues was significantly suppressed by the broad spectrum Nox inhibitor diphenyleneiodonium (DPI, 20μM). Further experiment using Nox2 specific inhibitor GSK2795039 (25μM) also attenuated the superoxide production in both brain tissues with 2/3 of the inhibition observed in the aortic tissue.

INTERPRETATION OF RESULTS

Western blots results with Nox2 protein band with specific molecular weight proves the existence of Nox2 molecules in PAG and PMC. The comparable density of Nox2 proteins in these brain regions to that of positive control cells suggests the abundance of Nox2 expression in these brain tissues. These Nox 2 proteins serve as a molecular basis for Nox-2 derived superoxide production. Measurement of NADPH-stimulated superoxide production, verified by superoxide scavenger Tiron, shows that PAG and PMC produce significant amount of NADPH-dependent superoxide, hence Nox-derived superoxide production. The magnitude of superoxide production, greater than that from the cardiac tissue, known to produce significant amount of reactive oxygen species and subject to oxidative damage, demonstrates the ability of the PAG and PMC to produce sufficient superoxide and hence cause oxidative damage. The significant inhibition of the superoxide production by the broad spectrum Nox enzyme inhibitor DPI proves that the source of superoxide is mainly from from the Nox enzymes in these brain tissues. The inhibition of the superoxide production by Nox2 specific inhibitor GSK2795039, comparable to that of aortic tissue, known to express mainly Nox2 subtype (3), supports the contribution from Nox 2 subtype in the PAG and PMC. The sustained superoxide production in both brain tissues compared with other peripheral tissues implies that Nox derived ROS in these brain regions, once initiated, produces long lasting oxidative damage to the tissue. This brain region specific mode of action of Nox driven superoxide production may serve as a molecular mechanism for chronic damage to these brain regions. As Nox 2 is a major pathologically important Nox subtype in the central nervous system, the findings from this work have pathological implications for neurogenic damage to micturition and bladder function.

CONCLUDING MESSAGE

Nox 2 subtype is expressed in the PAG and PMC with relatively high density. These brain regions have the ability to produce significant amount of NADPH-dependent superoxide, comparable to that of the peripheral tissues known to subject to oxidative stress. The source of superoxide is mainly from Nox enzymes with contributions from the Nox 2 subtype. The Nox-derived superoxide production in the PAG and PMC has sustained kinetics favouring chronic oxidative damage. The study provides the first evidence for Nox 2 subtype expression and Nox-derived superoxide production in these micturition regulatory structures in the central nervous system, with functional and pathological implications.

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SESSION 16 - BEST CONSERVATIVE MANAGEMENT 1

Abstracts 232-237
09:35 - 11:05, Hall K
Chairs: Dr Chantale L Dumoulin (Canada), Mrs Elisabeth Udier (Austria)

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BEST IN CATEGORY PRIZE: E-HEALTH

DEVELOPMENT OF A CONCEPTUAL FRAMEWORK AND DIGITAL PLATFORM FOR THE SELF-MANAGEMENT OF INTERSTITIAL CYSTITIS: ERICA (REMOTE ENGAGEMENT WITH INTERSTITIAL CYSTITIS AIDE)

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HYPOTHESIS / AIMS OF STUDY
Female patients with interstitial cystitis/bladder pain syndrome (IC/BPS) report low satisfaction with prescribed treatments (1). For chronic pain conditions, self-management has been shown to improve self-efficacy (2). This is the first study to develop an evidence-based digital platform that remotely delivers treatments including self-management strategies to patients with IC/BPS.

Aims: (1) to develop a conceptual framework for the self-management of IC/BPS; (2) To develop a digital platform that remotely delivers first- and second-line American Urological Association (AUA) treatments of IC/BPS; (3) To conduct feasibility testing of the newly developed platform for the treatment of IC/BPS.

STUDY DESIGN, MATERIALS AND METHODS
We used a process of contextual inquiry to develop a conceptual framework and digital platform for the self-management of IC/BPS. First, we conducted focus groups and detailed cognitive interviews of female patients with IC/BPS. Symptom data was collected using Interstitial Cystitis Symptom and Problem Index (ICSI and ICPI). Next, we integrated input from patients, providers (urogynecology and urology clinicians, psychologist, physical therapist) and health care innovation expert to develop a conceptual framework for the self-management of IC/BPS. We used this framework to inform the development of video modules that delivered self-management strategies to patients with IC/BPS. The video modules were designed to be delivered over a two-way texting platform that integrated with the electronic medical record and was compliant with regulations for protecting sensitive patient health information. Finally, we conducted a feasibility study in 10 women with IC/BPS eligible for first- and second-line treatments. Participants received video modules through the texting platform and participated in dialogue tree-based open-ended texting with a study coordinator for 6 weeks. Participants were instructed to 1) provide narrative feedback on the content; 2) request a call from a clinician as needed; and 3) assess ease of use of the platform (System Usability Scale, score range 0-100, higher score indicates easier use).

RESULTS
The median age of participants of our focus groups and cognitive interviews was 42 years. Median score (range) for the ICSI was 12 (4,20) and for the ICPI 10 (3, 16) indicating moderate symptom burden.

The following treatment related themes emerged: (i) patients prefer the term interstitial cystitis to bladder pain syndrome (ii) Patients are highly motivated to learn self-management strategies for their symptoms (iii) Patients want an organized plan that minimizes the need to contact a provider between scheduled visits (iv) Patients feel isolated and unsupported, especially when initiating a new treatment (v) Patients are very concerned about the side-effect of medications (vi) Patients have a strong interest in integrative approaches such as diet, pelvic PT, mind-body interventions (vii) Patients prefer remote interventions that minimize barriers (e.g., transportation, childcare, work).

Based on the above findings, a biopsychosocial framework for the treatment of IC/BPS emerged. According to this framework, biological (neuropathic pain, pelvic floor dysfunction), psychological (symptom-related fear and anxiety) and social (barriers in access to care, limited patient-provider communication) domains modulate a patient's biobehavioral response to pain (Figure 1). We used this model to develop video modules that deliver: 1) first- and second-line treatments and self-management strategies (Table 1) and 2) clinically validated messages offering support and guidance (Figure 1) using a structured dialogue tree.

Feasibility testing was performed in 10 participants (median age 40, median ICSI and ICPI were both 12). All patients received modules on patient education, bladder retraining and dietary triggers over two weeks. Each participant could then choose between cognitive behavioral therapy (CBT) for chronic pain, guided mindfulness practices, or pelvic floor physical therapy (PT) including myofascial trigger point release over four weeks. Four patients chose mindfulness, four chose PT, and two chose CBT. Median number of texts exchanged with each participant was 79 (range 49-120). Patient response rate was 89% indicating high engagement. In narrative feedback, patients expressed 1) appreciation for evidence-based treatments that they could access remotely on their own schedule and 2) confidence in implementing strategies for managing their symptoms. Qualitative comments included, "I felt like someone cared about me," "I felt empowered," and "I didn't feel like I was alone in figuring this out All 10 patients completed the program. Mean SUS was 87.8 $\pm$ 6 denoting high usability of the platform. Suggestions for improvement included making the platform more personalized. No participant requested a call back from a clinician indicating low health care utilization.

INTERPRETATION OF RESULTS
A biopsychosocial framework is useful for developing patient-centered treatments that promote the self-management of IC/BPS symptoms. IC/BPS patients are highly motivated to self-manage their condition with support from health care providers. IC/BPS patients prefer organized treatment plans that allow them to choose treatments and which they can access remotely in their own time. Low-cost text-messaging allows delivery of treatments using platforms that integrate with electronic medical records while protecting sensitive health information. When supported through a digital platform, few patients called their health care providers.

CONCLUDING MESSAGE
We developed a feasible low-cost patient-centered text message-based platform for the management of IC/BPS symptoms. The platform has the potential for improving self-management and reducing health care utilization. Future work will involve automating the dialogue tree and evaluating clinical effectiveness of the platform.

FIGURE 1

Video modules	Title	Length
Patient education & bladder health	What is IC?	4:01
	Bladder retraining 1 and 2	4:01 3:34
	Dietary triggers	2:13
Cognitive behavioral therapy for chronic pain	Introduction to CBT	0:29
	Understanding emotions	2:00
	Reversing the anxious spiral	2:41
	Opposite action	4:30
	Managing anxious thought	3:37
	Responding differently to our body	2:44
	Identifying values	3:29
	Expanding our lives	2:53
	Worry trap	4:02
Mindfulness video modules	Mindfulness introduction	4:44
	Mindfulness practice	4:24
Audio-guided mindfulness practice	Describe	4:42
	Observe	4:05
	Body Scan	5:23
	Loving Kindness	4:17
	Soften and allow	7:41
	Mountain meditation	5:33
	Lake meditation	4:58
Basics of pelvic floor PT	Introduction - The Pelvic Floor	2:44
	Diaphragmatic breathing	2:16
	Pelvic wand and trigger point release. Explanation and demonstration.	7:22
Hip adductors	Hip adductors - supine with support	1:43
	Hip adductors - supine without support	1:08
	Hip adductors - seated	0:58
	Hip adductors/ hamstrings stretch	1:23
Deep rotators and glutes	Deep hip rotators	1:20
	Deep hip rotators - internal	0:59
	Figure 4	0:59
Hip flexor and abdomen	Hip flexors stretch - standing	1:11
	Hip flexors stretch - supine	1:25
	Baby Cobra	1:09
Pelvic floor relaxation	Malasana	2:15
	Happy Baby	1:16
Low back	Cat Cow	1:05
	Child's Pose	1:19

Table 1: List of educational video modules on first and second line American Urological Association treatments

FIGURE 2

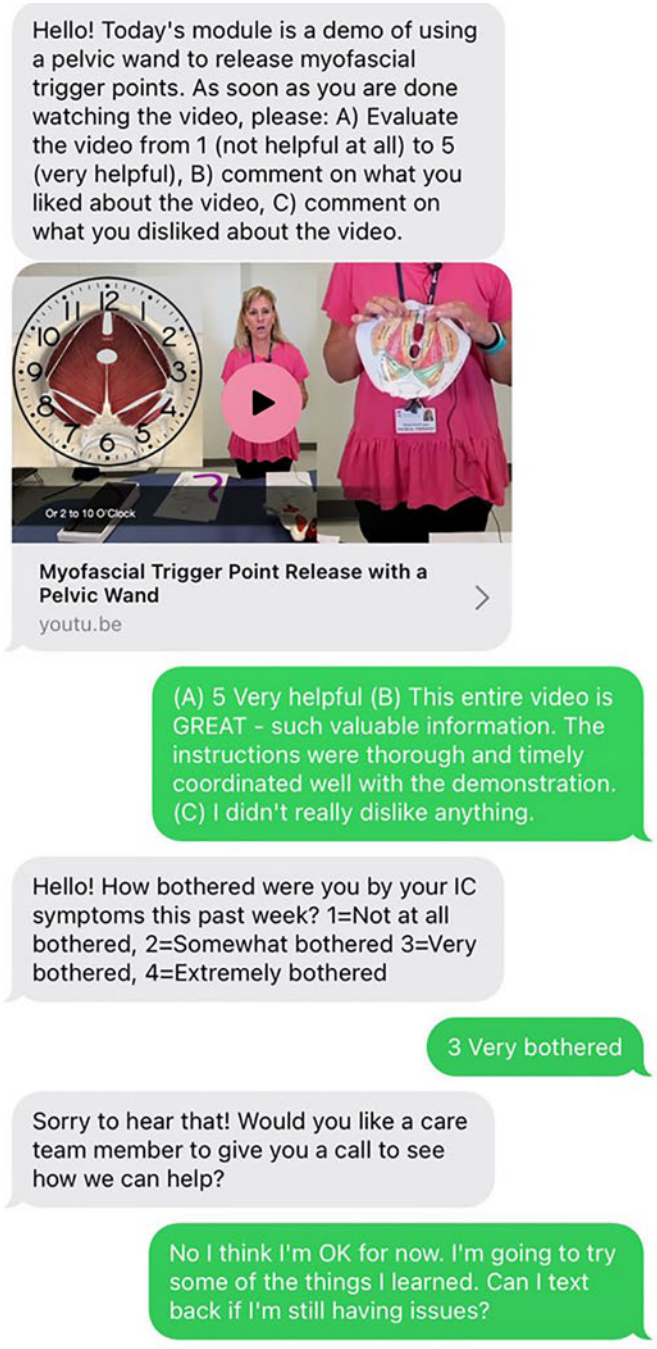

Figure 1: Screenshot of a conversation between ERICA and a participant.

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Funding American Urogynecological Society **Clinical Trial** No **Subjects** Human **Ethics Committee** University of Pennsylvania Institutional Review Board **Helsinki** Yes **Informed Consent** Yes

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MINIMUM IMPORTANT DIFFERENCE OF THE ICIQ-UI SF SCORE AFTER SELF-MANAGEMENT OF URINARY INCONTINENCE VIA A FREELY AVAILABLE MOBILE APP

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HYPOTHESIS / AIMS OF STUDY
To determine clinically relevant improvements after self-management of urinary incontinence with an app that supports pelvic floor muscle training (PFMT) and to evaluate Minimum Important Differences (MIDs) in relation to severity and type of urinary incontinence.

STUDY DESIGN, MATERIALS AND METHODS
A secondary analysis of data from a prospective cohort study evaluating the effect of a freely available app that supports pelvic floor muscle training [1]. Adult, non-pregnant, non-postpartum women who aimed to treat their urinary incontinence and had completed the Patient Global Impression of Improvement (PGI-I) at 3-month follow-up, were included. We registered their answers to the International Consultation on Incontinence Questionnaire (ICIQ-UI SF) at baseline and follow-up. The change in score was analysed for correlation (Spearman) and using one-way ANOVA to determine a MID. The MID in general and for each sub-group was set to the mean change of the women who reported being a little better.

RESULTS
In total 1,733 women with all types of urinary incontinence were included. Of those, more than half (54.8%) reported having symptoms of stress urinary incontinence only, 31.7% reported symptoms of mixed urinary incontinence and 10.8% of only urgency urinary incontinence. The mean age was 46.5 years (range 18-87). The mean baseline ICIQ-UI SF score was 8.92 (range 3-21). When divided into severity categories, 354 (20.4%) had a slight severity, 1,059 (61.1%) moderate, 300 (17.3%) severe and 20 (1.2%) very severe.

There was a significant correlation between the PGI-I and change in ICIQ-UI SF, Spearman rho -0.323 ($p < 0.001$). The one-way ANOVA revealed significant differences between PGI-I categories ($p < 0.001$) and the MID was set to 1.46 (95% Confidence Interval [CI] 1.26-1.67). Sub-group analysis could not determine a MID for the group with slight severity. For moderate severity the MID was set to 1.33 (95% CI 1.10-1.57) and for severe/very severe to 3.59 (95% CI 3.08-4.09). There was no difference in MIDs between different types of incontinence.

INTERPRETATION OF RESULTS
The results showed that women with a larger reduction in symptom score experienced a greater impression of improvement. For women who seek to self-manage urinary incontinence via eHealth, a reduction of 1.46 points on the ICIQ-UI SF score would be the minimum important difference. For the group with slight incontinence, a MID could not be determined despite the large sample size. For the group with moderate incontinence, 1.33 points was a clinically relevant reduction and for the group with severe incontinence 3.59 points was clinically relevant. We found no differences in MID between the different types of urinary incontinence, but this finding should be interpreted with caution.

CONCLUDING MESSAGE
The MID for self-management of urinary incontinence via a freely available mobile app was lower than for other types of conservative management. Differences in baseline severity should be taken into account when using a MID to interpret clinical trial results.

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LONG-TERM RESULTS OF APP-BASED SELF-MANAGEMENT OF URGENCY AND MIXED URINARY INCONTINENCE IN WOMEN

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HYPOTHESIS / AIMS OF STUDY

Urgency (UUI) and mixed (MUI) urinary incontinence are common conditions affecting up to a quarter of all women, often with a significant impact on quality of life. UUI is defined as urinary leakage upon a sense of urgency, and MUI is defined as a combination of urgency and stress-related urinary leakages.

The behavioral interventions recommended as first-line treatments for UUI and MUI include pelvic floor muscle training (PFMT) and lifestyle changes. In addition, bladder training, or scheduled voiding, is recommended in some cases. Pharmacological therapy is widely prescribed, but treatment satisfaction is lower than with behavioral interventions, and discontinuation is common – partly due to unwanted side-effects.

In the last years, telehealth interventions such as mobile apps have been shown to have potential as aids for long-term self-management in various chronical conditions, and an additional boost for telehealth has been predicted subsequent to the Covid-19 pandemic. Recent reviews have examined the effect and implementation of apps and other telehealth interventions in several urological conditions, including urinary incontinence, and found that they are an effective treatment alternative that can be implemented successfully. However, studies of the long-term result of behavioral interventions in general, and telehealth interventions in particular, targeting urinary incontinence are scarce.

A recent RCT showed that a new app was effective for self-management of UUI and MUI in women. After 15 weeks of treatment, women who received the app had a clinically relevant improvement in all outcomes, including incontinence symptoms and quality of life (1). However, there is a knowledge gap regarding the long-term effect of treatment specifically for UUI and MUI, both regarding app-based interventions and other interventions. Therefore, the aim of this study was to evaluate the long-term effect of the app for treatment of UUI and MUI in women.

STUDY DESIGN, MATERIALS AND METHODS

This was a long-term follow-up of a randomized controlled trial (RCT), including 123 women ≥18 years old with UUI or MUI, without red-flag symptoms, and ≥2 leakages per week. The original RCT was well powered and registered on ClinicalTrials.org and monitored on-site by an independent monitor (1).

All participants, regardless of their original allocation to intervention or control, had received the intervention, a treatment app, at the long-term follow-up. Long-term data was collected through web-based questionnaires 15 months after participants received the intervention.

The app was developed based on scientific evidence and clinical experience. It included pelvic floor muscle training, bladder training, psychoeducation, lifestyle advice, an exercise log, reminders, reinforcement messages, and tailored advice. The primary outcome was change in incontinence symptoms (International Consultation on Incontinence Questionnaire (ICIQ) – Urinary Incontinence Short Form (ICIQ-UI SF)), from baseline to follow-up. Other outcomes were urgency symptoms (ICIQ – Overactive Bladder Module (ICIQ-OAB)), quality of life (ICIQ – Lower Urinary Tract Symptoms Quality of Life Module (ICIQ-LUTSqol)), and improvement (Patient's Global Impression of Improvement (PGI-I)). The Incontinence Catastrophizing (IC) Scale (0-21 points) was used to assess the participant's tendency to catastrophize over their incontinence. It was adapted from the validated Pain Catastrophizing Scale (short version) and contains 7 items covering fear of leakage and urgency.

A paired t-test was used to estimate the change in mean score for continuous variables. Comparisons were made between baseline and long-term follow-up, and between short-term and long-term follow-up.

The software IBM SPSS version 25 was used for all analyses.

RESULTS

Of the 123 women, 102 (83%) completed the long-term follow-up. The ICIQ-UI SF mean score improved from 11.5 to 7.6 (mean difference 4.0, 95% CI 3.2-4.7). The ICIQ-OAB improved from 6.7 to 5.5 (mean difference 1.3, 95% CI 0.9-1.6), the ICIQ-LUTSqol improved from 38.0 to 30.9 (mean difference 7.1, 95% CI 5.7-8.5) and the IC score improved from 4.8 to 2.5 (mean difference 2.2, 95% CI 1.6 to 2.8). The difference between baseline and the long-term follow-up score was statistically significant for all outcomes (Table 1). There were no significant differences in any of the scores between the short-term and long-term follow-up (Figure 1).

According to the PGI-I, improvement in incontinence symptoms from baseline to the long-term follow-up was reported by 73% (74/102) of the women.

INTERPRETATION OF RESULTS

This is the first study of the long-term results of using a complex app for self-management of UUI and MUI specifically. The results show that treatment with the app resulted in significant and clinically relevant long-term improvement of UUI and MUI regarding all parameters measured: incontinence symptoms (ICIQ-UI SF), urgency (ICIQ-OAB), quality of life (ICIQ-LUTSqol), and catastrophizing (IC-Scale). Furthermore, the improvement at the short-term follow-up was sustained at the long-term follow-up for all outcomes. The full results of this study were reported in a paper published in March 2022 (2).

Our study participants had a mean ICIQ-UI SF score improvement of -4.0 points at the long-term follow-up. This improvement is of similar, or slightly larger, magnitude compared with other long-term studies. A recent long-term study found a mean improvement in the ICIQ-UI SF score of -2.17 for app-based treatment of UUI, MUI or stress urinary incontinence, compared with -3.43 for care-as-usual (3).

One limitation of this long-term follow-up study is the lack of a control group. The original control group from the RCT received the intervention after the initial follow-up and was analyzed together with the original intervention group.

CONCLUDING MESSAGE

This study showed that self-management with the app was effective for long-term reduction of urinary leakage and urgency symptoms, and improved incontinence-related quality of life, for women with UUI and MUI. An app providing an extensive intervention for these conditions might be a valuable addition to other first-line treatments, both over the short and long term.

FIGURE 1

Outcome	n	Mean value		Mean change	
		Baseline	Long-term follow-up	Mean (95% CI)	p-value[a]
Incontinence symptoms (ICIQ-UI SF)	101	11.5	7.6	4.0 (3.2 to 4.7)	<0.001
Urgency symptoms (ICIQ-OAB)	100	6.7	5.5	1.3 (0.9 to 1.6)	<0.001
Quality of life (ICIQ-LUTSqol)	100	38.0	30.9	7.1 (5.7 to 8.5)	<0.001
Incontinence catastrophizing (IC Scale)	99	4.8	2.5	2.2 (1.6 to 2.8)	<0.001

Table 1. Continuous outcomes at baseline and at the long-term follow-up. aAnalyzed using a paired t test.

FIGURE 2

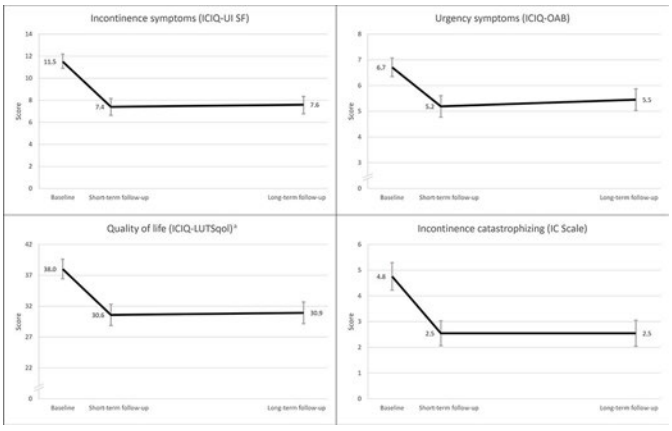

Figure 1. Overview of the change over time for the symptom mean scores. The error bars represent 95% CI. aPlease note that the lowest possible score for the ICIQ-LUTSqol is 19.

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BEST IN CATEGORY PRIZE: PREVENTION AND PUBLIC HEALTH

ZOOM TO SCALE? REAL WORLD IMPLEMENTATION OF ONLINE VERSUS IN-PERSON COMMUNITY-BASED CONTINENCE PROMOTION

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HYPOTHESIS / AIMS OF STUDY

(1) To characterize the impact of a small-group behavior change intervention implemented in communities on women's urinary and anal incontinence symptoms

(2) To compare intervention impact and evaluation data when implemented in person versus virtually

STUDY DESIGN, MATERIALS AND METHODS

Mind Over Matter: Healthy Bowels, Healthy Bladder (Mind Over Matter) is a small-group behavior change intervention for women aged 50 or older who want to prevent or improve urinary incontinence (UI) or anal incontinence (AI). Facilitated by a trained community member, the in-person program consists of three two-hour sessions delivered over one month, and in a 2017 RCT, participants achieved a 9-fold improvement in bladder symptoms and a 4-fold improvement in bowel symptoms compared to controls [1]. Statewide dissemination of Mind Over Matter began in 2019; in response to the COVID-19 pandemic, Mind Over Matter was transitioned to online delivery using Zoom in May 2020.

Voluntary questionnaires are completed by Mind Over Matter participants just prior to and following the program. Participants are asked about demographics, bladder and bowel symptoms, and related behaviors (pad use, pelvic floor muscle exercise frequency, care seeking). The International Consultation for Incontinence Questionnaire – Urinary Incontinence (ICIQ-UI) and St. Mark's (Vaizey) Incontinence Score (SMIS) assess symptoms [2, 3]; following completion, an evaluation survey and patient global ratings of satisfaction (PSQ), global perception of improvement (GPI), and estimated percent improvement (EPI) assess the program.

For this study, descriptive analyses characterized and compared participants in Mind Over Matter when implemented in-person versus virtually. Related samples were analyzed using paired t-tests, Wilcoxon signed rank tests, and McNemar's test; independent samples were analyzed using student's t-tests, Mann-Whitney U tests, and Chi-square tests. A p-value less than 0.05 was considered statistically significant.

RESULTS

Between April 2019 and December 2021, 85 workshops were held statewide (56 in-person, 29 online), reaching 708 women (481 in-person, 227 online). Table 1 describes the sample and compares in-person and online participants. Mean age of participants was (74.2 ± 8.5); the majority identified as non-Hispanic white, had education beyond high school, were insured by Medicare, and perceived themselves to be in good health. Participants in the online program were significantly younger than those who participated in-person (72.9 ± 8.3 vs. 74.6 ± 8.5 years, $p = .031$). Participants in the online program were more likely to live alone (66% vs. 54%, $p = .011$), have a bachelor's or graduate degree (53% vs. 44%, $p = .006$), and have access to someone to help around the house when needed (93% vs. 85%, $p = .007$). There were no significant differences between in-person and online participants as regards race, ethnicity, marital status, urban vs. rural dwelling, health insurance type, and general health status.

Table 2 describes changes from baseline to post-program symptoms and behaviors among in-person and online program participants. Urinary incontinence severity improved by one point on the ICIQ-UI for participants in both online and in-person programs. The proportion of women with mixed UI decreased from baseline to post-program among the sample overall and among in-person participants but not among online participants. There was a statistically significant improvement in AI severity by SMIS among online but not in-person participants. The amount of money spent per month on incontinence products decreased significantly from $5 to $2 among participants in both programs but there were not significant changes in types of products used. The proportion of participants who did pelvic floor muscle exercises routinely (often or always) was significantly higher at program completion than baseline among both groups of participants (16% → 77% in-person; 13% → 82% online, $p < .001$ for both). Plans to seek care did not differ between baseline and program completion for any group.

Regarding program evaluation, most participants heard about the program from a newsletter or friend / family member (Table 2). Those in the in-person program were significantly more likely to have heard about the program from a healthcare provider. The reasons cited for program participation did not differ between online and in-person participants; the most common reasons were to prevent or improve symptoms or because of liking the self-management approach.

Online participants were more likely than in-person participants to attend all three Mind Over Matter sessions ($p = .001$). The vast majority of participants in both online and in-person programs agreed that they felt comfortable in the program, thought the program was well-organized, and would recommend the program to others. Online participants were significantly more likely to agree that their voice was welcomed and less likely to agree that they learned from others through program participation. Online participants were significantly less likely than in-person ones (55 vs. 63%, $p = .031$) to feel completely satisfied with the program. Global perception of improvement (>85%) and estimated percent improvement (59%) did not differ between online and in-person participants.

INTERPRETATION OF RESULTS

A small-group behavior change program proven to improve incontinence in older women when administered in-person was successfully implemented virtually during the COVID-19 pandemic. The online program was more likely to reach those who live alone and have access to help around the house when they need it, and less likely to reach older women and those with a high school education or less, suggesting a role for both in-person and online programs to optimize program reach. Both in-person and online program participants saw improvements in both UI and AI symptoms following program completion, and the significantly increased rate of routine pelvic floor muscle exercise performance was similar to that seen in the RCT of the Mind Over Matter program, providing evidence of its impact when implemented in communities outside the research context. Of note, the significant decrease in money spent on incontinence products among in-person and online community program participants was not seen in the 2017 Mind Over Matter RCT participants, suggesting that real-world program implementation of Mind Over Matter may have even higher impact.

CONCLUDING MESSAGE

Mind Over Matter, a small-group behavior change program to improve UI and AI in older women, maintains similar impact when delivered online versus in-person. Participation is motivated by the desire to prevent or improve symptoms and the program's focus on self-management rather than recommendations from healthcare providers. Satisfaction with the program remains high, with the majority of participants reporting symptom improvement following participation. Both online and in-person versions of this program should be maintained beyond the pandemic given their differing reach.

FIGURE 1

Characteristic	All (N=708)	In-person (N=481)	Online (N=227)	P-value
Age (y) mean ± SD	74.2 ± 8.5	74.6 ± 8.5	72.9 ± 8.3	**.031**
Race or ethnicity				
White	585/589 (99)	432/435 (99)	153/154 (99)	.958
African American/Black	2/589 (0)	1/435 (1)	1/154 (1)	.442
American Indian/Alaskan Native	3/589 (1)	1/435 (0)	2/154 (1)	.109
Native Hawaiian/Pacific Islander	1/589 (0)	1/435 (0)	0/154 (0)	.552
Other	2/589 (0)	2/435 (1)	0/154 (0)	.399
Hispanic / Latinx / Spanish	5/587 (1)	3/430 (1)	2/157 (1)	.603
Marital status				.473
Married or partnered	291/579 (50)	212/439 (48)	79/140 (56)	
Widowed	173/579 (30)	138/439 (31)	35/140 (25)	
Single	27/579 (5)	21/439 (5)	6/140 (4)	
Divorced or separated	80/579 (14)	61/439 (14)	19/140 (14)	
Other	8/579 (1)	7/439 (2)	1/140 (1)	
Lives alone	326/572 (57)	226/420 (54)	100/152 (66)	**.011**
Education				**.006**
High school or less	128/601 (21)	109/447 (24)	19/154 (12)	
Technical or Associate's degree	197/601 (33)	143/447 (32)	54/154 (35)	
Bachelor's or graduate degree	276/601 (46)	195/447 (44)	81/154 (53)	
Residence type				.583
Rural	103/604 (17)	80/446 (18)	23/158 (15)	
Small town/Village	157/604 (26)	113/446 (25)	44/158 (28)	
City/Suburb of a city	344/604 (57)	253/446 (57)	91/158 (58)	
Considers overall health excellent/very good	322/565 (57)	236/411 (57)	86/154 (56)	.736
Has someone to help around the home	509/586 (87)	361/427 (85)	148/159 (93)	**.007**
Health insurance				
Medicare	495/592 (84)	366/436 (84)	129/156 (83)	.717
Medicaid	27/529 (5)	20/383 (2)	0/146 (0)	.251

Table 1. Description of Mind Over Matter: Healthy Bowels, Healthy Bladder participants, 2019-2021

FIGURE 2

Variable	Overall (N=708)			In-person (N=481)			Online (N=227)		
	Baseline	Completion	P-value	Baseline	Completion	P-value	Baseline	Completion	P-value
Incontinence Symptoms									
UI Severity (ICIQ-UI) - mean ± SD	7.3 ± 4.6	6.3 ± 4.2	**<.001**	7.4 ± 4.6	6.5 ± 4.3	**<.001**	6.8 ± 4.6	5.8 ± 3.8	**.012**
Stress UI	117/556 (21)	61/327 (19)	.890	84/406 (21)	56/301 (19)	.775	33/150 (22)	5/28 (19)	.999
Urgency UI	191/556 (34)	116/327 (36)	.268	137/406 (34)	103/301 (34)	.511	54/150 (36)	13/26 (50)	.289
Mixed UI	176/556 (32)	88/327 (27)	**.023**	133/406 (33)	81/301 (27)	**.045**	43/150 (29)	7/26 (27)	.453
AI severity (SMIS) - mean ± SD	6.1 ± 5.1	5.7 ± 4.5	.339	6.2 ± 5.2	6.0 ± 4.5	.868	5.7 ± 4.9	5.0 ± 4.6	**.045**
Absorbent incontinence product use									
Number used / 24 hours (median, IQR)	1 (0-2)	1 (0-2)	**.047**	1 (0-2)	1 (0-2)	.177	1 (0-2)	1 (0-1)	.096
Type: Pads (thin liners)	198/372 (53)	154/270 (57)	.999	137/272 (50)	104/193 (54)	.824	61/100 (61)	50/77 (65)	.581
Pads (regular thickness)	182/372 (49)	116/270 (43)	.296	143/272 (53)	88/193 (46)	.152	39/100 (39)	28/77 (36)	.999
Pull-on pads or all-in-ones (adult briefs)	35/372 (9)	26/270 (10)	.999	21/272 (8)	18/193 (9)	.999	14/100 (14)	8/77 (10)	.999
Dollars spent per month (median, IQR)	5 (0-12)	2 (1-2)	**<.001**	5 (0-12)	2 (1-2)	**<.001**	5 (0-15)	2 (1-2)	**<.001**
Behaviors to improve symptoms									
Routine pelvic floor muscle exercises	83/553 (15)	324/413 (79)	**<.001**	64/402 (16)	226/294 (77)	**<.001**	19/151 (13)	98/119 (82)	**<.001**
Plans to seek care	257/524 (49)	208/398 (52)	.630	193/382 (51)	144/281 (51)	.888	64/142 (45)	64/117 (55)	.648

Evaluation data	Overall	In-person	Online	p-value
Total sessions attended (median, IQR)	3 (2-3)	3 (2-3)	3 (3-3)	**.001**
Heard of program via … newsletter	128/303 (42)	69/171 (40)	59/132 (45)	.448
Friend/family	49/303 (16)	23/171 (14)	26/132 (20)	.143
Poster/Brochure	37/303 (12)	19/171 (11)	18/132 (14)	.506
Healthcare provider recommendation	11/303 (4)	10/171 (6)	1/132 (1)	**.019**
Strongest reason for taking program				
To prevent symptoms	174/324 (54)	94/176 (53)	80/148 (54)	.908
Frustrated with current symptoms	101/324 (31)	58/176 (33)	43/148 (29)	.450
Healthcare provider recommended	3/324 (1)	3/176 (2)	0/148 (0)	.111
Liked group approach	25/324 (8)	11/176 (6)	14/148 (10)	.281
Liked self-management approach	82/324 (25)	41/176 (23)	41/148 (28)	.363
Highly recommended by past participant	4/324 (1)	4/176 (2)	0/148 (0)	.065
Agree/strongly agree with statement:				
I felt comfortable	421/432 (98)	319/329 (97)	102/103 (99)	.245
Program was well-organized	431/442 (98)	318/328 (97)	113/114 (99)	.200
I felt my voice was welcomed	428/442 (97)	315/329 (96)	113/113 (100)	**.026**
I learned from others	389/440 (88)	295/326 (91)	94/114 (83)	**.021**
I would recommend this program	428/438 (98)	317/327 (97)	111/111 (100)	.062
Satisfied with program: Not at all	2/445 (0)	0/325 (0)	2/120 (2)	**.031**
Somewhat	174/445 (39)	122/325 (38)	52/120 (43)	
Completely	269/445 (60)	203/325 (63)	66/120 (55)	
Global perception: better or much better	389/441 (88)	288/323 (89)	101/118 (86)	.303
Estimated percent better – mean ± SD	59.2 ± 25.4	59.5 ± 25.6	58.5 ± 25.0	.732

Abbreviation key - IQR: interquartile range; UI: urinary incontinence; ICIQ-UI: International Consultation for Incontinence Questionnaire – Urinary Incontinence; SD: standard deviation; AI: anal incontinence; SMIS: St. Marks Incontinence Score.

Table 2. Impact of Mind Over Matter: Healthy Bowels, Healthy Bladder when implemented in-person versus online

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Funding None **Clinical Trial** No **Subjects** Human **Ethics not Req'd** This study did not require ethics committee approval because it is a program evaluation. **Helsinki** Yes **Informed Consent** No

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BEST IN CATEGORY PRIZE: QUALITY OF LIFE / PATIENT AND CAREGIVER EXPERIENCES

EXPLORING GYNECOLOGIC CANCER SURVIVORSHIP NEEDS, BARRIERS AND FACILITATORS TO VIRTUAL PELVIC HEALTH PHYSIOTHERAPY INTERVENTIONS: PHASE 1 RESULTS OF A PATIENT-ORIENTED MULTI-METHODS STUDY.

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HYPOTHESIS / AIMS OF STUDY

Vaginal pain during intercourse and urinary incontinence are common urogenital dysfunctions in women who have been treated for gynecologic cancer. With survival rates on the rise, there is a growing population of women impacted by these dysfunctions, which are known to affect their daily activities, sexual function and overall quality of life. Pelvic health physiotherapy interventions aim at reducing dysfunction in survivors of gynecologic cancers through education on the use of vaginal moisturizers, dilation therapy program and pelvic floor muscle exercises. Recent evidence suggest that pelvic health physiotherapy interventions can reduce dyspareunia and urinary incontinence in women who have been treated for gynecologic cancer.[1, 2] Given that time, travel and costs are obstacles to accessing pelvic health physiotherapy services, virtual pelvic health interventions presents a potential solution to mitigate accessibility issues. However, survivors' needs, barriers and facilitators towards virtual pelvic health interventions delivery remain unknown. Understanding the needs of survivors can inform the planning and delivery of virtual pelvic health education and exercise programming. With this mixed-method study, we aim to identify the needs, barriers, and facilitators of gynecologic cancer survivors towards virtual pelvic health physiotherapy interventions.

STUDY DESIGN, MATERIALS AND METHODS

Phase 1 of this patient-oriented mixed-methods study involves a cross-sectional online survey among adult who received at least one oncology treatment for a gynecologic cancer and who were able to read English. This study was approved by the local Health Research Ethics Board. The survey was designed to follow the Strategy for Patient-Oriented Research; patient-partners were recruited to be consulted and actively involved in decision-making throughout the various research activities of this study. The survey includes 50 multiple choice or open-ended questions spanning topics including health status, pelvic health knowledge, environmental factors and motivational factors. Formulation of questions were guided by evidence, clinical experience and input from patient-partners. The questions were informed by the Theoretical Domains Framework, a framework which stems from organizational behavior change theories and implementation science principles, and mapped to their related component of the Capability, Opportunity, Motivation - Behavior Change (COM-B) Model.[3] Participation was anonymous; invitations to participate in the survey were shared on social media platforms, patient support groups, lists of previous research participants, and through posters in medical offices. The survey is hosted on a secure, encrypted online platform (REDCap). Analysis: Responses to the survey provide quantitative data from categorical and ordinal scales, from which we derived descriptive statistics (frequency and percentages, mean and standard deviations) to summarize responses. An interpretive description thematic analysis method guided the qualitative analysis of the narrative content, where answers were first scanned and iterated for identification of possible themes, coded and further sorted into subcategories.

RESULTS

Phase 1 reports on the preliminary results from the English-respondents (n = 24) of this study. All 24 (100%) respondents identified their gender as woman; 15 (62.5%) were aged ≥55 years old; 18 (75.0%) were in a relationship; and 18 (75.0%) reported 2 or more previous pregnancies. They also reported having been treated for various types of gynecologic cancer: 12 respondents were diagnosed with uterine cancer (50.0%), 3 for cervical cancer (12.5%) and 9 for ovarian cancer (37.5%). Twenty-one respondents were treated with surgery (87.5%), 7 with radiation therapy (29.2%), 18 with chemotherapy (75.0%) and 6 with hormonal therapy (25.0%).

Only 5 (20.8%) of respondents felt confident in their ability to perform pelvic floor muscle properly, and 6 (25.0%) felt confident in their ability to perform dilation therapy adequately and safely. Knowledge on dilation therapy was low, with a mean score of 26.3(SD: 35.03) on a scale from 0 (Not at all) to 100 (Very Much). Fourteen (58.3%) respondents reported not discussing pelvic health with their healthcare provider at any point during cancer treatment, and only 2 (8.3%) sought out pelvic health information elsewhere on their own. A total of 9 (37.5%) respondents reported having refrained themselves from discussing pelvic health topics with their healthcare provider because of feeling embarrassed (n = 4), because of thoughts that pelvic health issues were not as important as being cancer free (n = 5), because of being unsure of who to discuss these topics with (n = 3), or because of lack of time and opportunity to bring the topic up (n = 5). Nineteen respondents believed it was difficult (n = 7; 29.2%) or somewhat difficult (n = 12; 50.0%) to access information on pelvic health interventions. They identified several barriers that hindered access to information on pelvic health interventions, as illustrated in Figure 1. The most identified barrier was "I don't know what exactly to look for" when accessing information (n = 13; 54.2%). Other reasons mentioned were the lack of resources in rural areas and the lack of opportunity during clinical telephone follow-ups in comparison to face-to-face visits.

All 24 (100%) respondents indicated that they believed that providing pelvic health physiotherapy interventions through an online format 'would' (n = 15; 62.5%) or 'maybe would' (n = 9; 37.5%) be helpful to an individual treated for gynecologic cancer. Qualitative analysis of narrative content revealed that respondents identified several facilitators to pelvic health interventions by the online format: 1) reducing the need to travel; 2) increasing access to services that are currently unavailable in rural and remote areas; 3) decreasing costs associated with in-person services (cost of private physiotherapy services, parking fees at the hospital, etc.); 4) reducing embarrassment ("removes some of the need for courage to bring it up"); and 5) facilitating access to care for those who are immune-compromised or too-sick to seek in-person care.

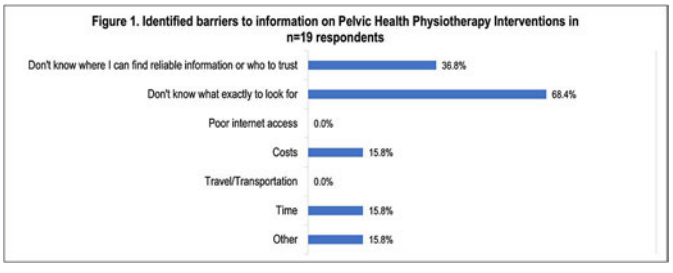
INTERPRETATION OF RESULTS

Preliminary results from this study highlighted that the English-speaking respondents reported little knowledge related to pelvic health interventions, recognized several barriers to accessing pelvic health care, including their lack of knowledge on what pelvic health is, and identified several facilitators from virtual delivery of pelvic health physiotherapy interventions. Reducing costs and travel were key facilitators identified by the respondents, as well as decreasing the time and travel burden for gynecologic cancer patients continuing active treatment.

CONCLUDING MESSAGE

By identify the needs and preferences of individuals treated for gynecologic cancer, the results from this work will provide a greater understanding of how best to delivery virtual pelvic health physiotherapy interventions as part of survivorship care. Findings have the potential to address a gap in access to pelvic health physiotherapy interventions and improve the health of survivors with gynecologic cancer.

FIGURE 1



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Funding Canadian Cancer Research Alliance **Clinical Trial** No **Subjects** Human **Ethics Committee** Health Research Ethics Board of Alberta – Cancer Committee (HREBA HREBA.CC-21-0498) **Helsinki** Yes **Informed Consent** Yes

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IS ONLINE GROUP-BASED PELVIC FLOOR MUSCLE TRAINING FEASIBLE FOR OLDER WOMEN WITH URINARY INCONTINENCE?

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HYPOTHESIS / AIMS OF STUDY
Urinary incontinence (UI) is one of the most prevalent health concerns among women aged 65 and over. The recommended first-line treatment for UI is individual pelvic floor muscle training (PFMT). [1] Yet, this treatment appears to be a resource-intensive approach that healthcare systems across the world are currently unable to meet. Recently, group-based PFMT was shown to be non-inferior to individual PFMT to treat UI in older women, despite using fewer resources. While group approaches thus appear promising, public health measures restricted group gatherings and interventions during the COVID-19 pandemic, which highlighted the importance of remote options. Therefore, this study aimed to assess the feasibility of online group PFMT for UI in older women.

STUDY DESIGN, MATERIALS AND METHODS
This mixed-methods clinical study investigated acceptability and feasibility from multiple stakeholders' perspectives, in addition to the short- and long-term clinical effects of online group PFMT on UI and UI-related symptoms. This abstract presents the study's feasibility component from the perspectives of the participants and the physiotherapist.

Population

We recruited community-dwelling women aged 65 and over, with symptoms of stress or mixed UI for three months or more, who reported at least three weekly episodes of urine leakage on a bladder diary. Stress/mixed UI was confirmed with the Questionnaire for Urinary Incontinence Diagnosis (QUID). [2] All participants were required to have internet access. Exclusion criteria included a body mass index (BMI) $\geq$ 35; significant pelvic organ prolapse (Baden-Walker score $>$ 2); physiotherapy treatment or surgery for UI or pelvic organ prolapse in the past year; any medication, co-morbidities or risk factors known to interfere with the effects of PFMT or with the pelvic floor muscle (PFM) evaluation.

Intervention

Pelvic floor physiotherapists established the eligibility of participants during an individual in-person initial evaluation session, where they also taught the participants how to contract their PFMs correctly through vaginal digital palpation.

Participants then took part in a 12-week online group-based PFMT program consisting of weekly one-hour training sessions from their home. A 13th optional session was offered at the end of the program as a catch-up session for any missed training. All participants received an exercise booklet, detailing the exercises and their progression, and a physical copy of the educational component of each session. An experienced pelvic floor physiotherapist delivered all sessions via Zoom to groups of seven to 11 women. Each session began with a one-to-three-minute individual meeting with the physiotherapist in a private breakout room to discuss weekly leakages and exercise adherence, while the rest of the group socialized in the 'main room' of the Zoom meeting. The session was then divided into a 10-15-minute educational component and a 30-45-minute PFM exercise component. The educational component covered various topics relevant to the aging pelvic floor as well as UI and pelvic health. The exercise component included four PFM exercises with a gradual increase in duration, difficulty, repetition and position (from lying down, to sitting, to standing). In addition to their attendance to the weekly sessions, participants were also expected to perform PFM exercises at home, for a total of five-days/week, during the intervention. Upon completion of the 12-week program, participants were asked to commit to a maintenance exercise regimen for six months.

Data collection

Data was collected before and throughout the 12-week intervention.

We collected baseline and demographic data before the intervention, including data on age, BMI, gynecological history and UI symptom severity with the ICIQ-UI SF and the Australian Pelvic Floor Questionnaire (APFQ). [3]

To assess the program's feasibility, we collected data on participant attendance to the online sessions, dropout rates and reasons for dropping out, program fidelity as delivered by the physiotherapist, participant adherence to weekly home exercises and any reported side effects throughout the 12-week intervention period.

Data analysis

We reported baseline and demographic data, attendance, dropout rates, program fidelity, participant adherence and side effects narratively and using descriptive statistics.

RESULTS
Description of the participants

From March 2021 to April 2022, a total of 34 older women were recruited to participate in the online group PFMT program and divided into four groups. Participants had a mean age of 70.1 (SD 4.2) years and a mean BMI of 25.3 (SD 4.0). Among them, mean parity was 1.4 (SD 1.2). Additionally, 44% used post-menopausal hormone therapy with a mean of 10 years of use. They had moderate UI symptoms before the intervention, with a median of 12 weekly leakages, and mean scores of 11.9/21 (SD 3.4) on the ICIQ-UI SF and 15.5 (SD 0.9) on the UI subscale of the APFQ [3]. The mean duration of UI symptoms was 12.9 (SD 15.5) years. Thirty-two (94.1%) had symptoms of mixed UI, and two (5.9%) of stress UI only.

Feasibility

Program attendance was excellent (91%) with an average of 12/12 (SD 1) attended sessions. Only one participant dropped out (3%) due to personal reasons. The program fidelity was overall good, with only minor adaptations noted to the program. The most important adaptation was an increase in the time allocated to the individual meeting period. This led to a 10- to 20-minute increase in the session's duration, depending on the number of women in the group. Additionally, the optional core and pelvis exercises were frequently skipped due to time constraints, while PFM exercises were prioritized. Lastly, the physiotherapist limited position changes during the sessions in order to avoid multiple camera angle adjustments by both the physiotherapist and women and to reduce time spent correcting participants' posture. The exercises performed during the weekly sessions were thus less varied and more like the home exercise program. Home PFM exercises were performed four to five times/week by 94% of the participants during the 12-week intervention period. No side effects were reported, apart from muscle soreness during the first weeks of training for one participant.

INTERPRETATION OF RESULTS
The high attendance compares favourably with previously reported attendance for in-person trials, showing good engagement from the older women in online treatment. Attrition was low, which is also in line with previous in-person interventions, showing no reduction in commitment to remote trainings. Fidelity was good and the physiotherapist was able to follow most of the program's steps, although the variety of exercise types and positions were reduced due to time constraints. The observed adaptations reflected the clinical judgement of the leading physiotherapist, who selected the most relevant exercises for PFM strengthening, considering the participants' levels and available time. Adverse events were minor and uncommon, also echoing previous findings from in-person interventions and supporting the safety of this program.

CONCLUDING MESSAGE
Online group PFMT appears to be a feasible option for older women. Further findings regarding the acceptability and clinical effects of online group PFMT on UI and UI-related symptoms are being collected and will soon be analyzed. Yet, these results are encouraging and constitute the first step into the study of online group PFMT in older women. Ensuring an online option would allow older women to receive safe UI treatment during pandemic periods and beyond.

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Funding This work was supported by the Advisory Committee for Clinical Research (CAREC) of the Research Centre of the Institut universitaire de gériatrie de Montréal (CRIUGM), and by Quebec Network for Research on Aging (RQRV) grant for pilot projects **Clinical Trial** Yes **Registration Number** ClinicalTrials.gov Identifier: NCT05182632, accessible from https://clinicaltrials.gov/ct2/show/record/NCT05182632 **RCT** No **Subjects** Human **Ethics Committee** Comité d'éthique de la recherche - vieillissement et neuroimagerie (CÉR VN) **Helsinki** Yes **Informed Consent** Yes

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SESSION 17 - NOCTURIA

Abstracts 238-249
09:35 - 11:05, Hall G
Chair: Prof Philip Edward Van Kerrebroeck (Belgium)

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EFFICACY AND SAFETY OF MIXTURE OF NOBILETIN AND TANGERETIN IN PATIENTS WITH NOCTURIA (NOT-NOCTURIA STUDY): A RANDOMIZED, PLACEBO-CONTROLLED, DOUBLE-BLIND, CROSSOVER STUDY

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HYPOTHESIS / AIMS OF STUDY

Nocturia is a very inconvinient lower urinary tract symptom. Nocturia is hard to cure clinically because the cause is multifactorial and is associated with disturbance of day–night differences in urine production and bladder capacity [1]. The objective of our study was to evaluate the efficacy of a mixture of nobiletin and tangeretin (NoT) in the treatment of nocturia and to confirm the safety of NoT in older adults. NoT are flavonoids, which are a class of polyphenol derived from the peel of Citrus depressa, a type of lemon that is native to Okinawa in Japan and is also found in Taiwan. There is emerging evidence that NoT modulate the circadian rhythm [2]. Therfore, we conducted a randomized clinical trial to investigate the efficacy of NoT in treating nocturia.

STUDY DESIGN, MATERIALS AND METHODS

This randomized, placebo-controlled, double-blind, two-sequence two-period crossover study included 40 patients with nocturia (Figure 1). Both men and women aged ≥50 years with nocturia were recruited, and each patient was confirmed to have a nighttime frequency ≥2 voids on a frequency volume chart (FVC). Included patients had an Eastern Cooperative Oncology Group performance status of 0-2 and were required to undergo regular checkups at our hospital. Patients were excluded if they had (1) global polyuria ≥40 ml/kg/24h, (2) postvoid residual ≥200 ml, (3) severe benign prostatic hyperplasia, overactive bladder, neurogenic bladder, or conditions considered unsuitable for inclusion in this study. Patients were allocated to AP (sequence 1, S1) or PA (sequence 2, S2) in a double-blind manner with stratified block randomization (A = active, NoT, P = placebo). Patients allocated to S1 group were orally administered a mixture of 50 mg of NoT (including 30 mg nobiletin + 15 mg tangeretin) once daily after dinner for 6 weeks. After a washout period of more than 2 weeks, the placebo was orally administered once daily after dinner for 6 weeks. The order of the NoT mixture and the placebo were reversed for the S2 group.

The primary endpoint was the change in nocturnal functional bladder capacity measured by the FVC. Secondary endpoints included: (1) change in the International Prostate Symptom Score (IPSS), (2) sleep quality measured with the Pittsburgh Sleep Quality Index (PSQI), (3) changes in items on the FVC (nighttime frequency, 24-hour urine volume, nocturnal polyuria index).

Data were presented as the mean ± standard deviation and statistical significance was determined by a paired t-test. Assuming a difference in mean bladder capacity change between the two groups of 20 and a standard deviation of 20, 16 patients were required for each group, based on a power of 80% to detect a significant difference at a two-sided level of 5%. A total of 40 patients were planned to be recruited to allow for dropouts.

RESULTS

A total of 40 patients (27 men and 13 women) with a mean age of 73.5 years were randomized (Table 1A) and 36 patients were completed the trial while 4 patients withdrew. The reasons for withdrawal were admission into a diabetes mellitus (DM) educational program, urinary tract infection, cancer of unknown primary, and poor drug compliance. No adverse events directly related to this study were observed.

The primary endpoint measure, mean changes in nocturnal bladder capacity were 6.2 ± 38.6 ml on NoT and 0.5 ± 47.9 ml on the placebo (difference: 5.7 ml, P = 0.61, not significant) (Table 1B). The secondary endpoints for FVC variables revealed that the mean change in nighttime frequency on NoT significantly decreased compared with that on placebo. The mean changes were −0.49 ± 0.86 times on NoT and 0.01 ± 0.82 times on placebo (difference: −0.50 times, P = 0.040). Other secondary endpoints did not differ significantly between NoT and placebo. The changes in the nocturnal polyuria index were −2.8 ± 8.1% on NoT and −0.2 ± 11.6% on the placebo (difference: −2.6%, P = 0.30, not significant). However, the change in the nocturnal polyuria index from baseline to the end of NoT administration significantly decreased from 42.7% to 39.9% (before–after difference: −2.8%, P = 0.048).

INTERPRETATION OF RESULTS

In patients with nocturia, NoT did not result in a significant change in the nocturnal bladder capacity compared with placebo. In contrast, NoT resulted in a significant decrease in the nighttime frequency. NoT appeared to influence the nighttime frequency by decreasing the nocturnal polyuria index. Further research is needed to elucidate the mechanism of action.

To our knowledge, this is the first study to show that NoT are effective for older adults (mean age 73.5 years) with nocturia. In addition, the present study is the first randomized, placebo-controlled, double-blind trial of NoT for nocturia patients as far as we know. Although the sample size was small, we believe that this randomized design provides a high level of evidence.

CONCLUDING MESSAGE

The present study demonstrated that NoT were well tolerated and resulted in a mild but significant improvement in the nighttime frequency of older adults with nocturia. The results suggest that NoT warrant further investigation in larger trials over longer periods of time.

FIGURE 1

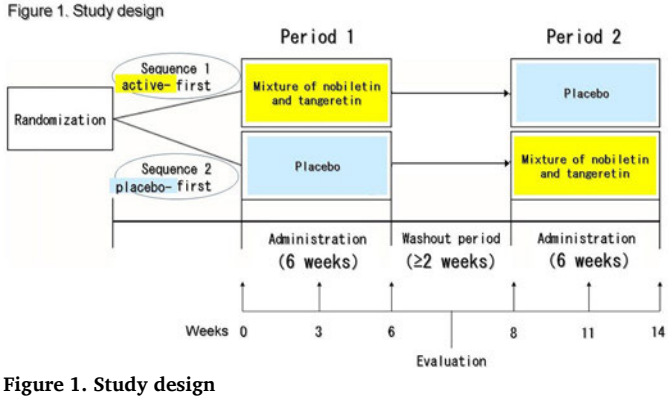

Figure 1. Study design

FIGURE 2

Table 1A. Baseline characteristics

	Sequence 1, active-first n=20	Sequence 2, placebo-first n=20	Overall cohort n=40
Age (years)	73.8±4.0	73.2±6.7	73.5±5.5
Sex	13 men, 7 women	14 men, 6 women	27 men, 13 women
Body mass index (kg/m^2)	23.4±3.7	24.0±3.6	23.7±3.6
Systolic blood pressure (mmHg)	133.4±19.1	134.9±16.6	134.2±17.9
Heart rate (beats/min)	74.9±12.1	74.9±12.0	74.9±12.0
Questionnaire scores			
IPSS-total	13.3±6.8	10.1±5.2	11.7±6.3
IPSS-Q7	3.05±0.59	2.55±1.07	2.80±0.90
IPSS-QOL	4.5±1.1	4.0±1.2	4.2±1.1
PSQI	8.6±2.9	8.8±4.5	8.7±3.8
Frequency volume chart variables			
Nocturnal bladder capacity (ml)	192.5±66.1	205.5±64.4	199.0±65.6
Nighttime frequency	2.85±0.72	2.72±1.06	2.78±0.91
24-hour urine volume (ml)	1483±341	1647±348	1565±354
Nocturnal polyuria index (%)	43.9±15.2	41.0±12.4	42.5±13.9
Hours of undisturbed sleep (h)	2.31±0.71	2.40±0.70	2.35±0.71
Laboratory data			
Post-void residual (ml)	19.8±25.5	27.5±31.2	23.6±28.8
BNP (pg/ml)	40.5±33.9	35.6±33.5	38.1±33.8
Daily salt intake (g/day)	8.79±2.38	8.77±2.99	8.78±2.70

Abbreviations: IPSS, International Prostatic Symptom Score; PSQI, Pittsburgh Sleep Quality Index; BNP, brain natriuretic peptide.

Table 1B. Efficacy measures

	Change from baseline NoT n=36	Placebo n=36	Difference	P value
Questionnaire scores				
IPSS-total	-0.64±3.20	-0.68±2.99	0.04	0.88
IPSS-Q7	-0.22±0.75	-0.21±0.80	-0.01	0.89
IPSS-QOL	-0.19±0.99	-0.06±1.11	-0.13	0.49
PSQI	-0.5±1.9	-0.2±2.0	-0.30	0.4
Frequency volume chart variables				
Nocturnal bladder capacity (ml)	6.2±38.6	0.5±47.9	5.7	0.61
Nighttime frequency	-0.49±0.86	0.01±0.82	-0.50	0.040
24-hour urine volume (ml)	-14±262	7±297	-21	.0.69
Nocturnal polyuria index (%)	-2.8±8.1	-0.2±11.6	-2.6	0.30
Hours of undisturbed sleep (h)	0.21±0.99	0.04±0.87	0.17	0.52

Abbreviations: NoT, nobiletin and tangeretin; IPSS, International Prostatic Symptom Score; PSQI, Pittsburgh Sleep Quality Index.

Table 1A. Baseline characteristics, Table 1B. Efficacy measures

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DIETARY SALT WITH NITRIC OXIDE DEFICIENCY INDUCES NOCTURNAL POLYURIA VIA ACTIVATED INTRARENAL OXIDATIVE STRESS-SPAK-NCC PATHWAY: AMELIORATION BY A NOVEL ANTIOXIDANT, SI-BASED AGENT

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HYPOTHESIS / AIMS OF STUDY

Nocturnal polyuria is a condition that significantly impairs quality of life and increased mortality. Its pathogenesis is not well understood and existing therapies have limited efficacy. We have reported a nocturnal polyuria mouse model to combine nitric oxide (NO) deficiency and salt loading, in which overactivation of the intrarenal SPAK(STE20/SPS1-related proline–alaninerich protein kinase)–NCC(sodium chloride co-transporter) pathway in the distal renal tubule suppresses sodium excretion during the day and causes nocturnal polyuria. We focused on the fact that the SPAK-NCC pathway is, in part, regulated by oxidative stress1, and we hypothesized that oxidative stress may cause nocturnal polyuria. We have recently developed a novel hydrogen-producing Si-based agent, which is orally ingestible and features sustained hydrogen generation by reacting with water in the intestine. Hydrogen is well known for its antioxidant properties and the efficacy of silicon-based agents has been reported in rat remnant kidney models, rat ischemia-reperfusion injury model and rat varicocele model2, all of which showed a reduction in oxidative stress. In this study, we aimed to show the effect of oxidative stress on nocturnal polyuria and to evaluate the efficacy of a novel antioxidant, Si-based agents, on nocturnal polyuria

STUDY DESIGN, MATERIALS AND METHODS

19-week-old C57BL6/J male mice were fed L-NAME (NO synthase inhibitor) and a 1% high-salt diet for 2 weeks to create a nocturnal polyuria model. Oxidative stress in kidney was assessed by immunohistochemical staining for 4-hydroxynonenal (4-HNE) and real-time PCR of NADPH oxidase subunit, which regulates the production of ROS. Si-based agent was used as antioxidant stress agents: The Si-based agent we co-developed is orally ingestible and features sustained hydrogen generation to inhibit oxidative stress production. Urine volume was measured by the aVSOP method3 after two weeks of treatment with the silicone-containing diet or silicone-free diet. Briefly, a roll of laminated filter paper, pretreated to turn urine dark purple, was rolled up under a water-repellent wire grid at a speed of 10 cm per h. Mice were housed for 4 days in cages with dimensions of 110 mm × 160 mm × 75 mm (H × D × W). Urination was counted, tracked, and converted to volume using software The diurnal polyuria index (inactive urine volume /daily urine volume) was calculated for the index corresponding to nocturnal polyuria in humans. Intrarenal NCC activation was assessed by phosphorylation of NCC using Western blotting.

RESULTS

First, renal oxidative stress was significantly increased in nocturnal polyuria mice compared to control mice (7.7 ± 1.4 vs 11.6 ± 2.1, $p < 0.05$). Treatment with the silicon component significantly reduced oxidative stress in nocturnal polyuria mice group (11.6 ± 2.1 vs 4.4 ± 1.1, $p < 0.01$). The mRNA expression of the subunit of NADPH oxidase, which regulates one of the pathways controlling the production of oxidative stress, was significantly up-regulated in the nocturnal polyuria mice group compared to the control mice group.

Second, treatment of the control mice with the Si-based agent did not significantly change DPi (0.12 vs 0.07, n.s.) or the daily urine volume (2220 μl vs 1991 μl, n.s.). On the other hand, administration of Si-based agent to the nocturnal polyuria mice group decreased the DPi (0.28 vs 0.17, $p < 0.01$) and did not change the daily urine volume (2489 μl vs 2607 μl).

Finally, treatment of the nocturnal polyuria mice with silicone component decreased phosphorylated NCC (0.99 vs 0.77, $p < 0.05$).

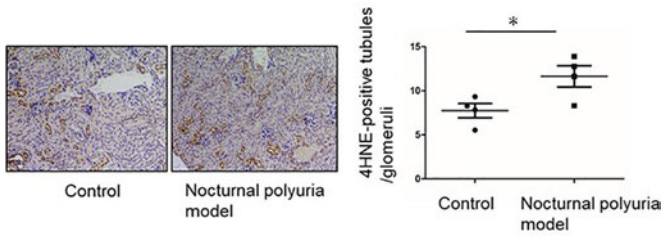
INTERPRETATION OF RESULTS

4-HNE-positive cells in the distal renal tubules and subunit of NADPH oxidase were significantly increased in nocturnal polyuria group compared with control ($P < 0.05$), indicating the association between oxidative stress and nocturnal polyuria. Si-based agent decreased oxidative stresse and inhibited phosphorylation of NCC, finally improving nocturnal polyuria.

CONCLUDING MESSAGE

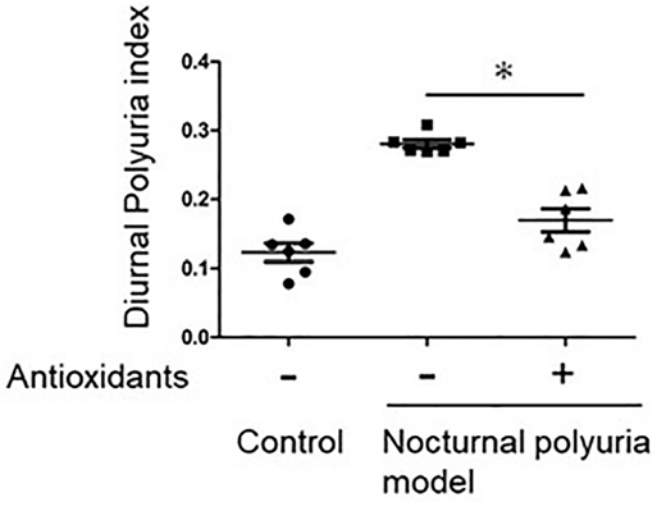
Oxidative stress causes nocturnal polyuria via intrarenal SPAK-NCC pathway .A newly co-developed antioxidant, Si-based agent, is a promising treatment for nocturnal polyuria by reducing oxidative stress.

FIGURE 1



Representative immunostaining of renal 4HNE in the control group and nocturnal polyuria model group.

FIGURE 2



The effect of antioxidant on nocturnal polyuria model.

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BEST IN CATEGORY PRIZE: NOCTURIA

THE FIRST TRIAL TO EVALUATE THE EFFECT OF WEARING COMPRESSION KNEE-HIGH SOCKS AND REGULAR KNEE-HIGH SOCKS ON NOCTURIA SYMPTOMS IN A DOUBLE-BLIND, RANDOMIZED, PARALLEL GROUP STUDY

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HYPOTHESIS / AIMS OF STUDY

Nocturia is the complaint of having to get up one or more times to urinate, after going to bed. In an international epidemiological survey, nocturia is a frequent lower urinary tract symptom that accounts for about half of those with nocturia symptoms regardless of gender or race. Nocturia affects both physical and mental health, is associated with death in patients over 60 years of age and impairs quality of life (QOL). In current medicine, it is difficult to alleviate nocturia symptoms with medication alone and the development of care to accompany medication is an urgent issue.

One of the causes of nocturia is increased venous return in the lower extremities at bedtime and it is said that wearing compression knee-high socks during the day is an effective treatment. However, currently, there are no comparative studies between the effects of compression knee-high socks and regular knee-high socks.

Therefore, the purpose of this study is to determine, for the first time, the effect of wearing compression knee-high socks versus regular knee-high socks during the day in participants with nocturia symptoms

STUDY DESIGN, MATERIALS AND METHODS

This study is a randomized, double-blind, controlled trial, parallel group study.

After approval by the Ethics Committee and a pretest, the study was conducted from December 2021 to March 2022 and followed the Consolidated Standards of Reporting Trials (CONSORT) reporting guideline.

Study participants were people aged 40-79 years who have nocturia and who were recruited from among the 300,000 members of a Japanese own web-based travel agency with a large proportion of senior citizen members.

Participants were stratified and randomized by age, gender, and pre-existing disease using a random number table by the web-based company. Using the double-blind method, participants were divided into two groups: the intervention group wore commercially available compression knee-high socks and the control group wore regular knee-high socks made of the same material as the intervention group (both made in Japan).

The compression knee-high socks worn by the intervention group were made of 32.7% cotton, 20.7% rayon, 20.7% nylon, 20.7% polyurethane, 4% ester, and 1.2% other materials, with compression values of 23.8 hPa at the sole, 17.2 hPa at the ankle, and 10.4 hPa at the calf.

The regular knee-high socks worn by the control group were made of 34.7% cotton, 27.2% rayon, 24.5% ester, 7.7% polyurethane, and 5.9% other materials, with compression values of 6.9 hPa at the sole, 5.0 hPa at the ankle, and 4.6 hPa at the calf.

The study was conducted for a total of 21 days, including a 7-day pre-observation period, the 3 days from day 5 to 7, during which the participants became accustomed to the study, were used as the baseline. Participants wore each pair of knee-high socks (washed daily) for at least 8 hours per day from morning to evening. The survey consisted of participants answering five questions, including the number of times they urinated at night, every day for 21 days. They also responded to the Japanese version of N-QOL at the baseline after 14 days of wearing the knee-high socks. Participants were given a double-blind telephone survey by the web company if they were unable to respond online. After the survey, all the knee-high socks were collected, and their condition of use and the presence of defects were verified by an expert.

Statistical sample sizes were calculated. The number of participants allowed adequate assessment of the effects of wearing knee-high socks. All study data was listed, summarized and plotted.

After confirming the normality of the percent change from baseline for the intervention and control groups, a t-test with a two-group correspondence was used. A welch t-test was used for the difference between the two groups in the frequency of nocturnal urination and the total points of the Japanese version of N-QOL. SPSS version 28 was used. (Statistical power 80 %, $P < .05$)

RESULTS

During the 14 days of recruitment, 2803 people visited the website. Of these, 637 were registered as participants. Excepting exclusion factors, statistical sample size calculations were conducted, and the 170 participants were distributed evenly across Japan. The purpose and methods of the study were explained to them via the Web and by phone, and their consent was obtained. Excluding two dropouts, 168 participants were included in the analysis.

There was no significant difference between the two groups: the intervention group consisted of 85 participants (54 women) with a mean age of 58.1 (±9.6) years and BMI of 22.8 (±2.7), and the control group consisted of 83 participants (51 women) with a mean age of 60.2 (±8.4) years and BMI of 23.3 (±2.9).

The mean frequency of nocturnal urination at baseline was 2.22 (±0.79) in the intervention group and 2.29 (±0.73) in the control- group, with no significant difference.

The mean frequency of nocturnal urination for the 3 days prior to the 12th-14th day of wearing the knee-high socks was 1.55 (±0.53) times in the intervention group and 1.73 (±0.67) times in the control group, with a significant decrease in urination frequency for the compression knee-high socks ($P = .03$).

The mean frequency of nocturnal urination for the 3 days prior to the 12th-14th day of wearing the knee-high socks was 2.22 (±0.79) times and 1.55 (±0.53) times in the intervention group, a significant decrease in frequency. ($P < .001$) Nocturnal urination frequency in the control group also significantly decreased from 2.29 (±0.73) times and 1.73 (±0.67) times. ($P < .001$)

The mean frequency of nocturnal urination for the 3 days prior to the 1st-3th day of wearing the knee-high socks was 1.94 (±0.75) times in the intervention group ($P < .001$) and 1.91 (±0.88) times in the control group ($P = .03$) with a significantly reduced compared to the baseline.

The total points for the Japanese version of N-QOL was 50.9 (±6.4) for the intervention group and 50.3 (±7.0) for the control group at baseline, which was not significant. The total points after 14 days of wearing knee-high socks was 64.9 (±7.1) for the intervention group and 63.2 (±2.3) for the control group. Although there was no difference in quality of life between the two groups ($P = .82$), both groups significantly improved their quality of life by wearing knee-high socks. ($P < .001$).

Participants had no adverse events from wearing the knee-high socks and wished to continue wearing them.

INTERPRETATION OF RESULTS

Nocturia symptoms were found to decrease the frequency of urination at night on days when knee-high socks were worn during the day. In addition, wearing compression knee-high socks increased venous return in the lower extremities during the day, suggesting that these socks were more effective than regular knee-high socks in decreasing nocturnal urinary frequency.

Since nocturia decreases QOL, a decrease in urination frequency significantly improves QOL. Therefore, wearing more effective compression knee-high socks is desirable. However, this study suggests that those who have difficulty wearing compression knee-high socks, may not have to give up but may instead be able to choose knee-high socks according to their preferences and circumstances.

CONCLUDING MESSAGE
For nocturia symptoms, wearing knee-high socks for 8 hours or more during the daytime decreased nocturnal urination frequency and improved quality of life, suggesting that compression knee-high socks were more effective in decreasing nocturnal urination frequency than regular knee-high socks.

Funding Products and research funding are provided by Okamoto corporation. **Clinical Trial** Yes **Public Registry** No **RCT** Yes **Subjects** Human **Ethics Committee Ethics Committee** of Daiichi University of Pharmacy(R03-0014) **Helsinki** Yes **Informed Consent** Yes

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NOCTURIA OVERVIEW: A SURVEY FROM GENERAL PRACTITIONER IN INDONESIA

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HYPOTHESIS / AIMS OF STUDY

Nocturia is described as the frequency with which urine is passed during the primary sleep phase. Following the first urination, each subsequent urination must be accompanied by sleep or the intention to sleep.(1) It is included in lower urinary tract symptoms and reported as the most bothersome and the most common. Nocturia causes long term sleep deprivation and lowering someone's quality of life. It leads to decreased work performance, difficulty sustaining focus, and mood changes. It increases with age and affecting both males and females. (1) Nocturia is commonly found in primary health care, managed by general practitioners (GPs). Thus, it is important for them to know how to diagnose and treat nocturia, including referral indications to specialist(s). The aim of this study is to review the management and diagnosis of nocturia among Indonesian general practitioners.

STUDY DESIGN, MATERIALS AND METHODS

This study was a cross sectional study. We collected the data by distributing self-constructed online survey covering the overview of nocturia among GPs in Indonesia, between October 2021 to March 2022. The questionnaire consisted of 15 questions, including general personal information of the respondents and the characteristic of nocturia patients, diagnostic modalities and management approach for nocturia patients. The primary outcome measures were data on nocturia diagnostic tools and management practiced by Indonesian GPs. The secondary outcome was characteristics of nocturia patients tended by Indonesian GPs.

RESULTS

There were 252 GPs in this study who filled out the questionnaire from October 2021 to March 2022. 77.8% of respondents came across 1-5 nocturia cases per month, more commonly encountered in elderly men compared to women (65.5% vs 17.5%). Most GPs were dealing with patient's age range of 50-65 years old (57.9%). The most common symptoms were nocturia accompanied by voiding symptoms (46.8%) and nocturia with storage symptoms (21.8%), and patients usually had had these symptoms for 2-4 weeks (32.9%) before they sought help. In terms of diagnostic tools, history taking and physical examination were routinely done, and most GPs implemented bladder diary (73%) and scoring system (62.3%). However, not many respondents used urinalysis or other further examinations, and only 46% referred their patients to urologist for further diagnosis. With regards to management, most GPs prescribed education and lifestyle changes (88.1%) and medication such as alpha blocker (19.8%) compared to desmopressin (13.5%). Only 65.5% of respondents would refer their patients to urologist for further treatment.

INTERPRETATION OF RESULTS

Nocturia is not an uncommon disease and mostly found in elderly men by GPs in Indonesia. It has negative impact for the quality of life however most patients seen by the GPs had waited several weeks before seeking help. This treatment seeking behaviour might be due to of low awareness that nocturia is a medical condition. Most of the general practitioners already understand the standard diagnostic approach for nocturia and did initial treatment. However, only small portions of respondents refer their patients to urologist or done more extensive examination. According to this study, only 73% used bladder diaries to diagnose nocturia on a regular basis. It is probably due to the fact that bladder diaries are considered to be time consuming and compliance plays a huge role (2). Low usage of urinalysis could have been related to Indonesia's inequitable distribution of facilities for laboratories. Desmopressin should be the primary choice for nocturnal polyuria caused by reduced nocturnal vasopressin, which is the most common cause of nocturia. However, only a few GPs prescribed desmopressin for patients with nocturia. The use of desmopressin in clinical settings is still uncommon probably because lack of standardised desmopressin doses and hyponatremia as its side effect, which can be life-threatening in the elderly. (3)

CONCLUDING MESSAGE

General practitioners in Indonesia face a difficulty in dealing with nocturia. Though the diagnostic modalities mostly are already in line with available guidelines, there were only 52% and 73% of GPs who used urinalysis and bladder diaries, respectively. Desmopressin was prescribed relatively less frequent to treat nocturia compared with alpha blockers. This lack of standardized approach highlights the prospective necessities to create awareness on nocturia and encourage Indonesian GPs to implement the current guideline available for nocturia.

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Funding None **Clinical Trial** No **Subjects** Human **Ethics Committee** Health Research Ethics Commitee - University of Indonesia and Cipto Mangunkusumo Hospital **Helsinki** Yes **Informed Consent** Yes

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INVASIVE TREATMENTS AND NOCTURIA: A SYSTEMATIC REVIEW OF CONTROLLED AND OBSERVATIONAL EVIDENCE.

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HYPOTHESIS / AIMS OF STUDY

Nocturia is a prevalent condition with impact on quality of life and also on morbidity and mortality. There are different treatments for nocturia. Lifestyle measurements are the first important step that should be initially considered; but there are also some pharmacological options to manage nocturia if conservative measures fail. Depending on the underlying cause: desmopressin, a synthetic ADH analog can be administered or in patients with an overactive bladder or bladder outlet obstruction as an underlying cause of nocturia, drugs like antimuscarinics and α-blockers can be used. Unfortunately, in some cases, patients may not present any improvement after initiation of treatment, or may need to interrupt it because of side effects. Causality of nocturia and nocturnal polyuria may involve the lower urinary tract (reduced bladder capacity due to overactive bladder [OAB] or post-void residual), the kidneys (aging, reversed circadian rhythm, nephrogenic diabetes insipidus, etc. …), the endocrine system (estrogen or testosterone deficiency, diabetes mellitus, and diabetes insipidus), sleep and neurologic diseases (sleep apnea, restless legs, insomnia and dopamine deprivation), the cardiovascular system (leg edema, heart failure, hypertension, and metabolic syndrome), and intake related disorders (polydipsia, high salt, or protein diet)(1).

The purpose of this study was to systematically review and to evaluate the effect of invasive treatments (such as surgical procedures, implantable devices…) on nocturia and/or nocturnal polyuria.

By doing so we aimed to investigate the options available and the existing knowledge about it when all the conservative treatments have failed.

STUDY DESIGN, MATERIALS AND METHODS

A systematic review was carried out by searching Pubmed and Embase articles on nocturia and invasive treatments that were published before April 2022. We followed the Preferred Reporting Items for Systematic Review and Meta-analysis (PRISMA) guidance and registered the details of the systematic review in PROSPERO.

Pubmed search, abstract selection and full text reviewing was aided by Silvi® (Silvi.AI, Copenhagen, Denmark), an artificial intelligence aided meta-analysis online platform.

Keywords of the literature search can be found in Figure 1.

We searched for invasive procedure related to the treatment of obesity, cardiac failure, veinous insufficiency, obstructive sleep apnea and Parkinson's disease.

Procedures related to uro-gynecology have voluntarily been not included in the research, owing the fact that there is already sufficient knowledge about invasive treatments such as sacral neuromodulation, botulinum toxin, prolapse surgery or intermittent self-catheterization and nocturia.

We included all observational and trial studies evaluating the effect of invasive procedure (surgical procedure, implantable device) on patients with nocturia and/or nocturnal polyuria.

Studies were excluded if they were reviews of mechanisms or clinical overview, if they addressed pediatric population and/or lifestyle advices or medical treatments. Commentary and review articles were also not included.

RESULTS

Searches identified 572 articles. After title and abstract screening,151 articles were retrieved among which 22 were selected for the review (see flowchart in Figure 1).

The selected reports concerned: invasive treatment of obstructive sleep apnea (n = 16) deep brain stimulation (n = 5), bariatric surgery (n = 1).

No study related to cardiac surgery or invasive treatment of venous insufficiency met the inclusion criteria.

Of the 22 papers included, 3 were randomized-controlled trials (RCT) (among which, one was a cross-over study), 5 were non-RCT and 14 were observational studies (majority of self-controlled case series (SCCS).

In RCTs there was no significant reduction in nocturia between the intervention group and the control group.

From the 3 RCT, only one found a statistically significant decrease of the systolic blood pressure that can explain a decrease in nocturia, when using Continuous Positive Airways Pressure (CPAP) and best supportive care (BSC) versus BSC alone (138,0 +/- 18,2 vs. 137,5 +/- 15,6; p = 0,04)

4 non-RCTs showed statistically significant improvement of nocturia, out of which 2 were based on non-validated questionnaires, and 2 validated questionnaires (DanPSS and NMSquest).

9 SCCS found a significant improvement of nocturia after invasive treatment; based on validated questionnaires.

Only one study evaluating uvulopalatopharyngoplasty for the treatment of obstructive sleep apnea syndrome (OSAS) has been included.

4 observational studies on CPAP have found a statistically significant improvement of nocturnal urine production on frequency volume chart or polysomnography.

One study evaluating the effect of bariatric surgery (sleeve gastrectomy and Roux-en-Y gastric bypass) on lower urinary tract symptoms showed an improvement of the IPSS total score (6,6 +/-6,4 vs. 5,6 +/-6,2; p < 0,001) and a reduction in nocturia episodes evaluated thanks to the question 7 of the IPSS questionnaire (1,9 +/- 1,2 vs. 1,1 +/- 0,9; p = 0,014).

Informations related to the studies included, outcomes and statistic informations are summarized in the table attached (Figure 2).

INTERPRETATION OF RESULTS

The findings are limited by the small size of the datasets. Comparison between studies on the same topic was restricted due to algorithms and datasets heterogeneity.

There is some evidence that CPAP, and implantable devices such as mandibular advancement devices, are effective treatment options for nocturia in patients with obstructive sleep apnea syndrome. Few articles have addressed the topic nocturia in patients undergoing deep brain stimulation for Parkinson disease or sleeve gastrectomy and Roux-en-Y gastric bypass tor the treatment of obesity.

No data has been found on the effect on nocturia of surgery for veinous insufficiency.

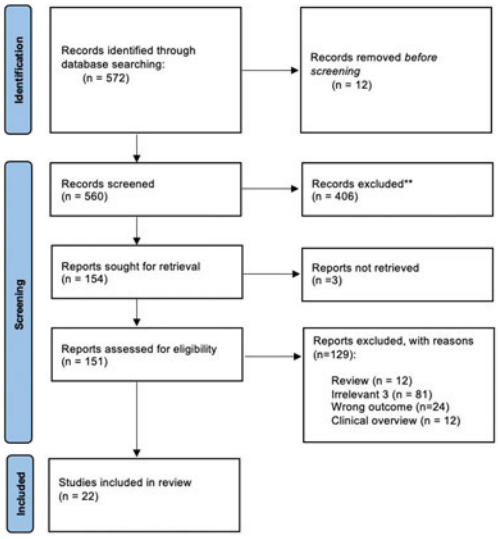
CONCLUDING MESSAGE

We synthetized available evidence on the effect of invasive procedure on nocturia.

The effect on nocturia of invasive treatments and surgical procedures out of the field of urology and gynecology has been little explored in the literature so far.

There is a need for prospective well-controlled, randomized and placebo-controlled trials in order to improve the care of patients with nocturia.

FIGURE 1



keywords of the literature search:

((nocturia) OR (nocturnal polyuria) OR (nocturnal enuresis))
AND ((cardiac surgery) OR (valvuloplasty) OR (coronary artery bypass surgery) OR (CABG) OR (venous insufficiency surgery) OR (phlebectomy) OR (surgical ligation) OR (saphenectomy) OR (vein stripping) OR (endovenous laser ablation) OR (radiofrequency ablation) OR (EVLA) OR (RFA)
OR (bariatric surgery) OR (Adjustable Gastric Banding) OR (excess weight loss) OR (gastric bypass) OR (duodenal switch) OR (biliopancreatic bypass) OR (sleeve gastrectomy)
OR (deep brain stimulation) OR (DBS)
OR (CPAP) OR (continuous positive airway pressure) OR (UVULOPALATOPHARYNGOPLASTY) OR (UPPP) OR (obstructive sleep apnea surgery) OR (adenoidectomy) OR (tracheostomy) OR (mandibular advancement device) OR (MAD))

Figure 1: Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow chart and keywords of the literature search

Figure 1: Preferred Reporting Items for Systematic Reviews and Meta-Analysis flowchart and keywords of the literature search

FIGURE 2

Causality	Study	n	Design study	Procedure	follow-up (months)	Category outcome	Outcome	controle group	post procedure	p
Neurology	Witte et al. 2017	128	RCT	DBS vs. medical ttt	12	Validated questionnaire	PDSS nocturia			NS
Pneumology	Yamamoto et al. 2019	45	RCT - cross over	CPAP vs. MAD		Non validated questionnaire	subjective impression of treatment of nocturia			NS
Pneumology	Mc Millan et al. 2015	278	RCT	CPAP + BSC vs. BSC alone	12	Non validated questionnaire	nocturia episodes			NS
						Clinical outcome	Blood Pressure Systolic	138,0+/-18,2	137,5+/-15,6	0,04
Pneumology	Kiely et al. 1999	56	n-RCT	nasal CPAP	4	Non validated questionnaire	nightly frequency of passing urine	0,8-1,4	1,3-1,9	<0,05
Pneumology	Zhang et al. 2019	120	n-RCT	surgery vs. CPAP vs. untreated	24	Non validated questionnaire	frequent nocturia			NS
Neurology	Soelzo et al. 2019	182	n-RCT	DBS vs medical ttt	12	Non validated questionnaire	nocturia episodes	significant reduction		
Neurology	Winge et al. 2012	107	n-RCT			Validated questionnaire	DanPSS nocturia score	1,1	2,7	0,001
							IPSS			NS
						Echography	Post void residual			NS
Neurology	Mridula et al. 2015	109	n-RCT	DBS vs medical ttt	12	Validated questionnaire	% of patients getting up regularly for urine	35	44	0,02
							NMS quest - urinary disturbances			NS
Pneumology	Miyazoto et al. 2015	53	SCCS	CPAP	3	Validated questionnaire	ESS	8,3 +/- 5,1	6,1 +/- 3,8	0,005
							IPSS total	7,6 +/- 5,5	5,0 +/- 4,3	0,005
							Q7 IPSS	2,1 +/-1,2	1,2 +/- 1,1	0,001
							QoL index	3,4 +/-1,5	1,9 +/-1,5	0,000
							OABSS	4,2 +/- 2,6	2,0 +/- 1,6	0,000
							Q3 urgency	1,2 +/-1,6	0,6 +/- 1,1	0,013
							ICIQ NQOL	75,9 +/- 18,5	89,6 +/- 12,5	0,000
						Clinical outcome	Blood pressure Systolic	140,0 +/- 20,1	135,3+/-16,6	0,091
							Blood pressur Diastolic			NS
						Biology	BNP			NS
						Frequency Volume Chart	Hours of uninterrupted sleep	193+/_132,1	287,3 +/- 136,4	0,001
							Nocturnal voided volume	723,3 +/- 498,4	453,6+/-251,4	0,007
							NPI	37,0 +/-16,2	28,6 +-14,7	0,011
							24h voided volume			NS
							Mean Voided Volume at night			NS
							Water intake per day			NS
Pneumology	Nimi et al. 2016	104	SCCS	CPAP	3	Validated questionnaire	Q2 OABSS	1,9+/-1,0	1,2 +/- 0,8	0,008
							Q7 IPSS	2,4 +/- 1,2	1,6 +/+0,9	0,008
						Frequency Volume Chart	Nocturnal. Urinary frequency	2,0 +/-1,7	0,9 +/-1,1	0,042
							Nocturnal Polyuria index	0,46 +/-0,13	0,35+/-0,17	0,023
Pneumology	Park et al. 2017	66	SCCS	uvulopalato-pharyngoplasty	3	Validated questionnaire	IPSS Q7	1,8 +/- 1,1	0,8 +/- 1,2	0,001
							IPSS total	9,3 +/- 6,9	5,9 +/- 5,9	<0,001
							IPSS QoL	1,8 +/-1,4	1,1 +/- 1,1	0,024
							OABSS	2,9 +/-2,2	2,0 +/-2,2	0,05
Pneumology	Maeda et al. 2017	150	SCCS	CPAP	3	Validated questionnaire	IPSS Q7	1,4 +/- 1,3	0,7 +/- 0,9	<0,01
							IPSS total	6,0 +/- 6,4	4,3 +/- 5,1	<0,01
							IPSS Voiding score	2,9 +/-4,2	2,3 +/-3,5	<0,01
							IPSS storage score	3,1 +/-2,9	2,0 +/-2,1	<0,01
							OABSS	2,7 +/- 2,6	1,7 +/- 1,7	<0,01
Pneumology	Miyazaki et al. 2015	666	SCCS	CPAP	3 to 6	Not validated questionnaires	nocturia episodes	2,2 +/- 1,6	1,0+/- 1,4	<0,0001
						Clinical outcome	Blood pressure Systolic	121,6 +/- 11,9	113,4+/-8,8	0,0002
						Biology	BNP	7 (15,0-144,4)pg/ml	48,5-111,7)pg/l	0,0006
Pneumology	Krieger et al. 1999	188	SCCS	CPAP	12	Questionnaire	Frequency nocturnal micturition	3,7	2,1	<0,001
Pneumology	Irer et al. 2018	126	SCCS	CPAP	3	Validated questionnaire	IPSS Q7	2,1 +/- 1,3	0,5 +/- 0,5	<0,001
							IPSS total	8,4 +/- 6,3	2,8 +/- 2,5	<0,001
							ICIQNIUTS Nocturia	2,0 +/- 1,2	0,6 +/- 0,5	<0,001
							ICIQ MLUTS Impact Nocturia on QoL	3,6 +/-2,8	0,7 +/-1,0	<0,001
							QS-NocturiaOABS V8	2,1 +/- 1,3	0,6 +/- 0,5	<0,001
						Frequency Volume Chart	Nighttime urine volume	547,0 +/- 285,5	95,6 +/-107,8	<0,001
							Frequency of nocturia	2,1 +/- 1,3	0,5 +/- 0,5	<0,001
Pneumology	Margel et al. 2006	97	SCCS	CPAP	1 to 3		awakenings to urinate per night	2,5 +/-2,4	0,7 +/- 0,6	<0,001
Pneumology	Vrooman et al. 2020	285	SCCS	CPAP	12		awakenings to urinate per night	3,1	2	<0,001
Pneumology	Miyauchi et al. 2014	98	SCCS	CPAP	12	Validated questionnaire	IPSS total	5,9+/-4,7	4,8+/-4,6	0,031
							IPSSQ7	1,6+/-1,3	1,1+-0,9	0,003
							OABSS Total			NS
							ICIQ NQoL			NS
						Frequency Volume Chart	Nighttime urine volume	542,4+/-289,9	354,0 +/-217,4	0,005
							Nighttime frequency	2,0+/-1,1	1,0+/-1,2	0,014
						Biology	Urinary Cl contents (mEq)	70,8+/-40,2	48,2+/-30,3	0,007
							Urinary Na contents (mEq)	76,2+/-36,2	51,5 +/-29,5	0,004
							Urinary K contents (mEq)	11,3+/-5,3	9,0+/-5,8	0,025
Pneumology	Coban et al. 2020	54	SCCS	CPAP	not stated	Validated questionnaire	Nocturia episodes	1,92 +/-1,51	1,24 +/-1,21	0,001
							IPSS total	10,38 +/-8,26	7,20 +/-6,65	<0,001
						Uroflowmetry	Qmax (mL/s)	19,03+/-10,21	22,40+/-13,62	0,041
							Qave (mL/s)	8,11+/-3,27	8,99+/-3,67	0,012
Pneumology	Yu et al. 2019	44	Observational	CPAP	0,5	Frequency Volume Chart	% of changes in nocturnal urine output	-26±27	6±49	0,04
							% of changes in nocturnal polyuria index	-21±30	9±27	0,005
							% of changes in nocturia			NS
Obesity	Liu et al. 2020	143	SCCS	sleeve gastrectomy and Rouxen-Y gastric bypass	36	Validated questionnaire	IPSS total score	6,6+/-6,4	5,6 +/-6,2	<0,001
							IPSS Q7	1,9 +/-1,2	1,1 +/-0,9	0,014
							IPSS QoL	1,9 +/-1,3	1,4 +/-1,2	0,005
						Biology	Creatinine (umol/L)			NS
Neurology	Liang et al. 2021	36	SCCS	DBS	6	Validated questionnaire	total OAB score	7,3 +/-3,7	3,7 +/-3,2	0,002

RCT: Randomized-Control-Trial; n-RCT= non randomized-Control Trial; SCCS= self-control case series; CPAP= Continuous Positive Airway Pressure; BSC= Best Supportive Care; MAD= Mandibular Advancement Device; NMS quest= Non Motor symptom Questionnaire

Figure 2: Summary of studies included in the review, with outcomes and data

Figure 2: Summary of studies included in the review, with outcomes and data

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ENHANCING SAFETY OF DESMOPRESSIN IN ELDERLY: VALIDATION OF CAPILLARY BLOOD SODIUM LEVELS

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HYPOTHESIS / AIMS OF STUDY

Nocturia affects more than 60% of adults above 65 years old and the prevalence only increases further with age with a significant impact on the patient's quality of life (1). As people grow older, nocturnal polyuria (NP), becomes the main cause of nocturia and is by itself caused by a loss of normal circadian rhythm of water and salt handling in the healthy aging kidney (2).

Desmopressin is the only type of medication with an evidence based effect on bothersome NP, but clinical implication remains limited in older people. Though rare, one of the most feared dose-dependent side effects is hyponatremia (<135 mmol/L), but even with the new low dose formulation, regular serum sodium monitoring remains necessary when initializing desmopressin in adults older than 65 years old (3). Therefore, we want to make desmopressin a safe treatment option for (older) patients at risk for hyponatremia, by introducing a new way of sodium monitoring. The goal is to reduce the risk of hyponatremia, enhance patient safety in desmopressin use and ultimately introduce self-monitoring of sodium levels. The first step in the aforementioned is to validate capillary sodium.

STUDY DESIGN, MATERIALS AND METHODS

All adult patients (M/V/X 18-99 years old) admitted to the urology ward that were planned to receive a standard venous blood collection were eligible to participate. There were no exclusion criteria. 100 capillary blood samples were collected through a single finger prick with a BD Microtainer® contact-activated lancet, in order to collect a couple of capillary blood drops (250µL) in a lithium-heparin tube. Venous blood was collected through regular venipuncture in a lithium-heparin tube. Venous and capillary plasma sodium were analyzed by indirect ion selective electrode (ISE) method.

Statistical analysis was performed using MedCalc version 20.015. Each patient acted as its own control for the capillary and venous blood sample. The primary outcome was the agreement between capillary and venous sodium, measured by the intraclass correlation coefficient (ICC). Inter-method differences were analysed by the method of Bland and Altman and a Passing-Bablock regression. Sodium results are reported in mmol/L and shown as mean, standard deviation (S.D.) and range (min, max).

RESULTS

Of the 100 paired blood samples, 3 samples were excluded due to insufficient capillary blood volume and hence the inability to analyse sodium levels. After sensitivity analysis of the difference between venous and capillary sodium, 1 outlier was identified and excluded from further data analysis. A total of 96 venous and capillary samples were statistically analyzed.

The median age of patients was 63 years old, ranging from 18-87 years, of which 71% were men.

The mean (S.D.) venous plasma value was 138,3 mmol/L (±3.3), ranging from 126 to 144 mmol/L, compared to a mean (S.D.) capillary plasma value of 138.5 mmol/L (±3.5), ranging from 127 to 145 mmol/L. There was no significant statistical difference observed between venous and capillary sodium (mean difference -0.23 mmol/L (0.2), p=0.374). The ICC for single measures between capillary and venous sodium was 0.82 (95% CI 0.75-0.88). The Bland-Altman plot visualizes the agreement between the two methods (Fig.1), indicating a mean difference of -0,23 mmol/L with a lower limit of agreement of -4.1 mmol/L and an upper limit of 3.4 mmol/L. The correlation between both groups was plotted by a Passing-Bablok regression (Fig.2) showing no systematic (intercept = 0.00), nor proportional (slope = 1.00) difference between venous and capillary sodium measurements.

INTERPRETATION OF RESULTS

With this research we show that there is no significant difference between venous and capillary indirect ISE sodium measurements in a real life clinical setting. It is however important to bear in mind as a clinician that there is inter- and intravariability (test-retest differences) between chemical analyses. In clinical practice, these minor differences become of particular interest in case of borderline hypo- or hypernatremia. However, in case of the latter and specifically for hyponatremia, clinical assessment will overrule borderline lab results and precocious measures will be taken to either prevent or treat hyponatremia.

This study is the first step in developing a patient centered method for preventing hyponatremia in elderly patients and other patients at risk taking desmopressin. Capillary blood collection has the advantage of being less invasive, using smaller blood volumes, having no need to gain venous access and having no hematoma formation compared to a standard venous blood collection, which is particularly of interest for older patients. In the future part of the study, we do recommend using more appropriate techniques for capillary blood collection. These methods have the benefit of being more patient friendly in use and less painful, leaving less margin for sampling error and requiring no difficult hand-eye coordination, so the patient can easily provide its own capillary blood collection without the need of another (trained) person. Patients participating actively in their own treatment and health will have a better outcome in therapy adherence. We hypothesize that patients being more involved in their treatment and having access to an easy, fast and painless method of sodium monitoring will develop less frequently hyponatremia and/or experience fewer hospital admissions, when taking desmopressin.

CONCLUDING MESSAGE

This study states that capillary blood sodium values are equivalent to venous blood sodium levels and that it is possible to accurately determine sodium levels on small capillary blood samples. This is the first step towards a simple and safe solution for frequent sodium monitoring in a patient population at risk for hyponatremia, with the possibility of future self-monitoring of sodium levels through minimal invasive capillary blood collection. The results are of direct clinical relevance to safely use desmopressin for NP in (older) patients at risk, resulting in a significant improvement in overall quality of life.

FIGURE 1

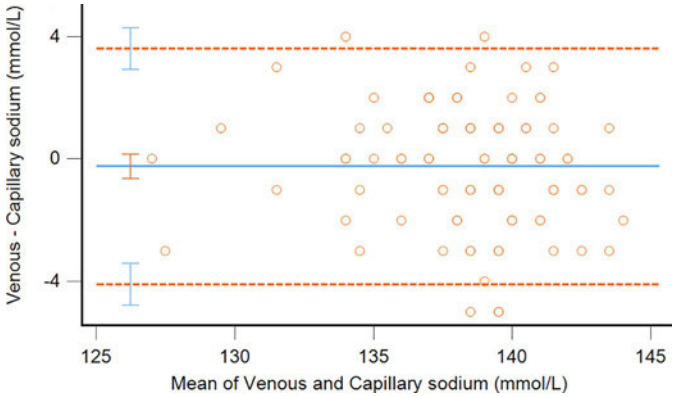

Fig. 1. Bland-Altman graph stating the overall agreement in sodium measurements between venous and capillary blood. Mean difference -0,23 mmol/L (95 %CI: -0,64 to 0,16), limits of agreement -4.1 mmol/L and 3,6 mmol/L.

FIGURE 2

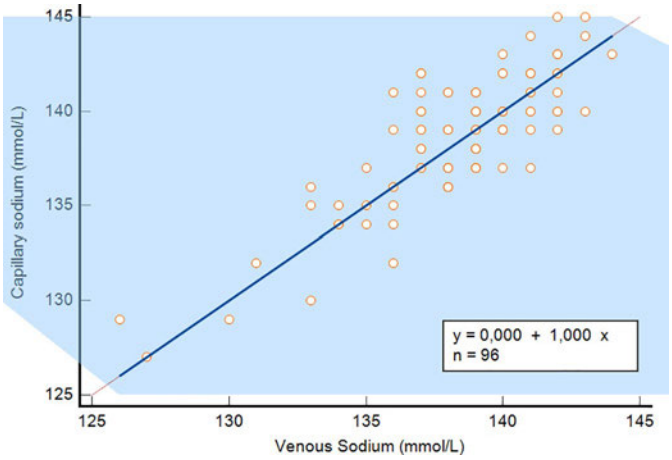

Fig. 2. Passing-Bablok regression showing no systematic, nor proportional difference between venous and capillary sodium measurements.

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NITE-SS, A NOCTURNAL BLADDER SYMPTOM SCORE FOR OLDER ADULTS.

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HYPOTHESIS / AIMS OF STUDY

Nocturia commonly occurs alongside other symptoms of bladder dysfunction at night, such as urinary urgency, urgency incontinence and enuresis (1). Quantification of nocturnal bladder dysfunction will enable evaluation of the impact of individualised treatment. A symptom-specific score for bladder dysfunction at night has recently been developed to capture clinically relevant domains (2). The aim of this study was to test the nocturnal bladder symptom score (NITE-SS) and to generate a robust short form.

STUDY DESIGN, MATERIALS AND METHODS

The NITE-SS measure was developed from a subjective patient-orientated perspective and refined following patient feedback (2). In this study, factor analysis was performed on completed measures with the aim of reducing the number of variables. Endorsement frequency was obtained for all items and sub-scales using counts; items with a high floor effect (i.e. >70% of responses 'never' or its equivalent) or >20% missing data were noted. Principal component analysis was used to extract the maximum variance explained by the first factors and then by subsequent factors. We report factor loading, eigenvalues and factor scores from a sample of 151 NITE-SS completed by individuals older than 70 years who were either inpatients at our hospital or attending outpatient clinics. Analyses justified items retained in the final NITE-SS. The institutional ethics committee (QA2021045) approved the study.

RESULTS

Of the 151 NITE-SS data sets, 98 were completed by inpatients and 53 by community-dwelling older adults attending a hospital continence clinic. Females comprised 68% of the responders. The data set contained no missing values. Nocturia of at least twice per night, frequent urinary urgency, incontinence while asleep and incontinence en route to the bathroom at night were reported by 70.8%, 47%, 20.6% and 19.8% of participants respectively.

Five items showed a floor effect. All correlation coefficients were <0.8 indicating no multi-collinearity. Kaiser-Meyer-Olkin = 0.83; Bartlett's test of sphericity was significant. Four factors returned an eigenvalue >1.0 explaining a cumulative variance of 59%. Specific items related to symptom description were retained. The decision tree for removing redundant items considered weighting in multiple components, inter-relationship, likelihood of change post-intervention and low endorsement frequency.

INTERPRETATION OF RESULTS

Three factors were identified in the measurement of bladder symptoms at night: sleep, incontinence and personal bother attributable to nocturnal LUTS. The final metric (Figure 1) contained 13 items each scored as 0 for lowest level of attribute through to 4 for most negative.

CONCLUDING MESSAGE

The new metric, NITE-SS, has undergone principal component analysis and been reduced to 13 items. Reliability and sensitivity are currently being established.

FIGURE 1

Figure 1: Final three factor version of NITE-SS

Your Bladder at Night this week

	SLEEP
1	How often has your bladder caused you to have broken or restless sleep? Never ☐ Occasionally ☐ Frequently ☐ Every night ☐
2	What is the most number of times you pass urine in one night? 0-1 ☐ 2 ☐ 3 ☐ 4 times or more ☐
3	How many hours do you usually sleep before waking to pass urine? 1- 2 hours ☐ 2-3 hours ☐ 3-5 hours ☐ 5 hours or longer ☐
4	How often do you have an **urgent need** to go to pass urine during the night? Never ☐ Occasionally ☐ Frequently ☐ Every night ☐
5	If you wake up wanting to urinate, but don't get up to go, do you have difficulty falling back to sleep? Never ☐ Occasionally ☐ Frequently ☐ Every night ☐
6	How often does your bladder feel empty after passing urine at night? Always ☐ Usually ☐ Occasionally ☐ Never ☐
	INCONTINENCE
7	How often do you lose urine while asleep? Never ☐ Occasionally ☐ Frequently ☐ Every night ☐
8	How often do you lose urine on the way to the toilet at night? Never ☐ Occasionally ☐ Frequently ☐ Every night ☐
9	How many pads or other protective items do you use each night? None ☐ 1 pad ☐ 2 pads ☐ 3 or more pads ☐
10	Would you worry that ignoring the urge to pass urine might cause a leak in bed? Never ☐ Occasionally ☐ Frequently ☐ Every night ☐
11	How would you feel if your bladder continued to function just the way it is now? Happy ☐ Mostly happy ☐ Unhappy ☐ Very unhappy ☐
	BOTHER
12	Describe the quality of your sleep Very good ☐ Good ☐ Variable ☐ Bad ☐ Very bad ☐
13	Are you fearful of falling if you get up to pass urine during the night? Never ☐ Occasionally ☐ Frequently ☐ Always ☐

Figure 1: Your Bladder at Night this week

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Funding Nil **Clinical Trial** No **Subjects** Human **Ethics Committee** Melbourne Health HREC **Helsinki** Yes

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245 | www.ics.org/2022/abstract/245

CONTROL OF BLADDER PERIPHERAL CLOCK AND DIURNAL MICTURITION PATTERN BY GLUCOCORTICOIDS

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HYPOTHESIS / AIMS OF STUDY

A variety of organisms have many physiological and behavioral processes with rhythmicity of approximately 24 hours, and this is called circadian rhythm. The central master clock located at the suprachiasmatic nucleus in mammals generates this rhythm through mechanisms of transcription-translation feedback loops. In addition to the circadian rhythm of whole body controlled by the central clock, each organ has its own functional circadian rhythm modulated by the peripheral clock. Several reports have shown that peripheral clocks are important for the circadian rhythm of each organ function (ref. 1), and the bladder is considered as well (ref. 2). However, the physiological cues to control the peripheral clock in the bladder has not been revealed yet.

STUDY DESIGN, MATERIALS AND METHODS

1) In vitro experiments. For the screening of physiological signals to modulate the peripheral clock in the urothelium, we created the hTERT-immortalized human urothelial cells stably expressing pBmal1-dLuc (Bmal1-Luc) by transfecting the lentiviral vector carrying it. After synchronization of the clock by serum shock, bioluminescence was continuously monitored for 3-5 days with administration of noradrenaline (10 μM), carbachol (10 μM), ATP (10 μM), and prostaglandin E2 (10 μM) and dexamethasone (0.1μM).

2) In vivo experiments. This study used 8-week-old male C57BL/6 mice. All mice were housed under a 14-hour light/10-hour dark (L/D) cycle condition [light-on at 0500 a.m. and Zeitgeber time (ZT) at 0]. To investigate the influence of corticosterone on the bladder clock and micturition behavior in mice, we created three models and their controls: a) bilateral adrenalectomy (ADx) or the sham operation b) corticosterone (0.2 mg/body) or the vehicle (methylcellulose) administration orally at a non-physiological timing of ZT1 (CORT), and c) ADx with oral CORT administration at ZT1 (ADx + CORT) or the vehicle. Both ADx and sham-operated mice were allowed to recover for 1 week postoperatively. All mice had free access to 1% NaCl solution after the operation. Bladders were extracted and genes expressions were evaluated by real-time qPCR. RNA sequences for the bladder samples were performed in the experiment c). The micturition behavior was measured using aVSOP method using a filter paper. The averages of 8 hours (4 hours before and after) were graphed starting from the beginning of the dark period. The amount of volume voided per micturition was averaged the amount of volume voided per micturition in the elapsed time. The amount of urine volume per hour was calculated by dividing the amount of total voided volume by the elapsed time.

RESULTS

1) In vitro experiments. After administration of noradrenaline, carbachol, ATP, and prostaglandin E2, the rhythm and amplitude of luminescence did not change, but only dexamethasone significantly decreased the amplitude, shifted the peak forward 10 hrs, and reduced the period from 24 hrs to 22 hrs. The amplitude of luminescence decreased after the administration of above 25 nM of cortisol, a physiological glucocorticoid (GC) in humans. The cortisol administration at the physiological timing after serum shock, a compatible to the time that the blood cortisol level in humans elevated, increased the amplitude but did not influence on the phase of the luminescence rhythm. However, the cortisol administration at non-physiological timing reversed the phase of the luminescence rhythm. These changes in phase and amplitude induced by the cortisol administration were inhibited when a mifepristone 10 nM, a glucocorticoid receptor inhibitor, was administered simultaneously with cortisol.

2) In vivo experiments. The ADx mice had little change on clock genes' expressions in the bladder compared with the sham mice, but the CORT mice and the ADX + CORT mice had significant alterations on the diurnal rhythm of clock genes' expressions compared with the controls. The peaks of Bmal1 and Rev-erbα shifted forward 4 hrs in the CORT mice and, of note, 8-12 hrs in the ADx + CORT mice (Fig. 1). Moreover, the RNA-seq revealed that the peaks of most of the clock genes shifted forward 8 to 12 hrs in the ADx + CORT mice. As for micturition behavior analysis, all model mice except the ADx + CORT maintained the diurnal rhythm of volume voided per micturition with decreased during the active period and increased during the inactive period; however, the ADx + CORT disrupted the diurnal rhythm of volume voided per micturition (Fig. 2).

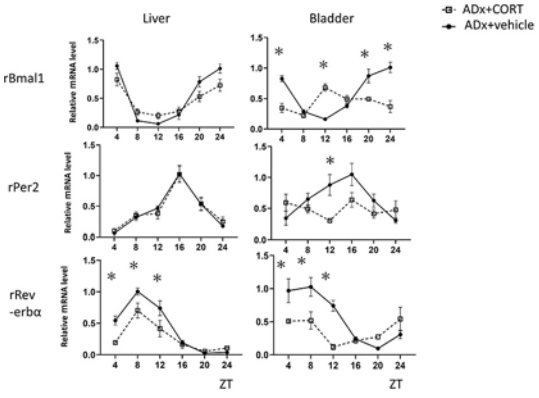
INTERPRETATION OF RESULTS

From the in vitro experiments, the GCs could be selected as a candidate physiological signal for the control of the peripheral bladder clock. From the in vivo experiments, the findings of the inversed rhythm of clock genes in the bladder of the ADx + CORT mice suggests that the peripheral bladder clock can be mainly controlled by the diurnal rhythm of cortisol level. The clock genes in the bladder of CORT mice, a model of non-physiological timing administration of corticosterone, shifted several hours forward only and kept their rhythms suggests that the maintained physiological peak of the corticosterone could attenuate the shift. The disrupted the diurnal rhythm of volume voided per micturition accompanied with the inversed rhythm of the bladder peripheral clock in ADx + CORT mice indicates that the synchronized rhythm of the central clock and the bladder peripheral clock is important for creating the diurnal rhythm of micturition.

CONCLUDING MESSAGE

The present study has demonstrated that the diurnal rhythm of GC signal is involved in the control of the bladder peripheral clock and in the formation of diurnal rhythms of volume voided per micturition. Clarifying more details of the regulatory mechanism for the peripheral bladder clock and the clock controlled genes would help us to understand the pathogenesis of nocturnal enuresis and nocturia and may lead to new therapeutic approaches.

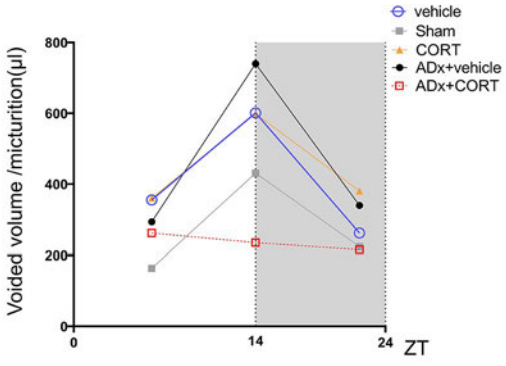
FIGURE 1



Temporal mRNA accumulation of Bmal1, Per2 and Rev-erbα in the liver and bladder from ADx+vehicle(solid line) and ADx+CORT(dash line). Each data series represents the mean +- SEM and 4 mice per time point. Differences were determined by two-way ANOVA and Sidak's multiple comparisons test.*p<0.01 v.s. ADx+vehicle.

Figure 1: Effect of bilateral adrenalectomy and corticosterone administration at the non-physiological timing.

FIGURE 2



The averages of 8 hours (4 hours before and after) volume voided per micturition were graphed starting from the beginning of the dark period. The amount of volume voided per micturition was averaged the amount of volume voided per micturition in the elapsed time. :No intervention (control), adrenal sham surgery only (sham), no surgery + corticosterone administration at ZT1 (CORT), bilateral adrenalectomy + methylcellulose administration at ZT1(ADx + vehicle), bilateral adrenalectomy + corticosteroneadministration at ZT1 (ADx + CORT) .

Figure 2: The diurnal rhythm of volume voided per micturition.

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NOCTURNAL POLYURIA IS COMMON IN PATIENTS WITH PURE AUTONOMIC FAILURE

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HYPOTHESIS / AIMS OF STUDY
Pure autonomic failure (PAF) is an uncommon sporadic alpha-synucleinopathy disorder affecting the periperhal innervation characterized by failure of blood pressure control and dysregulated cardiovascular reflexes, without other neurological symptoms and signs. 25% of patients however phenoconvert over time, and can present later with a central neurological disorder such as Multiple System Atrophy, Parkinson's Disease or Dementia with Lewy Bodies[1].

Cardiovascular autonomic failure , characterized by postural hypotension and supine hypertension, is the clinical hallmark finding in Pure autonomic failure (PAF), though other autonomic functions are often affected. A recent natural history study suggested that lower urinary tract symptoms (LUTS) and erectile dysfunction are common[2]. Nevertheless, systematic evaluation of LUTS, bowel and sexual symptoms has never been investigated and the prevalence of these symptoms and their associations with features of PAF remain unclear. This study aims to characterise LUTS, bowel and sexual dysfunction in PAF patients and explore their relationship with cardiovascular autonomic dysfunction.

STUDY DESIGN, MATERIALS AND METHODS
All patients fulfilled the diagnostic criteria of PAF and had been followed up for at least 5 years without other emerging neurological features.

PAF patients who underwent cardiovascular autonomic testing were prospectively recruited consecutively between November 2019- October 2021. Self-administered questionnaires evaluating lower urinary tract, gastrointestinal and sexual symptoms including Urinary Symptom Profile (USP), Constipation Scoring System (CSS), The Wexner incontinence score, The Arizona Sexual Experiences Scale (ASEX) and Quality of life questionnaire (SF-Qualiveen) were completed. A 3-day bladder diary measuring fluid intake and urine output were also evaluated. Demographic, clinical features, disease duration and related medical comorbidities were assessed. A subset of patients who underwent cardiovascular autonomic testing (head-up tilt test and 24-hour ambulatory blood pressure monitoring;24hr-ABPM) and urodynamic studies were examined.

RESULTS
25 PAF patients (10 males) were included (mean age 71 + 8 years; disease duration 13 + 8 years). All patients developed LUTS after orthostatic intolerance symptoms (median 4 years, IQR 2-9 years). Lower urinary tract symptoms were reported by 96% (24/25) using the Urinary Symptom Profile. Among these, overactive bladder symptoms (n = 23; 92%; median overactive subscore 8 (IQR 3-11)) were more frequently reported than voiding symptoms (n = 19; 76%; median low stream subscore 2 (IQR 1-3)). Four (16%) patients required catheterisation.

The CSS and the Wexner incontinence median score were 7 (IQR 4-13) and 7 (IQR 3-9), respectively. Sexual dysfunction was present in 91% (21/23) using ASEX with the median score of 17 (IQR 14-19). The median SF-Qualiveen score was 1.56 (IQR 0.69-2.31).

13 patients underwent uroflowmetry and 77% (10/13) had abnormal flow patterns including intermittent/irregular and prolonged flow. 31% (4/13) had a significant post-void residual urine (PVR > 100 ml) and required intermittent self-catheterisation. 6 patients underwent urodynamics, which showed detrusor overactivity and large bladder capacity (n = 2 for both), detrusor underactivity (n = 1) and early sensation during fill phase with no detrusor overactivity (n = 1).

22 patients completed a bladder diary and 19 (86%) had nocturnal polyuria (NP), defined as NP index > 0.3 (nocturnal urine volume/24-hour urine volume), mean NP index 0.45 (range, 0.20-0.73).

21 patients underwent autonomic function tests including a 10-minute tilt table test and 24hr-ABPM. All patients had confirmed cardiovascular autonomic failure and orthostatic hypotension on head-up tilt. With 24hr-ABPM, supine hypertension and reversed circadian blood pressure rhythm (average BP higher during night-time than daytime) was present in 81% (17/21) and 57% (12/21), respectively. There were no significant correlations between age, disease duration and cardiovascular parameters (orthostatic BP drop, supine hypertension and abnormal blood pressure circadian rhythm) with urogenital parameters including need for catheterisation and degree of NP ($p > 0.05$).

INTERPRETATION OF RESULTS
Our study demonstrated that LUTS, bowel and sexual symptoms are common in patients with PAF. Nocturnal polyuria is highly prevalent in patients with PAF. Possible mechanisms include improved renal perfusion due to supine hypertension when adopting a recumbent position at night and pressure natriuresis, and renal ischemia as a result of long-standing changes from postural hypotension [3]. However the lack of direct correlation between nocturnal polyuria and demographics or any of the measures of cardiovascular autonomic failure suggests that the pathophysiology of NP in Pure Autonomic Failure is likely to be multifactorial, and raises the possibility whether NP can occur independent of cardiovascular failure in this cohort. Longitudinal follow up is required to assess whether there is a relationship between NP and phenoconversion to other central neurological disorders later in the course of the disease.

CONCLUDING MESSAGE
Urogenital and bowel dysfunction is common in patients with Pure Autonomic Failure and majority of patients have nocturnal polyuria. Self-reported questionnaires and bladder diary are useful as part of uro-neurological assessment of patients with PAF. Screening for, and treating, pelvic autonomic symptoms in patents with PAF are strongly recommended given their impact on quality of life.

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Funding None **Clinical Trial** No **Subjects** Human **Ethics not Req'd** The Queen Square Clinical Audit Committee approved this study as an audit. There was a waiver of written consent because assessments were conducted as part of routine clinical management. **Helsinki** Yes **Informed Consent** Yes

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PARKINSON'S DISEASE AND NOCTURNAL POLYURIA

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HYPOTHESIS / AIMS OF STUDY

The question of whether Parkinson's disease (PD) patients have nocturnal polyuria (NP) has not yet been fully answered.

Objective is to determine whether NP was present in PD patients and if so, what its relevant factors were.

STUDY DESIGN, MATERIALS AND METHODS

This was a retrospective analysis. We had 36 consecutive referred PD patients: age, 71.5 years (range, 54-83 years); 24 men, 12 women; mean disease duration, 2.5 years (1.0-4.5 years); Hoehn and Yahr motor scale, 3.0 (2.0-3.5); all ambulatory; all on treatment. All PD patients completed a lower urinary tract symptom (LUTS questionnaire) and a bladder diary, and underwent urodynamics testing.

RESULTS

NP was identified in 56% of patients. NP was more common in patients with nocturia ($p < 0.05$), and in patients with urodynamic detrusor overactivity ($p < 0.01$). There was no relation between NP and gender, age, PD medications, blood pressure, or comorbid diabetes.

INTERPRETATION OF RESULTS

There may be two PD-related mechanisms in NP. First, hypothalamic arginine vasopressin (AVP) neurons (originating in the suprachiasmatic nucleus [SCN] and the paraventricular nucleus [PVN], which project fibers to the posterior pituitary gland, relevant to circadian rhythm generation, nausea, analgesia, antidiuresis [reabsorption of salt and water in the kidneys], etc.) are affected in PD, leading to either the syndrome of inappropriate antidiuretic hormone secretion (SIADH, clinically manifested as hyponatremia in rare cases) or the loss of nocturnal surge/increase of AVP (loss of NAVP, clinically manifested as NP).15 Similar conditions have been documented in multiple system atrophy that also affects hypothalamic AVP neurons. In 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP)-induced PD model dogs, NP and loss of NAVP were reported, and the administration of levodopa resumed NP and loss of NAVP. In another study, DAergic stimulation increased plasma AVP. Therefore, DA neurons are thought to facilitate NAVP. In the present study, NP was found to have a close relation with detrusor overactivity. Detrusor overactivity in PD is most probably a reflection of lesion in the nigrostriatal DA pathways. Considering the results of the present study, we postulate that in PD, loss of DA neurons leads to both NP (hypothalamic circuit) and detrusor overactivity (nigrostriatal circuit). However, it is important to note that loss of NAVP is not noted solely in brain diseases but also in general NP, at least in some cases. The second mechanism is orthostatic hypotension, although this relationship was not obvious in the present study. PD affects extra-brain periarterial noradrenergic (NAergic) fibers (innervating alpha1B receptors), producing orthostatic hypotension. In this condition, the glomerular filtration rate (GFR) depends on posture (on standing: diurnal peripheral fluid shift, edema and decreased GFR [immobility is also a factor]; on lying: nocturnal rostral fluid shift, increased GFR and NP). Other etiologies relevant to orthostatic hypotension, such as cervical spinal cord injury 22 and diabetic neuropathy, also cause NP.

CONCLUDING MESSAGE

A total of 56% of PD patients had NP, which had a close relation with detrusor overactivity ($p < 0.01$). These findings suggest that in PD, the loss of dopaminergic neurons leads to NP (hypothalamic circuit) and detrusor overactivity (nigrostriatal circuit).

FIGURE 1

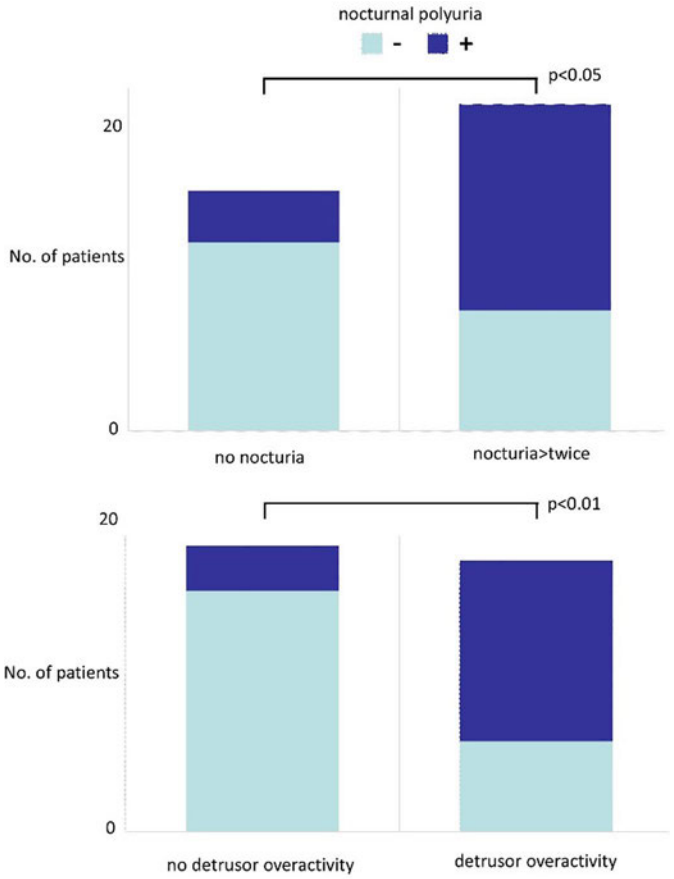

Figure 1. Relationship between nocturnal polyuria and other factors in Parkinson's disease (PD).

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NOCTURIA AS A RISK FACTOR FOR ALL-CAUSE AND CARDIOVASCULAR DISEASE MORTALITY

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HYPOTHESIS / AIMS OF STUDY

Nocturia has been associated with many comorbidities including cardiovascular diseases (CVD), and endocrine disorders. It has also been associated with chronic illnesses, such as chronic respiratory disease, neurological disease, and malignancy. Considering its associations with these many chronic comorbid conditions, several studies have reported a relationship between nocturia and mortality. However, related evidence in the literature is limited. The National Health and Nutrition Examination Survey (NHANES), a nationally representative population-based sample of the United States, was conducted by the National Center for Health Statistics of the Centers for Disease Control and Prevention. To date, only a few studies have investigated nocturia [1] or its association with mortality using NHANES data [2]. Only one study reported an association between nocturia and mortality risk using NHANES III 1988–1994, but the data used is about 30 years old [2]. Therefore, we investigated the relationship between nocturia and mortality risk in the United States using the NHANES data collected between 2005 and 2010.

STUDY DESIGN, MATERIALS AND METHODS

Data were obtained from the NHANES 2005-2010. Mortality data were obtained by linking the primary database to death certificate data found in the National Death Index with mortality follow-up up to December 31, 2015. Nocturia was defined based on symptoms reported in the symptom questionnaire. We categorized patients into two groups: mild nocturia (2–3 voids/night) and moderate-to severe nocturia ($\geq$4 voids/night). We estimated hazard ratios (HR) using multiple Cox proportional hazard regression analyses to investigate the effect of nocturia on all-cause mortality and CVD mortality. Moreover, considering the heterogeneity of the confounding variables according to nocturia, we conducted subgroup analysis with propensity score matching data (1:1 matching).

RESULTS

This study included 9,892 adults (4,758 men, 5,134 women). Nocturia occurred in 3,314 individuals (33.5%). Nocturia was more common in older individuals, women, smokers, and those with higher BMI and metabolic diseases. In addition, the prevalence of CVD was significantly higher in those with nocturia at the baseline survey. In the follow-up data up to 2015, adults with nocturia showed a significantly higher incidence of all-cause and CVD mortality than those without nocturia.

Kaplan-Meier survival curves revealed a significantly higher rate of all-cause mortality and CVD mortality in participants with nocturia than in those without nocturia. In the multiple Cox regression analysis, nocturia was significantly associated with all-cause mortality (HR: 1.23, 95%CI: 1.10–1.39, $p<0.001$) and CVD mortality (HR 1.55, 95%CI: 1.19–2.01, $p=0.001$). Mild and moderate-to-severe nocturia were both significantly associated with all-cause mortality (HR 1.17, 95%CI: 1.03–1.32, $p=0.014$; HR 1.67, 95%CI: 1.36–2.06, $p<0.001$, respectively) and CVD mortality (HR 1.49, 95%CI: 1.14–1.96, $p=0.004$; HR 1.90, 95%CI: 1.20–2.99, $p=0.006$, respectively). Considering the heterogeneity of the participants with nocturia, additional analysis was performed using 1:1 propensity score matching. With propensity score matching, nocturia was still significantly associated with all-cause mortality (HR 1.25, 95%CI: 1.10–1.41, $p<0.001$) and CVD mortality (HR 1.58, 95%CI: 1.2–2.07, $p=0.001$). Mild and moderate-to-severe nocturia were significantly associated with all-cause mortality (HR 1.18, 95%CI: 1.04–1.34, $p=0.012$; HR 1.69, 95%CI: 1.37–2.09, $p<0.001$, respectively) and CVD mortality (HR 1.52, 95%CI: 1.15–2.02, $p=0.004$; HR 1.94, 95%CI: 1.23–3.08, $p=0.005$, respectively).

In subgroup analysis according to sex, nocturia was significantly associated with all-cause mortality and CVD mortality in men. In women, moderate to severe nocturia was significantly associated with all-cause mortality and CVD mortality. In subgroup analysis according to cardio-metabolic diseases, nocturia was associated with CVD mortality in patients with diabetes mellitus, hypertension, dyslipidemia or CVD at baseline. In subgroup analysis of patients without diabetes mellitus, hypertension or CVD, nocturia was significantly associated with all-cause mortality.

INTERPRETATION OF RESULTS

Our population-based study demonstrated that mortality was significantly associated with mild and moderate-to-severe nocturia in men and women after adjusting for major confounding factors. Our study also showed that CVD mortality was associated with nocturia in a dose-dependent manner.

CONCLUDING MESSAGE

Our study provides strong support for the previously established relationship between nocturia and mortality.

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Funding None **Clinical Trial** No **Subjects** Human **Ethics Committee** The National Center for Health Statistics' Research Ethics Review Board **Helsinki** Yes **Informed Consent** Yes

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STRUCTURAL HEART DISEASE EVALUATED BY ECHOCARDIOGRAPHY CAN BE PREDICTED BY NOCTURIA

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HYPOTHESIS / AIMS OF STUDY

Nocturia is the most common and bothersome lower urinary tract symptoms (LUTS). Except for urological disorders, nocturia is also caused by systemic diseases. Heart failure and uncontrolled hypertension lead to clinically significant nocturia. Cardiac diseases with left ventricular hypertrophy (LVH) and left atrial enlargement (LAE) identified by electrocardiographic (ECG) had association with nocturia. We aim to investigate the relationship between nocturia and cardiac structural abnormalities on cardiac sonography.

STUDY DESIGN, MATERIALS AND METHODS

We included the adult patients in cardiology outpatient department whom received the cardiac sonography from June 1, 2021 to July 31, 2021. All the patients were asked of the times of nocturia in the past six months before the echocardiographic examination. Univariate and multivariate analyses were done with logistic regression to evaluate the predictive value of nocturia on echocardiographic abnormalities. Statistical analysis was performed by Pearson's chi square test and p value of < 0.05 was considered to be statistically significant.

RESULTS

A total of 299 patients were included, and up to 267 (89.3%) patients reported to have nocturia. Besides, 109 patients met the criteria of LAE (36.5%) and 85 patients had LVH (28.4%). In all patient, age older than 65 years (2.0 +/- 1.1 versus 1.4 +/- 1.0, p = 0.0001), diabetes mellitus (2.0 +/- 1.1 versus 1.7 +/- 1.1, p = 0.027), LAE (2.1 +/- 1.1 versus 1.7 +/- 1.1, p = 0.001), LVH (2.1 +/- 1.2 versus 1.7 +/- 1.1, p = 0.014), and moderate AR (2.1 +/- 1.2 versus 1.8 +/- 1,1, p = 0.048) were associated with higher times of nocturia. In patients older than 65 years of age, LAE (2.3 +/- 1.1 ver sus 1.9 +/- 1.1, p = 0.008) and LVH (2.3 +/- 1.1 versus 2 +/- 1.1, p =0.012) had higher times of nocturia. On multivariate analysis, the presence of nocturia could be predictive factor of LAE (odds ratio 1.347, 95% CI 1.062 – 1.710, p = 0.014). In subgroup of patients older than 65 years of age, nocturia was not only predictive of LAE (odds ratio 1.362, 95% CI 1.034 – 1.793, p=0.028), but also LVH (odds ratio 1.397, 95% CI 1.057 – 1.846, p=0.019).

INTERPRETATION OF RESULTS

In the present study, we found that old age, diabetes, and echocardiographic evidence of LAE and LVH were significantly associated with higher times of nocturia. Moreover, nocturia could be predictive of LAE and LVH, especially among the elderly. The elevation of atrial natriuretic peptide (ANP) levels in patients with LAE is thought to associate with nocturia. ANP increases the glomerular filtration rate (GFR), renal plasma flow and sodium excretion, which cause diuresis and natriuresis. LVH increases the risks of both systolic and diastolic heart failure, which leads to nocturia.

CONCLUDING MESSAGE

Patients with old age, diabetes, and echocardiographic evidence of LAE and LVH had higher times of nocturia. Moreover, nocturia could be predictive of structural heart disease including LAE and LVH. Referral to cardiologists should be considered for nocturia patients without other significant LUTS.

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SESSION 19 - FEMALE STRESS URINARY INCONTINENCE

Abstracts 273-284
11:30 - 13:00, Hall D
Chair: Dr Rufus Cartwright (United Kingdom)

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MISCONCEPTIONS OF THE MINIMAL IMPORTANT DIFFERENCE ANALYSIS OF PATIENT-REPORTED OUTCOMES RELATED TO FEMALE URINARY INCONTINENCE: PRELIMINARY RESULTS OF A SYSTEMATIC REVIEW

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HYPOTHESIS / AIMS OF STUDY
Many results related to the effectiveness of surgical and non-surgical procedures for treating urinary incontinence (UI) are reported in the literature. Following the principles of evidence based-practice, besides the interpretation of study results based on statistical significance, authors should consider evaluating the clinical relevance of treatment effects in this field.

The minimal important difference (MID) of clinical outcomes could be used to assess the clinical relevance of interventions. MID is defined as “the smallest difference in score in the domain of interest that patients perceive as important, either beneficial or harmful, and which would lead the clinician to consider a change in the patient’s management”[1]. One common way to obtain MID for outcomes of interest is by using anchor-based methods. These methods apply one anchor that analyzes the change in the patient's health status according to the patient’s perception.

However, MIDs should be provided according to appropriate calculations and methods and based on the definition of a MID. However, there are a lot of misconceptions and misunderstandings related to the MID. These misunderstandings have led to incorrect reports of these values. Moreover, it is still not known which criteria the authors considered during the analysis of the MID in the Women’s Health area. Therefore, with this preliminary report, we aimed to identify and report all anchor-based methods to estimate MIDs for outcomes measures related to UI available in the literature; and analyze which concepts and levels of improvement in the health status of the patient have been considered by the authors to calculate the MID.

STUDY DESIGN, MATERIALS AND METHODS
This systematic review was conducted according to PRISMA guidelines. The study protocol was registered in the PROSPERO database (CRD42022299686). A systematic search was performed using Ovid Medline, Embase, Web of Science, and Scopus from May to June 2021. Any study generating MIDs for UI that included women with more than 18 years, stress urinary incontinence (SUI), urgency urinary incontinence (UUI) and/or mixed urinary incontinence (MUI) was included. The primary outcome was the MID for outcomes related to UI. No limits were applied on the databases for the date, language or publication range.

Studies were classified into three categories according to the level of improvement in health status assessed by the anchor and considered by the authors during the MID calculation: 1) slight improvement: if authors included participants that evaluated their health status as “a little better” in their analysis; 2) moderate improvement: if authors considered women that reported a “better” or a “much better” status of the condition; or 3) strong imporvement: if all patients that improved (“very much better” or if authors grouped all the patients that improved in one single category) were considered in one group against other group that did not report any improvement. After classifying the papers, we counted and reported how many studies were considering only the minimal level of improvement to reported the MID, according to previous definition and recommendation.

RESULTS
The initial electronic search resulted in a total of 1,662. After removing duplicates (n = 719), 943 were screened, and at the end of the selection stages, nine papers that reported anchor-analysis were included in this preliminary report. Seven studies included women with SUI (total sample size = 2,436), while one study included only women with UUI (n = 307), and the other one evaluated women with SUI and MUI (n = 288). Six studies analyzed data and provided the MID after a non-surgical treatment of UI, while three analyzed the results after surgery to correct UI. Eleven different questionnaires to measure the patient-related outcomes related to UI with their MIDs were identified. All the tools were related to measuring the impact, distress, or quality of life of women with UI.

Different anchors were used to analyze MID, including scales that evaluated the improvement and satisfaction of the patient, and the visual analogue scale, measures of urinary leakage and questionnaires that measure the severity and impact of UI. The MID of six tools was determined according to the smallest difference detected by the patients, using the Patient Global Impression of Improvement questionnaire and the self-reported satisfaction to assess the change of the condition. Most of the MIDs (n = 28, 80%) were miscalculated considering a moderate or a strong improvement of the patients, and not a minimal improvement as suggested by the literature (Table 1).

INTERPRETATION OF RESULTS
Although previous systematic reviews have reported the psychometric properties of different questionnaires to measure UI outcomes, this is the first study to analyze methods of obtaining MIDs for UI outcomes from the patients perspective (anchor based methods). All the tools with their respectives MIDs were related to the impact, distress, and/or quality of life of women with UI. The use of these outcomes measures is in line with the associated impairments of social, psychological, financial, and sexual aspects of a women’s life produced by UI.

Most of the authors in this field did not consider the smallest difference identified by the participants to calculate the MID, which does not follow the original definition of MID proposed by Jaeschke et al.,1 This could generate underestimation or over-estimation of MID, which may directly impact the interpretation of the findings from the clinical trials[2] and biased interpretation of the results of the clinical significance from the interventions used to manage female UI. Therefore, the interpretation of the clinical significance related to UI outcomes should be done with caution.

CONCLUDING MESSAGE
Few studies that aimed to calculate the MID using anchor-based methods for outcomes related to female UI were found in the literature. Eleven different questionnaires to measure the outcomes related to UI with their MIDs were identified. However, most studies had not considered the smallest change of improvement (as perceived by the patients) in their analysis, which does not follow the definition of the MID. This could impact decision making. Future research should provide clear guidelines on how to calculate, report, and interpret MIDs in this field.

FIGURE 1

Table 1. Level of improvement used by the authors to group participants and to calculate the minimal important difference.

Questionnaires	Anchors	Level of improvement in health status considered by the authors to calculate MID
Urogenital Distress Inventory (UDI)	Patient Global Impression of Improvement questionnaire	Moderate
	Incontinence Severity Index	**Slight***
	Voiding diary	Moderate/Strong
	Global Perception of Improvement	Moderate
	Patient Satisfaction Questionnaire	Moderate
Urogenital Distress Inventory - Irritative Subscale	Voiding diary	Moderate
	Global Perception of Improvement	Moderate
	Patient Satisfaction Questionnaire	Moderate
Urinary Distress Inventory – Stress Subscale	Patient Global Impression of Improvement questionnaire	**Slight**
	Incontinence Severity Index	Moderate
	Voiding diary	Moderate
Urinary Impact Questionnaire (UIQ)	Patient Global Impression of Improvement questionnaire	**Slight***
	Incontinence Severity Index	Moderate
	Voiding diary	Moderate
Overactive Bladder Questionnaire (OAB-q) - Symptom Severity (SS)	Voiding diary	Strong
	Global Perception of Improvement	Moderate
	Patient Satisfaction Questionnaire	Moderate
Incontinence Quality of Life (I-QOL)	Patient Global Impression of Improvement questionnaire	**Slight***
	Pad Test	Strong
	Voiding diary	Strong
Pelvic Floor Impact Questionnaire (PFIQ)	Self-reported satisfaction	**Slight***
	Visual analogue scale	Moderate
Pelvic Floor Distress Inventory (PFDI)	Self-reported satisfaction	**Slight***
	Visual analogue scale	Moderate
International Consultation on Incontinence Questionnaire - Short Form (ICIQ-SF)	Patient Global Impression of Improvement questionnaire	**Slight**/Strong
	Satisfaction	Strong
	Pad test	Strong
	Voiding diary	Moderate/Strong
	Urogenital Distress Inventory	Strong
	Incontinence Impact Questionnaire	Strong
ICIQ-Lower Urinary Tract Symptoms Quality of Life (ICIQ-LUTSqol)	Patient Global Impression of Improvement questionnaire	Strong
	Satisfaction with the treatment	Strong
	Pad test	Strong
	Voiding diary	Strong
Australian Pelvic Floor Questionnaire	Patient Global Impression of Improvement questionnaire	**Slight***

Table 1. Level of improvement used by the authors to group participants and to calculate the minimal important difference.

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A PHASE 2, RANDOMIZED, PLACEBO-CONTROLLED, DOUBLE-BLIND STUDY OF TAS-303 IN FEMALE PATIENTS WITH STRESS URINARY INCONTINENCE

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HYPOTHESIS / AIMS OF STUDY

TAS-303, a selective noradrenaline reuptake inhibitor, is in development for the treatment of stress urinary incontinence (SUI) aiming for an effective and safe drug. The present randomized, placebo-controlled, double-blind study was conducted based on the results of an early phase 2 study, which was carried out for an exploratory assessment of the efficacy and safety of TAS-303 3 and 6 mg [1].

The primary objective was to assess the efficacy of TAS-303 18 mg, as measured by the percent change in stress urinary incontinence episode frequency (SUIEF) per 24 hours, by 12-week treatment in female patients with SUI compared with placebo. The secondary objectives were to assess efficacy, as measured by changes in the 24-hour pad weight test, patient reported outcome measures such as the International Consultation on Incontinence Questionnaire – Short Form (ICIQ-SF), Patient Global Impression of Improvement (PGI-I) score, and Incontinence Quality of Life (I-QOL) score; and safety, as measured by the occurrence of adverse events (AEs).

STUDY DESIGN, MATERIALS AND METHODS

This study included female Japanese patients with SUI, including stress predominant mixed urinary incontinence (MUI), aged at least 20 years who had symptoms of SUI for at least 12 weeks and had positive 1-hour pad test results. Aside from these criteria, patients who met the following criteria based on a 7-day bladder diary entry proceeded to the treatment period: mean SUIEF per 24 hours of ≥ 1. Randomization was undertaken using an interactive web response system and stratified by mean SUIEF <2 or ≥2 per 24 hours at baseline and age <60 years or ≥60 years. In this study, after completion of a single-blind observation period receiving placebo once daily for 3 to 4 weeks, the patients orally received TAS-303 18 mg or placebo once daily for 12 weeks in the double-blind treatment period. The primary endpoint was the percent change in mean SUIEF per 24 hours from baseline to week 12. For the primary analysis of the primary endpoint, the differences between the TAS-303 and the placebo group were evaluated using analysis of covariance (ANCOVA) adjusted by the covariate (baseline urinary incontinence weight measured by 24-hour pad test) with a two-sided significance level of 5%. The sample size was determined to have a minimum of 186 subjects, which provide at least 80% power to detect a treatment difference from placebo of 20% in the percent change in SUIEF and the standard deviation assumed to be 46% for both groups.

RESULTS

A total of 231 patients were randomized, and the per protocol set (PPS) was 221 patients (110 in the TAS-303 group, 111 in the placebo group). The mean age in the TAS-303 group was 53.9 years and 54.2 years in the placebo group. 100/110 (90.9 %) patients were diagnosed as SUI in the TAS-303 group and 103/111 (92.8 %) in the placebo group. The mean SUIEF per 24 hours at baseline was 1.99 and 2.16 in the TAS-303 and placebo group, respectively. The percent change in LS mean SUIEF per 24 hours at week 12 in the PPS was -57.50% in the TAS-303 group and -47.35% in the placebo group (Table 1). The difference between the two groups was -10.16 % (ANCOVA p = 0.047; 95% confidence interval -20.17, -0.14), indicating a significant decrease in the TAS-303 group compared with placebo. As for the secondary endpoints, the change in the mean SUIEF per 24 hours at week 12 was -1.14 in the TAS-303 group and -0.90 in the placebo group. The rate of ≥50% reduction in mean SUIEF per 24 hours at week 12 was 64.5 % in the TAS-303 group and 54.1 % in the placebo group. The mean change in the 24-hour pad test at week 12 was -9.33 g in the TAS-303 group and -7.93g in the placebo group. The mean change in ICIQ-SF at week 12 was -3.0 and -2.8, and the mean change in I-QOL at week 12 was +11.1 and +9.9 in the TAS-303 and placebo group, respectively. More patients in the TAS-303 than in the placebo group rated themselves as “very much better”, “much better” using the PGI-I rating at week 12 (TAS-303 53.6%, placebo 42.3%). The incidence and severity of AEs in the TAS-303 group was similar to that in the placebo.

INTERPRETATION OF RESULTS

It was shown that in the TAS-303 group, percent change in mean SUIEF per 24 hours from baseline at week 12 significantly decreased compared to the placebo group. This study suggests that TAS-303 may be an effective and favorable treatment option for SUI by increasing basal urethral pressure.

CONCLUDING MESSAGE

As a superior effect and safety of this drug is suggested in SUI patients, further research with a larger number of patients is needed to confirm the therapeutic effect in SUI patients.

FIGURE 1

An intergroup comparison of Percent Change from Baseline in mean frequency of Stress Urinary Incontinence episodes per 24 hours (PPS-1)

	Placebo (N =111)	TAS-303 18 mg (N =110)
ANCOVA		
Percent Change from Baseline in mean frequency of Stress Urinary Incontinence episodes per 24 hours at Week 12 (%)		
LS Means	-47.347	-57.503
95%CI	[-54.409 , -40.285]	[-64.597 , -50.410]
Difference of LS Means		-10.157
95%CI		[-20.173 , -0.140]
P Value		**0.047**

Analysis Set: PPS-1
Fixed Effects: Group (TAS-303 18 mg) (Base:Placebo), 24-hour Pad weight Test

Table 1. Percent change in LS mean SUIEF per 24 hours at week 12

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TRANSURETHRAL INJECTION OF AUTOLOGOUS MUSCLE PRECURSOR CELLS FOR THE TREATMENT OF FEMALE STRESS URINARY INCONTINENCE – A PROSPECTIVE AND RANDOMIZED PHASE I CLINICAL TRIAL

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HYPOTHESIS / AIMS OF STUDY

To investigate the safety and feasibility of a tissue-regenerative approach to treat stress urinary incontinence (SUI) in female patients with a novel transurethral injection therapy using autologous muscle precursor cells (MPCs) in a combination with neuro-muscular electromagnetic stimulation (NMES).

STUDY DESIGN, MATERIALS AND METHODS

We conducted a prospective and randomized clinical trial using ultrasound-guided injections of autologous MPCs into the external urinary sphincter (EUS) muscle of female patients with SUI to assess the safety and feasibility of this therapy. Main inclusion criteria were female gender, age 20–60 years and clinical diagnosis of SUI grade ≥I since at least 6 months. Exclusion criteria were a history of anti-incontinence or prolapse surgery, urgency urinary incontinence due to urodynamically proven detrusor instability, history of urogenital cancer or pelvic radiotherapy, pregnancy or <12 months post-partum or an unstable systemic, neurological or genetically determined muscular disease. Standardized 1h pad test, incontinence and quality of life questionnaires (ICIQ), urodynamic studies, and MRI of the pelvis were performed at baseline and follow-up visits. MPCs were gained through an open surgical biopsy from the Soleus muscle of the lower limb. A muscle specimen ≥200mg was then transported in biopsy medium to the GMP facility for processing and cell expansion. Eighty to 100 x 106 cells were re-suspended in collagen solution for injection of the final product. The cooled (2-8°C) final product was then implanted with 8-12 injections under ultrasound guidance in the EUS using a Bard needle (20cm, 18G). After the injection, the study nurse unveiled the randomisation to the two treatment groups of either MPCs alone (Group A) or MPCs + NMES (Group B). NMES included two sessions per week for 20 minutes for 6 weeks (total of 12 sessions) on a BioCon-2000WTM chair (Marly Products, Germany). Follow-up visits were arranged at the first or second postoperative day and thereafter 1, 3 and 6 months after the injection. To analyse the safety and feasibility of our therapy, primary outcome was defined as any adverse event (AE) during the follow-up period. Secondary outcomes were 1h pad test, bladder capacity, functional urethral length (resting and stress profiles), urethral pressure profiles (resting and under stress), ICIQ questionnaires to evaluate quality of life, and the change in sphincter diameter in the follow-up MRI of the pelvis at 6 months. Paired Wilcoxon signed-rank test was used to compare medians between baseline and follow-up visits. Statistical significance was regarded as $p < 0.05$.

RESULTS

Ten female patients were included in the study, of which 9 received treatment and completed all follow-up visits during the study period between 01/2020 and 09/2021. Patients had SUI grade ≥I, a median age of 45 years (range: 32-58 y) and a median BMI of 24 kg/m2 (range 21.0-29.4 kg/m2). After MPC injection, patients were subsequently randomized either into Group A (n=5) or Group B (n=4). Eight adverse events (AEs) were registered, of which 2 (25%) were potentially related to the treatment. One urinary tract infection (UTI) was diagnosed three weeks after injection of MPC and was successfully treated with a single dose of oral Fosfomycin. Dysuria as of burning micturition was treated conservatively in one further patient. No severe AEs (SAEs) were registered. Median urethral closure pressure was 79 cmH2O at baseline compared to 71 cmH2O at 6 months follow-up (95% CI: -9 to 28.5, p = 0.859). Median functional urethral length (FUL) under stress was significantly shorter with 25 mm at baseline compared to 30mm at 6 months follow-up (95% CI: 2.5 to 7, p = 0.009). Median maximum bladder capacity was 610ml at baseline and 670ml at follow-up (95% CI: -45 to 140, p = 0.343). QoL questionnaires showed an improvement ICIQ-scores from median 7 points at baseline to median 4 points at 6 months follow-up (95% CI: -7 to -2.5, p-value = 0.035). The evaluation of MRI of the pelvis revealed no evidence of aberrant tissue formation or necrosis. Diameter of EUS muscle was measured with a median of 1.8 mm at baseline and 1.9 mm at follow-up (95% CI: 0.10 to 0.25, p = 0.009).

INTERPRETATION OF RESULTS

Our analysis demonstrated an objective improvement of the median FUL under stress in the urodynamic study 6 months after injection of autologous MPCs into the EUS muscle. Further, the subjective QoL improved with a lower median ICIQ-score 6 months after the intervention. However, these results need to be interpreted with caution since this was a phase I trial investigating safety and feasibility solely. Efficacy and durability of the treatment needs to be confirmed with larger patient cohorts and longer follow-ups in particularly designed and powered phase II and III trials.

CONCLUDING MESSAGE

The transurethral ultrasound-guided injection of autologous MPCs into the EUS muscle for the treatment of SUI in female patients can be regarded as safe and feasible. Only a minimal number of expected AEs were documented, and all AEs were well-treatable and healed without sequelae. No severe or unexpected AEs were diagnosed.

Funding This project has received funding from the European Union's Horizon 2020 research and innovation program under Grant Agreement No. 731377. **Clinical Trial** Yes **Registration Number** ClinicalTrials.gov, NCT03439527 **RCT** Yes **Subjects** Human **Ethics Committee** Kantonale Ethikkommission Zürich (KEK-ZH-Nr. 2014-0547, BASEC Nr. PB_2017-00621) and Swissmedic (Ref. Nr. 2014TpP1009) **Helsinki** Yes **Informed Consent** Yes

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TREATMENT OF MILD TO MODERATE STRESS URINARY INCONTINENCE WITH A NOVEL POLYCAPROLACTONE-BASED BIORESORBABLE URETHRAL BULKING AGENT

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HYPOTHESIS / AIMS OF STUDY

There is a wide range of treatment options available for Stress Urinary Incontinence (SUI), including non-surgical therapy (pelvic floor muscle training, electric stimulation, change in fluid intake and drug therapy) and surgical treatment. The most widely used surgical treatment for SUI is the midurethral sling (MUS) procedure; the retropubic (TVT) or the trans obturator sling (TOT).

With the recent safety concerns and suggested underestimation of complications such as urethral obstruction requiring surgery, vaginal, bladder and/or urethral erosion requiring surgery, and refractory chronic pain associated with MUS procedures, there is a growing interest for alternative less invasive treatment options for SUI without major risks for complications. One of such alternative minimally invasive treatment option for SUI is the urethral injection of a bulking agent. A fully bioresorbable polycaprolactone-based bioresorbable bulking agent was evaluated for safety and efficacy in female patients with mild to moderate stress urinary incontinence who attempted and failed prior pelvic floor muscle training.

STUDY DESIGN, MATERIALS AND METHODS

In this multicenter study, female subjects of 18 years and older were eligible for inclusion. Inclusion criteria consisted of subjects who suffer from predominantly SUI as determined by the Questionnaire for Urinary Incontinence Diagnosis (QUID); Total Stress Score (Sum Q1-3) of $\geq$ 4 and Total Urge Score (Sum Q4-6) of $<$ 6. Subjects must have attempted or failed prior pelvic floor exercises while incontinent, suffer from mild to moderate SUI as confirmed by the Stamey Grading Scale (SGS) 1 or 2, able to comply with trial follow-up procedures, schedule, and are willing to provide written informed consent for their participation in the trial. Fifty female subjects were treated by transurethral sub-mucosal injection. Over a period of 24 months safety was evaluated during a 24-monts follow-up period. At the 12-month visit, a cystoscopy was performed for visual inspection of the injected area. Efficacy was assessed with the same intervals with the Stamey Grading System (SGS) among others.

RESULTS

Only 6/50 subjects reported transient mild adverse events. The results show for the SGS grade more than 55% of the participants had an improvement in SGS grade of whom 40% were cured within the first 12 months after treatment. During the second year of follow-up the effect seems to falter with an improvement of 50% of the subjects of whom 25% were cured.

INTERPRETATION OF RESULTS

The aim of the study was to evaluate treatment safety and efficacy of a novel PCL-based bioresorbable bulking agent used for the treatment of mild to moderate SUI in female subjects. In this study the two-year follow-up results are presented. The results of the study suggest that treatment of mild-to-moderate SUI with a bioresorbable PCL-based bulking agent is a safe and effective alternative to permanent bulking agents and intermediate treatment option before the use of the permanent MUS.

CONCLUDING MESSAGE

A polycaprolactone-based bioresorbable bulking agent was evaluated as a new minimally-invasive treatment option for adult females with mild- to moderate SUI.

Funding This study was sponsored by AQLANE Medical BV, The Netherlands and was performed in collaboration with the Clinical Research Organization Medpace (Maastricht, The Netherlands). **Clinical Trial** Yes **Registration Number** Trial Registration: Reference NL5760 (NTR6002) (Netherlands); Reference 80M0633 (Belgium). **RCT** No **Subjects** Human **Ethics Committee** Ethical Committee approval was obtained in The Netherlands and Belgium. **Helsinki** Yes **Informed Consent** Yes

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BULKAMID® INJECTION AS A SALVAGE TREATMENT OPTION IN PATIENTS WITH RECURRENT STRESS URINARY INCONTINENCE: MEDIUM TERM OUTCOMES FROM A TERTIARY UNIT

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HYPOTHESIS / AIMS OF STUDY
The outcomes for Bulkamid® injection as a primary procedure for stress urinary incontinence (SUI) have been well reported. However, the outcomes for patients with previous failed SUI surgery are less known. The aim of our study is to identify the factors which could predict the outcomes of Bulkamid® injection as a salvage treatment alternative.

STUDY DESIGN, MATERIALS AND METHODS
Data collected prospectively between 2017-2021 was analysed retrospectively. All patients had had at least one previous anti-incontinence operation. Data including demographics, urodynamic parameters, type and number of previous anti-incontinence procedures, number and total injected amount of Bulkamid® were analysed. Outcomes were assessed with number of pads where possible, and were categorised as dry, improved or wet according to patient satisfaction. Shapiro-Wilk tests of normality were performed.

RESULTS
Results are shown on Table 1. Twenty patients with mean age of 63 (range 32-88) years were treated with a mean follow up 17 (range 2-52) months. Fourteen patients had one set of injections and six had two injections. The overall success rate was 35% (10% dry, 20% improved and 70% failed) with 30% successful after one injection and 35% after two injections.

Four of eight patients with Type III SUI had a 50% chance of success (37.5% dry and 12.5% significantly improved after the first injection), whereas no improvement was observed in the 5 patients with Type IIA / IIB SUI (100% failure). One patient with mixed urinary incontinence had no improvement after the Bulkamid® injection.

The success rate for patients with one previous procedure was 37% (25% dry, 12.5% improved), whereas the success rate for patients with two or more previous procedures was 25% (0% dry, 25% improved).

Patients who had previous TOT/TVT-O insertion, autologous rectus fascial sling or Macroplastique® injections showed higher success rate (63% dry or improved), whereas patients with TVT, colposuspension, SNS/Botox or complex reconstruction were poor responders (16% dry or improved).

Injection of more than 2.2ml of Bulkamid® had better outcomes compared to smaller volumes (55% versus 35% success).

INTERPRETATION OF RESULTS
Patients with multiple previous procedures seemed to do less well than those with a single previous procedure. Interestingly, patients with Type III SUI did better than those with persistent Type IIA/IIB SUI, and those with previous obturator tapes and autologous slings seemed to do better than those with TVT or colposuspension, which may suggest that bulking injections treat sphincteric deficiency better than hypermobility.

CONCLUDING MESSAGE
The success rate of Bulkamid® injection as salvage therapy was significantly lower than reported in the literature as a primary therapy. Further prospective studies of Bulkamid® are in process for patients with recurrent SUI.

FIGURE 1

			N (%)	Pre-operative pad Mean (SD)	Post-operative pad Mean (SD)	Outcomes		
						Dry N (%)	Improved (but not completely dry) N (%)	Failed N (%)
Age	<63 years old		9/20 (45%)	4.7 (1.4)	3.3 (2.05)	1/9 (11%)	1/9 (11%)	7/9 (78%)
	≥63 years old		11/20 (55%)	4.4 (2.2)	3.9 (2.7)	1/9 (11%)	3/9 (33%)	5/9 (56%)
BMI	18.5 to 24.9		5/20 (25%)	4.7 (1.5)	4.5 (1.3)	0/5 (0%)	0/5 (0%)	5/5 (100%)
	25 to 29.9 (overweight)		4/20 (20%)	3.5 (0.7)	5 (7)	1/4 (25%)	0/4 (0%)	3/4 (75%)
	30 to 39.9 (obese)		4/20 (20%)	5.25 (2.1)	3.1 (0.85)	0/4 (0%)	1/4 (25%)	3/4 (75%)
	≥ 40 (severely obsess)		1/20 (5%)	7	4	0/1 (0%)	1/1 (100%)	0/1 (05)
Gender	Female		18/20 (90%)	4.6 (1.9)	3.6 (2.4)	2/18 (11%)	4/18 (22%)	12/18 (67%)
	Male		2/20 (10%)	4 (2.8)	4 (2.8)	0/2 (0%)	0/2 (0%)	2/2 (100%)
Type of incontinence (confirmed with urodynamics)	Type IIA		2/20 (10%)	5	5	0/2 (0%)	0/2 (0%)	2/2 (100%)
	Type IIB		3/20 (15%)	4.3 (1.5)	4 (1)	0/2 (0%)	0/2 (0%)	3/3 (100%)
	Type III		8/20 (40%)	4.9 (2.2)	3.7 (2.9)	3/8 (37.5%)	1/8 (12.5%)	4/8 (50%)
	MUI		1/20 (5%)	3	3	0/1 (0%)	0/1 (0%)	1/1 (100%)
	No SUI or UUI		2/20 (10%)	NA	NA	0/2 (0%)	0/2 (0%)	2/2 (100%)
	NA		5/20 (25%)					
No Previous SUI operations	1 operation		8/20 (40%)	3.7 (1.8)	3.1 (3.6)	2/8 (25%)	1/8 (12.5%)	5/8 (62.5%)
	≥1 operations		12/20 (60%)	4.9 (1.8)	4 (1.1)	0/12 (0%)	3/12 (25%)	9/12 (75%)
Type SUI Operations	Mesh	TVT	5/20 (25%)	5.2 (2.9)	3 (2.3)	1/5 (20%)	0/5 (0%)	4/5 (80%)
		TVT-O	5/20 (25%)	3.2 (1.2)	2.2 (1.5)	1/5 (20%)	2/5 (40%)	2/5 (40%)
		TOT	1/20 (5%)	4	2	0/1 (0%)	1/1 (100%)	0/1 (0%)
	Colposuspension		8/20 (40%)	5 (1.7)	4.8 (2.7)	0/8 (0%)	2/8 (25%)	6/8 (75%)
	Autologous Rectus Fascial Sling		2/20 (10%)	3.5 (0.7)	2.5 (0.7)	0/2 (0%)	1/2 (50%)	1/2 (50%)
	Botox		6/20 (30%)	5.2 (1.5)	4.2 (0.8)	0/6 (0%)	1/6 (17%)	5/6 (83%)
	Sacral Neuromodulator		2/20 (10%)	3	3	0/2 (0%)	0/2 (0%)	2/2 (100%)
	Macroplastique		4/20 (20%)	5 (1.7)	3.3 (1.1)	0/4 (0%)	2/4 (50%)	2/4 (50%)
	Others (ileocystoplasty, AUS, neobladder and mitrofanoff)		3/20 (15%)	4.5 (2.1)	4.5 (2.1)	0/3 (0%)	0/3 (0%)	3/3 (100%)
Number of injections	2		2/20 (10%)	3.5 (3.5)	0.5 (0.7)	1/2 (50%)	1/2 (50%)	0/2 (0%)
	3		5/20 (25%)	5.2 (2.6)	3.5 (0.6)	0/5 (0%)	2/5 (40%)	3/5 (60%)
	4		12/20 (60%)	4.4 (1.3)	4.2 (2.6)	1/12 (8.3%)	2/12 (16.7%)	9/12 (75%)
Total volume of injected Bulkamid	<2.2 ml		11/20 (55%)	3.8 (1.2)	3.8 (2.8)	2/12 (16.7%)	0/12 (0%)	10/12 (83.3%)
	≥2.2 ml		7/20 (35%)	6.2 (1.3)	3.8 (1.4)	0/7 (0%)	3/7 (42.8%)	4/7 (57.2%)

Table 1. Outcomes of Bulkamid® injections for recurrent SUI

Funding None **Clinical Trial** No **Subjects** Human **Ethics Committee** Audit department of our hospital **Helsinki** Yes **Informed Consent** Yes

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MESH EXPOSURE AFTER MIDURETHRAL SLINGS. A NATIONAL OBSERVATIONAL STUDY OF 9 YEARS OF PRACTICE IN DENMARK

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HYPOTHESIS / AIMS OF STUDY

Stress urinary incontinence (SUI) is a common diagnosis amongst women. A popular and effective surgical treatment is the minimal invasive midurethral slings (MUS). Up to 85% of women treated with these operations are cured or experience significant improvements after surgery. Overall, the complications are few. A common long-term complication to MUS is exposure of the mesh to the vagina, urethra, or bladder. This complication is difficult to diagnose as symptoms vary considerably. Symptomatic treatment may include local estrogen, covering the mesh with vaginal tissue, or ultimately removal of the mesh, resulting in recurrence of urinary incontinence. Therefore, prevention of mesh exposure is paramount. It has been suggested that mesh complications after insertion of MUS is related to presence of inflammation and infection. There is no consensus about prophylactic use of perioperative antibiotics. Current use of prophylactic antibiotics for MUS is depending on local tradition, surgeon's experience, and individual preoperative evaluation of patient risk. The Retropubic MUS (R-MUS) and the Trans-obturator MUS (O-MUS) are placed anatomically differently; the R-MUS has a close relation to the bladder, which might increase the number of bladder exposures, while the O-MUS has a more horizontal approach in the vagina, which might increase the risk of vaginal exposures.

The aim of the study was to estimate the effect of single dose perioperative antibiotics on mesh exposure in patients undergoing MUS surgeries in a Danish national cohort study. Secondary, we wanted to compare the exposure rate after R-MUS compared to O-MUS.

STUDY DESIGN, MATERIALS AND METHODS

We included women undergoing MUS during 2010-2018 in this nationwide register-based cohort study and followed them until December 31, 2018.

Data was collected from the Danish Urogynecological Database (DugaBase). The DugaBase contains clinical data from all urogynecological surgical interventions performed in Denmark since 2006.

The Dugabase was supplemented with data from the Danish National Patient Registry (DNPR). The DNPR includes diagnoses and surgical interventions at all Danish hospitals since 1977. In Denmark, it is mandatory to register surgical procedures in both databases, which ensures high data validity and completeness of data. The outcome, mesh exposure, was retrieved through diagnosis or procedure codes from the DNPR.

Patients who previously underwent pelvic organ prolapse (POP) surgery with mesh and

SUI surgeries were identified via the DNPR and excluded. Patients undergoing POP surgery with mesh after initial MUS were censored.

We conducted Cox regression analyses to determine if a single dose perioperative antibiotic affected the risk of mesh exposure. We adjusted for patient age, body mass index (BMI), income, education, smoking habits, alcohol consumption, American Society of Anesthesiologist's (ASA) score, surgeon's experience and type of MUS.

To investigate the risk of mesh exposure after R-MUS versus O-MUS, we conducted Cox regression analyses adjusted like mentioned above plus for antibiotics.

Due to the observational and register-based nature of this non-interventional study, a sample size calculation was not computed.

RESULTS

A total of 6,706 women were included, out of whom 5,178 (77.2%) were given antibiotics perioperatively, while 1528 (22.8%) women were not. Mean age was 52.1 in both groups. Furthermore, the groups were comparable according to BMI, ASA score, surgeon's experience, smoking habits, level of income and education.

Totally 3,991 women underwent R-MUS surgery and 2,715 women underwent O-MUS surgery. Likewise, these groups of women were comparable. However, a higher proportion of women undergoing R-MUS received perioperative antibiotics (81.9%) compared with women undergoing O-MUS (70.4%).

A total of 1.3% (87/6706) mesh exposures were diagnosed within the 9 year study period, 1.2% (62/5178) in the group that received perioperative antibiotics and 1.6% (25/1528) in the group that did not. 0.9% (34/3991) of the women were diagnosed with mesh exposures after R-MUS and 2.0% (53/2715) after O-MUS.

We found an insignificant tendency toward reduced risk of mesh exposure when perioperative antibiotics were administrated in the total population (HR = 0.7 (CI 0.4-1.1)). However, it was very different for the two types of MUS. After O-MUS significantly fewer women were diagnosed with mesh exposure if perioperative antibiotics were administrated HR = 0.4 (CI 0.3-0.8). The same tendency was not found for women undergoing R-MUS (HR = 3.1(CI 0.7-13.1)).

We found that the type of MUS highly affected the risk of mesh exposure. Undergoing R-MUS significantly reduced the risk compared with undergoing O-MUS: HR = 0.4 (CI 0.3-0.6).

Cumulative incidence plots for mesh exposure comparing R-MUS and O-MUS (Figure 1) and comparing use of perioperative antibiotics or not in the women undergoing O-MUS surgery (Figure 2) are presented.

INTERPRETATION OF RESULTS

This nationwide cohort study found a significantly reduced risk of mesh exposures after O-MUS if perioperative antibiotics are administered. We did not find same significant association in the R-MUS group and in the total group.

This could reflect a type II error as few women undergoing R-MUS did not receive perioperative antibiotics and the number of mesh exposures was low. The findings indicate that perioperative antibiotics should be administered to women undergoing O-MUS to reduce the risk of mesh exposure. Whether perioperative antibiotics should be standard care for women undergoing R-MUS operation may be debated.

Furthermore we found that women undergoing O-MUS surgery have significantly more mesh exposures compared with women undergoing R-MUS surgery.

CONCLUDING MESSAGE

The risk of mesh exposure after O-MUS surgery is significantly reduced if perioperative antibiotics are administered.

Significantly fewer mesh exposures are seen after R-MUS, which might be preferred.

FIGURE 1

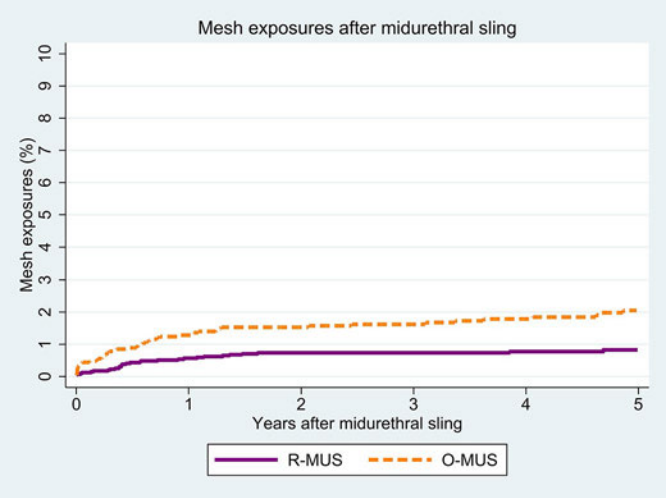
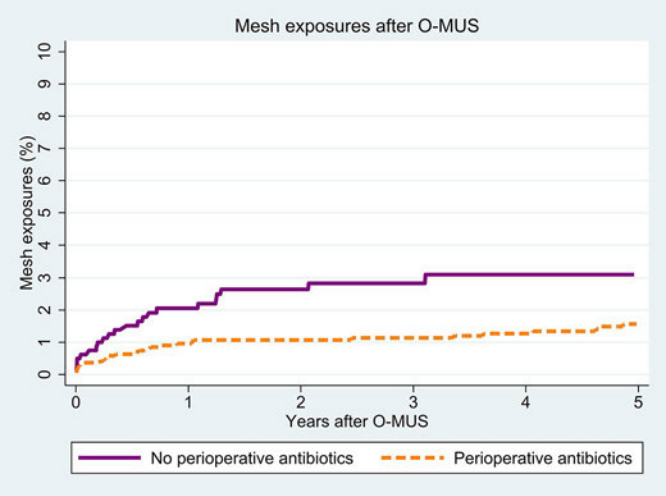


FIGURE 2



Funding None **Clinical Trial** No **Subjects** Human **Ethics not Req'd** According to Danish law, ethical approval is not required for register-based studies **Helsinki** not Req'd This was a register based study **Informed Consent** No

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PVDF VS PP TAPES IN THE MANAGEMENT OF FEMALE STRESS URINARY INCONTINENCE: INITIAL SINGLE-CENTER EXPERIENCE.

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HYPOTHESIS / AIMS OF STUDY

Midurethral slings are currently composed mostly of polypropylene (PP). PP has been proven to cause fewer complications, mainly due to the fact that it is inert, not sifting, not allergic, and not causing inflammatory reactions. Nevertheless, common complications related to PP tapes are postoperative voiding problems, tape erosions in the vagina or adjacent organs, voiding problems, recurrent urinary infections, etc. Therefore, it is of paramount value to discover novel materials with different and if possible minimal complication profiles in the management of stress urinary incontinence (SUI). It seems that polyvinyldihydrofthoride (PVDF) is theoretically a useful alternative in SUI treatment. PVDF has been massively used in other prosthetic fields of medicine (cardiac valves, orthopedics) and it is related to reduced rates of rejection, erosion, inflammatory reactions, pain or dysfunction (1,2).

The aim of the study is to compare the effectiveness and safety of PP and PVDF transobturator tapes (TOT) for the treatment of female SUI.

STUDY DESIGN, MATERIALS AND METHODS

This is a clinical, cross-sectional, single-centre study in an academic urogynecologic unit. As no relevant literature exists, a convenience sample of two groups from 30 patients each was considered as adequate for a non-inferiority study. Sixty female patients with SUI who consecutively underwent TOT surgery with PVDF (group PVDF: 30 patients) or PP (group PP: 30 patients) sling between January 2018 and December 2021. Inclusion criteria were: (a) women over the age of 18, (b) Greek speakers, and (c) women with at least moderate SUI/MUI. Informed consent was obtained as appropriately by all the participants and the study protocol was approved by the Ethics Committee of the hospital. All patients before surgery had a clinical examination and a standardized cough test. Symptoms were measured with the use of the ICIQ-UI (short form) questionnaire and the patients had a full urodynamics investigation (uroflowmetry, filling cystometry, pressure-flow studies, and urethral profilometry). All patients had pelvic floor sonographic evaluation (PFUS: urethral mobility assessment, bladder wall thickness (BWT) assessment). All patients had a transobturator mid-urethral sling (PVDF or PP) with a standardized inside-out technique. Then, both groups were examined 6 months post-operatively with: (a) clinical exam and standardized stress test, (b) check for tape erosions, (c) urethral mobility and sling mobility, (d) PGI-I and PGI-S score. Urethral and sling mobility were analyzed according to a standardized and reproducible method described by Schaer et al (1,2). Statistical analysis was performed with MedCalc. An independent paired t-test was used to compare the pre- and post-operative results of the PVDF and PP groups. Statistical significance was defined as p 0.05.

RESULTS

60 patients were recruited. The PVDF group mean age was 61.2 ± 8.0 years and the PP group was 61.6 ± 5.9 years ($p = 0.84$). The mean BMI in the PVDF group was 29.3 ± 3.4 and in the PP group was 29.5 ± 3.3 kg/m2 ($p = 0.89$). The mean parity was 2.1 ± 1.0 for PVDF group and 2.1 ± 0.8 for PP group (p-value: 0.45). In PVDF group 24/30 (80%) and in PP group 22/30 (73%) of patients underwent prolapse surgery simultaneously ($p = 0.542$). Pre-operatively, 83% of the patients in PVDF group and 80% of the PP group had moderate or severe SUI ($p = 0.866$). The main urethral length was 3.33 ± 0.41cm for PVDF group and $3,43 \pm 0,35$cm for PP group ($p = 0.19$). Pre-operatively, mean Bladder Neck Mobility (BN-MOB) in PVDF and PP groups was 1.26 ± 0.36 and 1.20 ± 0.35, respectively ($p = 0.48$).

In the 6 months examination, 28/30 (93.3%) of PVDF group and 25/30 (83.3%) of PP group had a negative stress test ($p = 0.644$). No tape erosion into the vagina was identified in PVDF group, although in PP group there was an incidence of erosion (1/30, 3.3%). No post-operative pain or dyspareunia was reported by any of the patients, and there was no pathological post-void residual (PVR) in both groups. PVDF group had a statistically significant better PGI-S score than PP group (1.37 vs 2.03, $p = 0.02$) and there wasn't any statistically significant difference in PGI-S score between the two groups. The mean distance of the sling from the inside urethra orifice was 1.9 ± 0.4cm in PVDF group and 1.9 ± 0.3cm in PP group ($p = 0.35$). The patients in the PVDF group exhibit higher but not statistically significant decrease of urethral mobility post-operatively (0.63 ± 0.34cm vs 0.49 ± 0.56cm, $p = 0.22$). Also, we found a higher but not statistically significant sling mobility in PVDF group (0.82 ± 0.69 vs 0.71 ± 0.24 cm) ($p = 0.41$).

INTERPRETATION OF RESULTS

Incontinence surgery is facing a challenge due to the constant improvement of techniques and materials used. Initial approaches with polypropylene meshes of various types and weaves had the result that numerous varieties of materials were gradually abandoned from clinical practice because of increased complications or decreased success rates. Macroporous type I PP tapes were established as the ideal type of material for suburethral incontinence operations. Nevertheless, the inherent disadvantages of PP tapes are the erosion, the migration, and the diminishing of the successful outcome over time. This study provides an initial insight into the use of PVDF tapes. Early experience seems to be promising, with results comparable to those of the PP tapes.

CONCLUDING MESSAGE

This is one of the first studies where PP slings are compared to PVDF slings for the surgical treatment of SUI. Initial experience with the use of PVDF tapes as sub-urethral slings appears to be satisfactory in terms of safety, functionality, and effectivity. Large, prospective, non-inferiority studies have to be performed in order to demystify the exact efficacy of these tapes in the field of pelvic surgery.

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BEST IN CATEGORY PRIZE: FEMALE STRESS URINARY INCONTINENCE (SUI)

SERIOUS COMPLICATIONS AND RECURRENCE AFTER STRESS URINARY INCONTINENCE SURGERY BY MID-URETHRA SLING IN THE VIGI-MESH REGISTER: DESCRIPTION AND MEDIUM-TERM INCIDENCE FOR 2683 WOMEN

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HYPOTHESIS / AIMS OF STUDY

Surgery for stress urinary incontinence (SUI) by mid-urethral sling (MUS) has become a standard widely used in routine clinical practice. The retropubic procedure is the one for which there is the most long-term data. Transobturator route (out-in or in-out) has been developed with the intention of simplifying the surgical procedure and reducing the risk of complications.

In the 2010's, growing awareness was raised of serious complications of surgical meshes used in urogynecological surgery.

Unlike clinical trials, the registries offer the possibility of specifying the occurrence of rare events in routine clinical practice.

Our objective is to specify the incidence and to describe the serious complications related to surgery by MUS in routine clinical practice according to the type of sling (retropubic or transobturator) using the long-term data from the French VIGI-MESH registry(1). We also aimed to compare the reccurence rate of both approach.

STUDY DESIGN, MATERIALS AND METHODS

All patients who benefit of the MUS by retropubic or transobturator route since February 2017 were included in the analysis.

We collected all serious complications (Grade III and Grade IV according to modified Clavien-Dindo classification) and reoperation for recurrence of SUI.

Intra-operative injuries requiring cancelled placement of the sling were counted as grade III. Declared complications were analysed to assess imputability of the MUS procedure. In accordance with the design of the registry, the surgeons reported complications and reoperations on a specific form during follow-up. To ensure the completeness of the surgeons's reports (for complications and reoperations), we checked the data collected by each hospital's data department to link and monitor medical events after the index surgery. Annual follow-up questionnaires were also sent to seek for new unknow complications. The end of the study period was October 2021.

To balance the baseline differences between both groups, we used a propensity score approach with inverse probability of treatment weighting with pre-specified variables (age, body mass index, smoking, diabetes, previous hysterectomy, previous surgery for SUI or pelvic organ prolapse, physical status score and menopausal status).

Two Cox proportional hazard's models with a frailty term taking into account the centre effect and the occcurence of concomitant hysterectomy or prolapse surgery were used to compare both approach.

RESULTS

Between February 2017 and October 2021, 3316 women underwent surgery for SUI among which 2683 benefited of MUS by retropubic (1831 women) or transobturator (852 women) route: 211 out-in and 639 in-out (2 unkown).

Women in the transobturator group were older than the others (58.8 years vs 56.9 years, $p < 0.001$) and history of SUI surgery was more frequent in the retropubic group (13.1% vs 3.2%, $p < 0,001$).

The maximum follow- time was 88 months. We observed serious complications for 124 women: 100 patients in the retropubic group and 24 in the transobturator group.

25 complications occurred in the retropubic group during surgery or within the first 48 hours following surgery: 8 grade III intraoperative injuries (4 bladder wounds, 3 urethral wounds and 1 vascular injury), 1 intraoperative hemorrhage, 13 obstructed micturitions, 2 postoperative hematomas and 1 neuropathic pain on the obturator territory.

In the transobturator group, 5 complications were reported during surgery or within the first 48hours: 3 grade III intraoperative injuries (2 vaginal and 1 urethral wounds), 1 obstructed micturition; and 1 neuropathic pain on the obturator territory. Post-operative neuropathic pain was treated by the removal of the mesh. Postoperative hematomas were taken care by drainage by coelioscopy or laparotomy.

From 48 hours to 2 months after the initial intervention, there were 38 complications in the retropubic group and 8 in the transobturator group. In the retropubic group, we observed 32 obstructed micturitions, 3 vaginal exposure et 3 mesh infections. Mesh infections were treated by removal of the mesh. In the transobturator group, 6 women had obstructed micturition, a woman needed a laparotomy due to infected haematoma of Retzius space and one woman needed to return to the operative room to evacuate a suburethral thrombus that had resulted in obstructed micturition.

From 2 months to 12 months after initial intervention, there were 31 complications in the retropubic group: 23 mesh exposure (20 vaginal exposure, 2 urethral exposure, 1 non described exposure), 5 obstructed micturitions et 3 chronic pain (among one patient with pain during sexual intercourse).

During this period, there was 6 complications in the transobturator group: 2 obstructed micturitions et 4 vaginal exposure. For the 3 women requiring reintervention for chronic pain, the mesh was removed in 2 cases (by vaginal route or laparotomy). The women presenting pain during sexual intercourse benefited of vaginal trimming without resection of the mesh.

Beyond 12 months after initial intervention, there was 6 complications in the retropubic group: 3 obstructed micturitions and 3 chronic pain. Women with chronic pain benefited of the removal of the sling by vaginal route or laparotomy or of vaginal trimming without resection of the mesh.

During this period, 5 women in the transobturator group had complications: 1 vaginal exposure, 1 urethral exposure, 2 obstructed micturitions and one women with a painful vaginal polyp removed surgically by vaginal route.

In both groups during the study period, obstructed micturitions were treated either by loosening of the sling vaginally when diagnosed early after surgery (41 women), section of the sling (11 women) or removal of the sling (12

women). Mesh exposure were treated either by vaginal trimming without resection of the mesh (3 patients) or by removal of the mesh (28 patients).

The survival curve without serious complication showed a significant difference between MUS types in favor of the retropubic route (Logrank-p value = 0.001 and Figure 1). The estimated incidence at 36 months of serious complications was 5.9% in case of retropubic sling, and 2.8% in the case of a transobturator sling. Taking into account potential confounders, the risk of complication was more than two time lower in the transobturator approach (HR = 0.43; IC95% = 0.31 to 0.59).This difference remain significant after exclusion of patient with previous history of SUI.

The risk of reoperation for recurrence of SUI was similar between groups (HR = 0.97; IC95% = 0.58 to 1.69 and Figure 2).

INTERPRETATION OF RESULTS

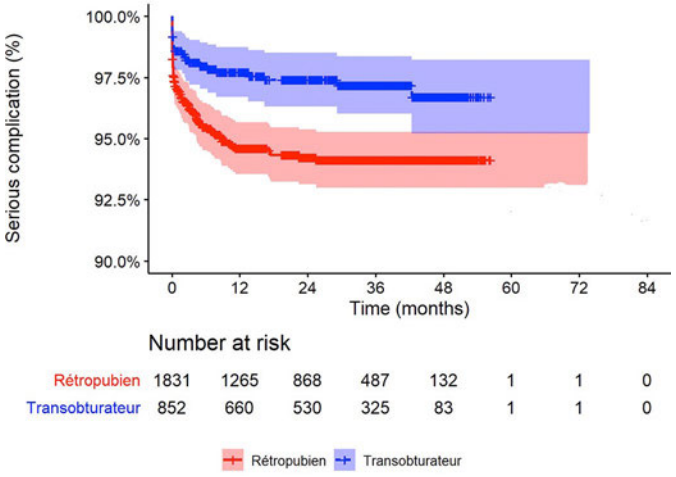
The retropubic route was associated with a higher risk of complication than the transobturator route. On the other hand, there was no difference in recurence rate needing reoperation between both approach. These results are in line with a previous clinical trial comparing both approach(2). However, more recent meta-analyses did not confirmed those differences(3). Differences between both groups were related mostly to voiding obstruction. On the other hand, other perioperative events and other medium term events were also more frequent in the retropubic group. Baselines characteristics were different in particular an history of SUI procedure was more frequent in the retropubic group, nonetheless the difference in serious complications rate remains after excluding these women.

CONCLUDING MESSAGE

Analysis of long term results in our registry show higher risk of serious complication in the surgical treatment of SUI with the retropubic route compared with transobturator (in-out or out-in) with a similar efficacity.

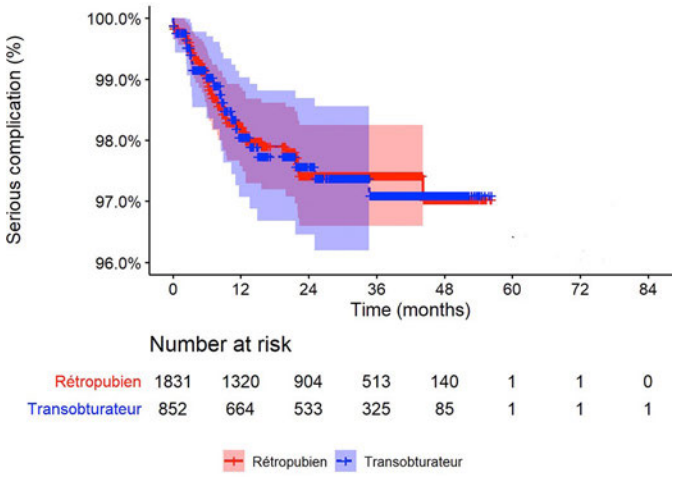
However, the design of our study ignore complications requiring medical treatment, including painful symptoms that may impact the quality of life. It now remains to analyze the typology of the complications to explain which would be related to the difference in route.

FIGURE 1



Kaplan–Meier curve: free of serious complication (Clavien– Dindo grade III or higher) as a function of time (months) and of surgical group

FIGURE 2



Kaplan–Meier curve: free of reoperation for SUI recurrence as a function of time (months) and of surgical group.

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A SYSTEMATIC REVIEW ON CONTENT VALIDITY OF MEASUREMENT INSTRUMENTS USED TO ASSESS QUALITY OF LIFE (QOL) IN WOMEN WITH STRESS URINARY INCONTINENCE (SUI).

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HYPOTHESIS / AIMS OF STUDY
Stress urinary incontinence (SUI) affects as many as one in five adult women (1), with a high socioeconomic burden. Patient reported outcome measures (PROMs) are increasingly used in clinical research for the assessment of the efficacy of interventions in pelvic floor disorders. QoL is a significant outcome domain of impact of SUI on women as well as of treatment efficacy. The aim of this study was to evaluate the content validity of the most commonly used and reported PROMs in published trials on SUI interventions, assessing their suitability for inclusion as core outcome and outcome measure sets (COS and COMS) in research and clinical practice.

STUDY DESIGN, MATERIALS AND METHODS
Search terms were based on a previous systematic review (2) combined with an adjusted PROM and construct validity filter (3). We considered for inclusion PROMs in published randomised trials, which assessed QoL.

A literature search was conducted using EMBASE, MEDLINE and PsycINFO databases. The search filter used in PubMed, was modified for other databases (3). Hand searches on Google scholar were additionally undertaken.

To assess content validity, any report regarding the development of the identified PROMs was included, irrespective of the published format. Studies were eligible if the population included adult women (18 years or older), with SUI. Studies had to be conducted on humans, available as full-text articles, and published in English, or with an available English translation. Studies concerning cross-cultural adaptation and translation of a PROM were included as content validity studies if they performed a pilot study to evaluate cross-cultural comprehensibility.

To evaluate PROM development 35 standards were assessed across two domains; the initial domain involving general design requirements for the PROM, subsequently followed by the assessment of the quality of the cognitive interview study. Each standard was rated using the four-point scale as either: “inadequate”, “doubtful”, “adequate”, or “very good”.

To assess the quality of the content validity studies, a further set of COSMIN (www.cosmin.nl) guidelines were used. Thirty-one standards reported relevance, comprehensiveness, and comprehensibility of the PROM by professionals and patients. Again, using the four-point scale.

Total scores for each domain were calculated by using the ‘worst score counts’ method (using the lowest grade of any standard in that box).

Evidence synthesis comprised of two steps. The PROM development studies, content validity studies, and the content of the PROM, were rated against the 10 established criteria of good content validity.

Quality of evidence of the PROM development studies, was then assessed by applying a modified GRADE (Grading of Recommendations Assessment Development and Evaluation) approach.

RESULTS
We selected the seven most commonly used and reported PROMS in randomised trials on SUI interventions in female populations. We evaluated the Urinary Distress Inventory (UDI), Urinary Distress Inventory 6 (UDI-6), International Consultation of Incontinence Questionnaire – Short Form (ICIQ-SF), International Consultation of Incontinence Questionnaire – bladder diary (ICIQ-Bladder Diary), Incontinence Impact Questionnaire (IIQ), Incontinence Impact Questionnaire-7(IIQ-7), and Patient Global Impression of Improvement (PGI-I). Only one PROM (PGI-I), was developed in a population with diagnosed stress urinary incontinence. Of the remaining PROMS, 4 (UDI, IIQ, UDI-6, IIQ-7) were designed to specifically assess QoL in women with urinary incontinence, and the ICIQ-SF to assess QoL in women as well as men.

The overall quality of PROM design was deemed inadequate for 5 PROMs (UDI, IIQ, UDI-6, IIQ-7, and PGI-I). This was due to the lack of an appropriate interview guide, and no obvious recordings of interviews, meaning concept elicitation was scored as inadequate. Despite this, 4 (IIQ, UDI, ICIQ-SF, ICIQ Bladder Diary) of the 7 PROMs assessed did involve patients in concept elicitation.

Of the 7 PROMs, only 2 (ICIQ-SF, ICIQ-Bladder diary) had cognitive interviews in their development process. The comprehensibility of the ICIQ-SF was deemed doubtful, as it was unclear if guides were used to conduct interviews, and if these were in turn transcribed or recorded. With regards to comprehensiveness of ICIQ-SF, this too was scored as doubtful, again due to the lack of clarity surrounding the interview process, and adaptation of the PROM.

Comparatively, the ICIQ-Bladder Diary scored adequately in terms of comprehensibility, the main attributing factor being the inclusion of interview recordings. An adequate rating was also given for comprehensiveness. The authors documented problems faced by patients when answering the questionnaire, and appropriately addressed these issues (Table 1).

We identified one study evaluating content validity of a single PROM – ICIQ Bladder Diary. The study assessed relevance, comprehensibility, and comprehensiveness. All 5 domains were classified as doubtful, as it was unclear if interviews were based on an appropriate topic or guide, or if an appropriate approach was used to analyse the data.

No high-quality evidence was available for the 7 PROMs included in this review (Table 2). Only the ICIQ- Bladder diary, was deemed moderate across the board, suggesting this PROM likely has the best content validity for QoL in women with stress urinary incontinence.

INTERPRETATION OF RESULTS
Overall, there is a clear lack of content validity studies, with our searches returning only one content validity paper, assessing relevance, comprehensiveness, and comprehensibility of one PROM (ICIQ-Bladder Diary).

Development should be undertaken in a population reflective of the population of interest, to ensure relevance and comprehensiveness. Only 3 out of 7 PROMs used in this study involved patients in the development process. Comparatively, only 2 out of 7 PROMs conducted cognitive interviews suggesting that information regarding content modification was not extensively considered. Patients were not given an opportunity to report problems with relevance or comprehensibility of the measurement tool, meaning data may have been incorrectly recorded or missed altogether.

Despite recommendations existing to aid development of PROMs with high content validity, our findings concur with other literature highlighting the issue with poor reporting of qualitative research regarding content validity. Guidelines suggest that as a minimum development of a PROM should include: 1) a literature review, 2) concept elicitation reviews or the use of focus groups, 3) data analysis, 4) item generation, and 5) performing cognitive interviews. In 2016 COSMIN methodology provided an approach to assess content validity, prior to this a clear framework was missing, leading to a lack of standardisation of development. Studies previously published have not assessed content validity.

This study was completed as part of a wider project to establish COS and COMS in research and clinical practice for women with SUI. COS/COMS aims to reduce the variation of outcome reporting in clinical trials. Inconsistencies within outcome reporting in women with SUI have been highlighted by previous systematic reviews. COSMIN and COMET guidelines outline a methodological approach to aid developers when producing a COS.

CONCLUDING MESSAGE
This review has highlighted gaps in the quality of evidence surrounding content validity for PROMs used to assess QoL in women with SUI. To collect clinically relevant data from patients and ensure we can record QoL in a meaningful way, it is imperative that development of PROMs is based on robust methodological principles.

FIGURE 1

PROM	Concept elicitation study – quality [i]	Concept elicitation study – patient involvement	Cognitive study performed	Cognitive study – quality [i]	Overall quality of PROM development study [i]
UDI	Inadequate	Yes	No	n/a	Inadequate
IIQ	Inadequate	Yes	No	n/a	Inadequate
UDI-6	Inadequate	No	No	n/a	Inadequate
IIQ-7	Inadequate	No	No	n/a	Inadequate
PGI-I	Inadequate	No	No	n/a	Inadequate
ICIQ-SF	Doubtful	Yes	Yes	Doubtful	Doubtful
ICIQ-Bladder Diary	Adequate	Yes	Yes	Adequate	Adequate

Abbreviations: UDI; Urinary Distress Inventory, UDI-6; Urinary Distress Inventory 6 (Short Form), ICIQ-SF; International Consultation of Incontinence Questionnaire – Short Form, ICIQ-Bladder Diary; International Consultation of Incontinence Questionnaire – bladder diary, IIQ; Incontinence Impact Questionnaire, IIQ-7; Incontinence Impact Questionnaire-7 (Short Form), PGI-I; Patient Global Impression of Improvement.

Notes

i. Quality rated as very good, adequate, doubtful, inadequate, or not applicable

Table 1: Evidence synthesis on PROM development for female SUI

FIGURE 2

PROM	Relevance rating[i]; quality[ii]	Comprehensiveness rating[i]; quality[ii]	Comprehensibility rating[i]; quality[ii]
UDI	+/- ; very low	- ; very low	- ; very low
IIQ	+/- ; very low	- ; very low	- ; very low
UDI-6	? ; very low	- ; very low	- ; very low
IIQ-7	? ; very low	- ; very low	- ; very low
PGI-I	- ; very low	- ; very low	- ; very low
ICIQ-SF	+; low	+; low	+; low
ICIQ-Bladder Diary	+ ; moderate	+ ; moderate	+; moderate

Abbreviations: UDI; Urinary Distress Inventory, UDI-6; Urinary Distress Inventory 6 (Short Form), ICIQ-SF; International Consultation of Incontinence Questionnaire – Short Form, ICIQ-Bladder Diary; International Consultation of Incontinence Questionnaire – bladder diary, IIQ; Incontinence Impact Questionnaire, IIQ-7; Incontinence Impact Questionnaire-7 (Short Form), PGI-I; Patient Global Impression of Improvement.

Notes

i. Ratings can be (+) sufficient, (-) insufficient, (±) inconsistent, (?) indeterminate
ii. Quality can be high, moderate, low, and very low

Table 2: Evidence synthesis on content validity for QoL instruments for female SUI

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COLPOSUSPENSION, DOES SUTURE MATERIAL MATTER?

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HYPOTHESIS / AIMS OF STUDY

In the wake of the now known complications associated with the use of non absorbable material in the management of pelvic floor disorders such as stress incontinence there has been a move towards discussing and giving patients choice between absorbable and non absorbable sutures at colposuspension for stress incontinence. There has been minimal data on the differences at success rates between absorbable and non absorbable sutures during colposuspension and traditionally this procedure has been performed using non absorbable sutures, at our unit prior to Mesh scandal we would use Ethibond. Since pause in insertion of retropubic tapes for stress incontinence, colposuspension surgeries have had a surge. Previous studies and literature reviews is limited with largely comparing use of staples versus permanent sutures. Our study aimed to compare cure rate in those patients who had colposuspension (open or laparoscopic) performed using absorbable sutures and those performed using permanent suture.

STUDY DESIGN, MATERIALS AND METHODS

This was a retrospective reviews of the operation notes to ascertain suture material used and patient reported resolution of their symptoms at post operative clinic review or reported recurrence of symptoms within the 12 months following the procedure. Failure rate was defined as persistent stress incontinence/ recurrence of stress incontinence within 12 months of the Burch Colposuspension.

The patients cohort was identified from the British Society of Urogynaecologists (BSUG) database as input by the named consultant. A total of 69 patients were identified between 2017 - 2021. Operation notes were sought from the archived hospital database of clinical notes, current electronic operative notes and patients's written notes. We are yet to review all the notes therefore unable to fully report our results prior to the deadline for the this abstract.

RESULTS

Preliminary results appear to show higher failure rate when absorbable suture material was used during the operation with an initial cure rate and a later reported complete recurrence of stress incontinence within the first 6 months after Burch Colposuspension was performed. There also appeared to be a slight higher rate of failure with laparoscopic colposuspension in comparison to the open approach.

INTERPRETATION OF RESULTS

The full results of our analysis is yet to be completed but there is suggestion that permanent (non-absorbable) sutures may be superior in achieving the success rates that are normally quoted for colposuspension (85% success rates) at 12 months. The data on permanent suture material migration for Burch colposuspension is very scanty leading to the conclusion whether use of absorbable material confers additional benefit.

CONCLUDING MESSAGE

It is difficult to fully analyse our results as analysis of the notes is ongoing and although we have seen some differences in the success rates we are aware that this is not a randomised control study and our data and results may be surgeon specific but nonetheless when there is ongoing discussions with regards to use of permanent suture materials and the long term effects reported by many women, our small scale study hopes to open discussions and more research so as to give women more informed choices when deciding on incontinence surgery.

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MODERATE TO SEVERE LOWER URINARY TRACT SYMPTOMS COULD BE PREDICTIVE OF AORTIC REGURGITATION IN WOMEN WITH CARDIAC SYMPTOMS

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HYPOTHESIS / AIMS OF STUDY
Lower urinary tract symptoms (LUTs) is well established as being an independent risk factor for cardiovascular disease (CVD). However, the association between structural heart disease and LUTs remains unclear. Echocardiography is the main examination to assess structural heart disease. Therefore, the current study aimed to investigate the relationship between LUTs and structural heart disease via application of echocardiography.

STUDY DESIGN, MATERIALS AND METHODS
This single center, prospective cross sectional study included adult female patients with LUTs who had undergone echocardiography for suspected cardiac abnormalities from February to March 2021. Doppler echocardiography was implemented following a standard protocol recommended by the European Society of Cardiology. All the participants were asked to complete the questionnaires composing of general demographic information and International Prostate Symptom Score (IPSS) questionnaire. LUTs severity was categorized based on the IPSS. The Chi-squared test was used to compare the differences between mild and moderate to severe LUTs (defined as IPSS $\geq$ 8). Multi-variable logistic regression analyses adjusted for demographic covariates and comorbidities were conducted to determine whether moderate to severe LUTs was predictive of echocardiographic abnormalities. A two-sided p-value less than 0.05 was accepted as statistically significant.

RESULTS
Total 165 female patients (mean age 69.96 $\pm$ 10.20 years) were enrolled in the study. All the participants were categorized into two group based on the IPSS. Among the participants, 132 patients (80%) were found to have mild LUTs and 33 patients (20%) were found to have moderate to severe LUTs.

INTERPRETATION OF RESULTS
The prevalence of moderate to severe aortic regurgitation (AR) was significantly higher in patients with moderate to severe LUTs compared to those with mild LUTs (33.3% vs. 13.6%, $p = 0.008$). Other parameters did not differ significantly in patients with moderate to severe LUTs compared to those with mild LUTs. On multi-variable logistic regression analyses, moderate to severe LUTs could predict moderate to severe AR independently [odds ratio (OR) 3.56; 95% confidence interval (CI) 1.409-8.993, $p = 0.007$]. Furthermore, it was IPSS storage sub-score rather than voiding sub-score having significant association with moderate to severe AR (OR 1.285; 95% CI 1.111-1.486, $p = 0.001$).

CONCLUDING MESSAGE
Moderate to severe LUTs, especially storage symptoms, was an independent predictor for the co-existence of moderate to severe AR in female patients. This correlation may be concerned in clinical practice, urologists should recognize cardiac manifestations that develop in female patients coexisting with AR and moderate to severe LUTs. Early referral to cardiologist may provide collaborative treatment and improvement of general health for these patients.

Funding To the best of our knowledge, the named authors have no conflict of interest, financial or otherwise **Clinical Trial** No **Subjects** Human **Ethics Committee** The **Ethics Committee** of Taipei City Hospital (Institutional Review Board number: TCHIRB-11002002) **Helsinki** Yes **Informed Consent** Yes

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TAKING A CUE FROM THE HOST IMMUNE SYSTEM: URINARY WHITE BLOOD CELLS DISTINGUISH FRIEND FROM FOE IN THE HEALTHY HUMAN BLADDER

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HYPOTHESIS / AIMS OF STUDY

This study presents a novel experimental design to distinguish potential pathogens from commensal bacteria in healthy human bladder. It is hypothesized that the bladder immune system is constantly at work to maintain immune homeostasis and suppress the activity of pathogens from causing an overt infection. The aim is to identify the presence of these potential pathogens by isolating bacteria associated with white blood cells in urine samples of healthy volunteers.

STUDY DESIGN, MATERIALS AND METHODS

Six healthy female volunteers (Samples A to F) were recruited and informed consent was obtained before participating in the study. They answered a 39-point questionnaire on lower urinary tract symptoms (LUTS) grouped into storage, stress incontinence, voiding and pain. The questions were close-ended with a yes or no response. Urine samples were then collected and separated into sediment and supernatant by centrifugation. These were designated as "neat urine". The cells in the sediment were labelled with CD45 microbeads (Miltenyi Biotec, Germany) and sorted with magnetic-activated cell sorting (autoMACS® Pro Separator, Miltenyi Biotec, Germany) into CD45-positive "white blood cell (WBC)" and CD45-negative "non-WBC" fractions. Individual aliquots of the supernatant and sediment of neat urine, WBC and non-WBC fractions were cultured on chromogenic agars (chromID® CPS® Elite). After 24-hour incubation at 37oC, colony growth was observed and recorded. The cells in the sediments were also stained with DAPI for cell nuclei and bacteria, wheat germ agglutinin (WGA) for cell membrane, anti-lipoteichoic acid antibody for Gram-positive bacteria and anti-lipid A antibody for Gram-negative bacteria. The fluorescently-labelled cells were examined using a TCS SP8 deconvolution laser scanning confocal microscope (Leica Microsystems, Germany).

RESULTS

The volunteers (mean age 25 ± SD 5 years) were all healthy with only two respondents scoring one point each on the questionnaire. Culture of supernatant fractions provided information on planktonic bacteria present in the urine while sediment fractions showed bacteria associated with white blood cells (WBC) in the WBC fraction and epithelial cells in the non-WBC fraction. The bacterial colonies were presumptively identified based on the manufacturer's documentation. Possible organisms were Enterococcus sp. (turquoise), Proteus sp. (brown), Escherichia coli (red to burgundy) and Klebsiella, Enterobacter, Serratia, Citrobacter (KESC group) (blue to blue-green). However, the diversity of colours that were observed in this study could not be grouped entirely into these four classes and will, therefore, be described solely based on colour when mentioned. Samples A and B did not show any colony growth from all cultured fractions. In Sample C (Figure 1), five types of colonies were observed in the sediment of neat urine and WBC fraction. They were E. coli (burgundy), Enterococcus sp. (turquoise), KESC group (blue), Proteus sp. (brown) and white colonies. The turquoise, blue and brown colonies were similarly present in the neat urine supernatant while the white colonies were present in the non-WBC sediment. Supernatant of non-WBC and WBC fractions did not show any growth. In Sample D, Proteus sp. (brown) and yellow colonies were observed in the sediment of neat urine. The same yellow colony was also present in the sediment of WBC fraction, with additional green-white and white colonies. Non-WBC fraction as well as the supernatant of neat urine and WBC fraction did not show any growth. In Sample E, three types of colonies were present in all fractions. They were Enterococcus sp. (turquoise), white and blue-coloured lawn. In Sample F, six types of colonies were observed in the sediment of neat urine – E. coli (burgundy), KESC group (blue, dark blue and green), yellow and white. All were also present in the supernatant of neat urine and non-WBC fraction except for the white. In the non-WBC fraction, all were present except for E. coli in the sediment. In the WBC fraction, all were present except for the green KESC group in the sediment while the supernatant showed the blue KESC group, yellow and white colonies. White blood cells and both Gram-positive and Gram-negative bacteria could be observed in the sediment of WBC fractions on confocal microscopy (Figure 2).

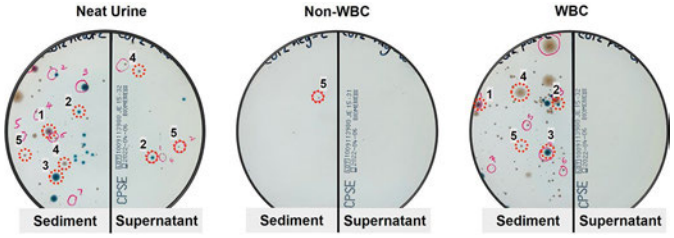
INTERPRETATION OF RESULTS

It has been shown, in recent years, that the urine is not sterile [1] and bacteria are ubiquitously present in health and disease. The emerging field of the urobiome has complicated the diagnosis of urinary tract infection, particularly in respect to standard culture methods. White blood cells that are shed into the urine provide a useful means to study bacteria implicated in immune system activation, subsequently aiding in distinguishing pathogens from commensals. Even though this study examined healthy pre-menopausal females, differential bacterial growth could be observed in three out of six urine samples, suggesting transient subclinical infections which are being successfully subdued by the host immune response. Asymptomatic bacteriuria occurs in healthy individuals and is thought to be a beneficial colonization of commensals which can persist in the bladder by modifying host gene expression [2]. However, the observation in this study shed new light on this clinical presentation where the lack of symptoms could be due to an active engagement of the immune system in preventing the infection from manifesting.

CONCLUDING MESSAGE

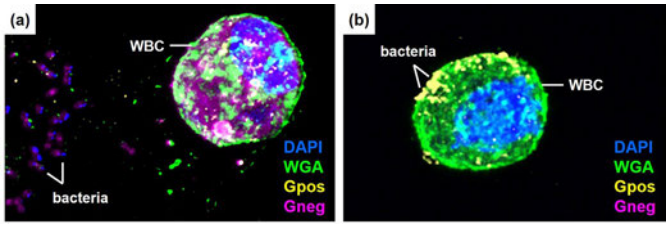
This study demonstrates a workflow for isolating bacteria that are being targeted by the immune system. The presence of bacteria that is unique to the WBC sediment fraction indirectly distinguishes pathogens from commensals in the bladder. The same approach can be applied to urine samples from patients with urinary tract infection to single out aetiological pathogens and potentially characterize deficiencies in their immune response that lead to symptomatic infections. More samples from healthy and diseased individuals are planned for future work to compare between the groups and accurately identify pathogenic microorganisms of the urinary tract.

FIGURE 1



Mixed growth of bacteria being targeted by the immune system of healthy control shown in the sediment of WBC fraction. The bacteria were (1) Escherichia coli, (2) Enterococcus sp., (3) KESC group, (4) Proteus sp. and (5) unknown white colony.

FIGURE 2



Maximum projection deconvolution laser-scanning confocal micrographs showing bacteria associated with white blood cells (WBC). (a) WBC with extracellular Gram-negative (Gneg) bacteria stained with DAPI. (b) WBC with Gram-positive (Gpos) surface bacteria.

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Funding Chronic UTI Grant Code 558771 **Clinical Trial** No **Subjects** Human **Ethics Committee** UK Health Research Authority (HRA) **Helsinki** Yes **Informed Consent** Yes

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SESSION 20 - BEST CONSERVATIVE MANAGEMENT 2

Abstracts 285-290
11:30 - 13:00, Hall K
Chairs: Dr Kathleen Frances Hunter (Canada), Mrs Barbara Goedl-Purrer (Austria)

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BEST IN CATEGORY PRIZE: REHABILITATION

DESIGN AND CONTENT VALIDITY OF THE RUNNING AND RELATED ACTIVITIES URINARY INCONTINENCE SYMPTOMS QUESTIONNAIRE – A DELPHI STUDY

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HYPOTHESIS / AIMS OF STUDY
Physical activities such as running, jogging and brisk walking can trigger urinary incontinence (UI), but our ability to assess the relationship between the nature and duration of activity and the experience of UI is limited. Recommended UI symptoms questionnaires include a limited number of items that address physical activity, but do not assess the characteristics of the aggravating activity. Customized questionnaires have been used in individual studies to gain a more detailed understanding of the relationship between UI and physical activity [e.g., 1]. However, these questionnaires are often poorly described and lack reporting of their measurement properties. The lack of a reference standard for reporting UI symptoms associated with running, jogging or brisk walking makes comparisons among studies difficult and limits our ability to assess the effectiveness of interventions designed specifically to address UI experienced by females during physical activities.

The primary aim of this study was to develop a new questionnaire, the "Running and Related Activities Urinary Incontinence Symptoms Questionnaire" (RARA-UISQ) and to establish its content validity through consultation with an expert panel.

STUDY DESIGN, MATERIALS AND METHODS
This study received ethical approval from the local institutional research ethics board with informed consent to participate being obtained from each panelist. A draft questionnaire was developed through focus-group consultation with three local physiotherapy clinicians who treat UI, two local patients who experience UI during exercise and four academic researchers who study UI. Next, a Delphi process was used to refine the questionnaire and to establish its content validity. Health care practitioners located in Canada and the United States, including medical doctors who had completed surgical fellowship training in urogynaecology as well as physiotherapists working in women's health and with experience managing UI in female patients. In addition, females who experience UI during running, jogging and/or brisk walking were invited to participate in the remote expert panel consultation.

Panel members were presented with the draft questionnaire and responded by either agreeing or disagreeing with each included construct and with each individual question, providing explanatory comments for each response. All comments were anonymized and shared with the other panel members in the next round. Consultation rounds continued until consensus was achieved for each construct and question, where consensus was defined as >66% agreement amongst panelists.

RESULTS
The panel was comprised of four urogynaecologic surgeons, three physiotherapists and three females who regularly experience UI during running, jogging or brisk walking. The initial questionnaire consisted of six sections with 22 questions. Two rounds of consultation were required to reach consensus. The final version of the questionnaire has five sections, including: Screening (to determine if an individual experiences UI and/or a sense of urgency with running, jogging and/or brisk walking), Exercise Characteristics, Urgency Urinary Incontinence Symptoms, Stress Urinary Incontinence Symptoms and Management Strategies, resulting in a total of 45 questions across these categories.

INTERPRETATION OF RESULTS
Overall, the expert panel provided feedback that focused the scope of the RARA-UISQ as a research tool, while increasing the amount of detail that is provided by research participants. The screening, exercise characteristics and urgency UI sections underwent the largest changes, with the number of questions in each section more than doubling. In the case of the urgency UI section, changes were made to account for individuals who experience urinary urgency while running, without associated leakage. The initial questionnaire included a section to screen for co-morbidities but this was removed following feedback from the expert panel. Instead, use of previously validated questionnaires for co-morbid pelvic symptoms (e.g., ICIQ modules for urinary, vaginal and bowel symptoms) will be recommended for use alongside the RARA-UISQ.

The knowledge and experience of the panelists (urogynaecologic surgeons, physiotherapists, or individuals with UI) influenced responses. Urogynecologic surgeons more frequently commented that questions around the characteristics of the physical activity (e.g., frequency, distance travelled, total number of hours) were not relevant, while physiotherapists and panelists with UI agreed that these were important factors to report, as severity of leakage may be associated with volume or intensity of activity.

The most contentious aspect of the questionnaire was the separation of symptoms by UI subtype (i.e., stress vs urgency). Some panelists interpreted the separation of symptoms in this way as an attempt to diagnose questionnaire respondents as having stress, urgency or mixed UI. Indeed, the RARA-UISQ is a patient reported outcome that focuses on symptoms of UI associated with running, jogging and brisk walking with an intended use of evaluating the efficacy of interventions for UI experienced predominantly during physical exercise. It is not intended to be used for diagnosis. The consensus was to retain this separation for symptom reporting.

CONCLUDING MESSAGE
Through a focus group followed by a Delphi process, the content validity for the RARA-UISQ has now been established. The evaluation of its measurement properties (test-re-test reliability, construct, and concurrent validity) is now underway.

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Funding The Canadian Institutes of Health Research (McLean 202003PJT-436744-CIC-CECA-117551) The Natural Sciences and Engineering Research Council of Canada (Klahsen PGSD3-559887-2021; 2020-2023) **Clinical Trial** No **Subjects** Human **Ethics Committee** The University of Ottawa Health Sciences and Science Research Ethics Board **Helsinki** Yes **Informed Consent** Yes

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PRIMARY RESEARCH ON SPECIFIC INTERVENTIONS FOR FEMALE ATHLETES WITH PELVIC FLOOR DYSFUNCTION ARE NEEDED: A SCOPING REVIEW OF THE LITERATURE

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HYPOTHESIS / AIMS OF STUDY
This scoping review aimed to a) provide a comprehensive overview of all studies addressing pelvic floor dysfunction (PFD) interventions in female athletes, summarizing studies according to PFD classification provided by the International Continence Society (ICS) standardized terminology, the type of sport and treatments; b) to identify any gap in the knowledge of the topic.

STUDY DESIGN, MATERIALS AND METHODS
The present review was conducted following the Joanna Briggs Institute methodology[1] for scoping reviews. The entire selection process was recorded and reported according to the latest published version of the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA 2020) flow diagram[2]. The Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) Checklist[3] for reporting was used. The scoping review protocol was prospectively registered in MedRxiv.

MEDLINE, Cochrane Central, Scopus, CINAHLComplete, Embase, PEDro and SPORTDiscus were searched up on 9th May 2021 with no date limit. Additional studies were identified through grey literature and the reference lists of articles included.

Studies considering female athletes practising sports at any performance level with any type of PFD were eligible for inclusion. Any clinical intervention (i.e. preventive, conservative, pharmacological, surgical) and any context were considered. No language, study design and publication type restrictions were applied.

Two authors independently screened all abstracts and full-text studies for inclusion. An ad-hoc data collection form was developed by the research team to extract the characteristics of included studies. The results were presented numerically and thematically according to scoping reviews methodology.

RESULTS
From 2625 initial records, 2590 were excluded and 35 articles met inclusion criteria.

Figure 1 synthesizes the main characteristics of the studies ranging from the year of publication to categories of intervention (Figure 1).

The majority of research designs were narrative review (n = 19; 54.3%), while seven (20%) were primary research. Only two randomized controlled clinical trials (RCTs) were conducted on female athletes over the years.

Studies were identified from 12 different countries and in four languages (English, French, Spanish, and Slovenian).

In the majority of articles (n = 27; 77.1%), authors defined participants as “athletes,” but performance level was not clearly reported. A few of them reported about particular subgroups, such as post-partum triathletes, adolescents, and wheelchair athletes.

Regarding the PFD, urinary incontinence was the most common pelvic floor symptom explored (n = 24; 68.6%). In most cases, athletes suffered from stress urinary incontinence (SUI) (n = 19, 54.9%). For other disorders, in 10 studies (28.6%) more than one PFD was considered.

Nearly 70% of articles included more than one sport, mainly the high-impact ones. Considering those that focused only on one sport, volleyball (n = 3; 8.6%) and running (n = 2; 5.7%) were the most frequently investigated.

Authors discussed a wide range of interventions. In particular, 23% of considered articles (8 out of 35) described only preventive interventions to manage PFD.

Conservative approaches (n = 35) were suggested by all authors of the included studies.

Among these, Pelvic Floor Muscle Training, alone or combined with other treatments, is explicitly cited as an effective treatment in 85.7% of studies. Figure 2 graphically illustrates the pooled results of all the conservative interventions that were considered (Figure 2).

More specifically, the analysis of treatments proposed for SUI showed several possibilities, including biofeedback, bladder training, lifestyle interventions, education, electrical stimulation, hypopressive techniques, intra-abdominal pressure management, modification of the sport technique, vaginal tampons, pads, and vaginal cones.

Pharmacological options (n = 12; 34.3%) and surgical procedures (n = 10; 28.6%) for PFD were rarely cited and in general, were not supported by the opinion of the authors.

INTERPRETATION OF RESULTS
Although authors discussed a wide variety of interventions ranging from preventive or conservative treatments to surgery, the present scoping review confirmed that only a few authors evaluated the effectiveness of interventions dedicated to this population.

Athletes are a unique group of patients who have higher functional demands than the general population and may need a different and specific approach than nonathletic women.

Indeed, as happens with other disorders, like the musculoskeletal ones, the overall management should be specific and tailored to the athlete, considering the type of PFD and other factors such as: (a) training volume, (b) type of sport, (c) performance level, (d) other associated disorders (e.g., musculoskeletal), and (e) individual risk and contributing factors within multidisciplinary management.

To provide better guidance for clinical practice and to fill the current gaps, these variables should guide high-quality research.

CONCLUDING MESSAGE
This is the first scoping review to provide a comprehensive overview of the topic.

The authors discussed different interventions for PFD among female athletes. Among these, the conservative approach was the most frequently suggested. Besides the great number of listed interventions, specific programs and RCTs for female athletes are still limited.

The findings of the present study showed that suggestions for clinical practice were basically supported by the transferability of the nonathlete population's results or by the expert opinion. Therefore, there is a great need of primary research considering individual characteristics, related-variables sport, and PFD within multidisciplinary management.

FIGURE 1

Variable[a]	No. of studies (%)
Year of publication	
1984 - 1990	1 (2.8)
1991 - 2000	3 (8.6)
2001 - 2010	11 (31.4)
2011 - 2020	19 (54.9)
Up to 2021	1 (2.8)
Study design	
Primary research	7 (20)
Case series	1 (2.8)
Pre-post study	1 (2.8)
RCT	2 (5.7)
Case report	3 (8.6)
Secondary research	2 (5.7)
Systematic review	2 (5.7)
Traditional sources	25 (71.4)
Conference proceeding	1 (2.8)
Editorial	1 (2.8)
Narrative review plus case report	1 (2.8)
Book chapter	3 (8.6)
Narrative review	19 (54.9)
Protocol	1 (2.8)
Level of performance	
Agonistic	1 (2.8)
Elite/High level	7 (20)
Not reported level	27 (77.1)
Sport	
Basic Combat Training	1 (2.8)
Soccer	1 (2.8)
Triathlon	1 (2.8)
Running	2 (5.7)
Volleyball	3 (8.6)
Not reported	3 (8.6)
Multiple sport	24 (68.6)
PFD	
Pelvic pain	1 (2.8)
Multiple PFD	10 (28.6)
UI	24 (68.6)
SUI	19 (54.9)
Interventions	
Preventive, conservative	4 (11.4)
Preventive, conservative, surgical	1 (2.8)
Preventive, conservative, surgical, pharmacological	3 (8.6)
Conservative	16 (45.7)
Conservative, pharmacological	2 (5.7)
Conservative, surgical	2 (5.7)
Conservative, surgical, pharmacological	7 (20)

PFD = Pelvic Floor Dysfunction; UI = Urinary Incontinence; SUI = Stress Urinary Incontinence

[a] Not reported level = Population defined as "athlete" by the authors, but specific level of performance was not specified.

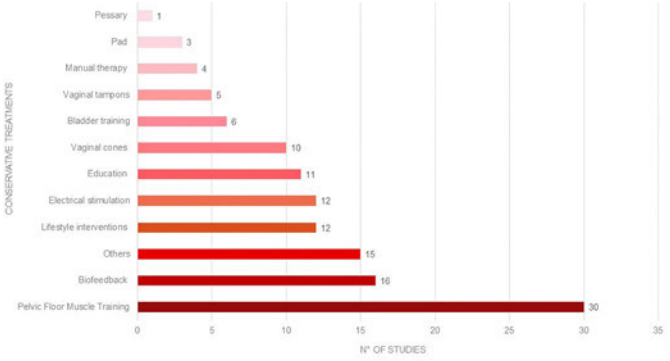
Multiple sport = Studies in which authors considered different type of sport (more than one).

Multiple PFD = Studies in which authors considered more than one PFD.

RCT = Randomized Controlled Trial

Summary of main characteristics of included studies.

FIGURE 2



Electrical stimulation category includes different type of interventions such as Percutaneous Tibial Nerve Stimulation, and Transcutaneous Electrical Nerve Stimulation.

Others: Heat/cold; Intermittent catheterization; Intra-abdominal pressure management; Multidisciplinary management; Muscle strengthening; "Physiotherapy" intervention not clearly specified; PFM Synergistic Training (Breathing techniques, Hypopressive technique); Running technique. Vaginal dilators.

Overall conservative treatments for PFD among female athletes.

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BEST IN CATEGORY PRIZE: ANATOMY / BIOMECHANICS

PELVIC FLOOR MUSCLES ACTIVATION PATTERN DURING PREGNANCY AND POSTPARTUM COMPLICATED BY GESTATIONAL DIABETES

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HYPOTHESIS / AIMS OF STUDY

Gestational diabetes mellitus (DMG) has been associated with higher prevalence of both pregnancy-specific urinary incontinence (PS-UI) and urinary incontinence (IU) postpartum, with worsening of severity and quality of life during pregnancy and over first year postpartum compared to non-GDM women.[1] Experimental studies in moderate diabetic rat models have shown that the periurethral and rectus abdominis muscles present deterioration, such as atrophy, thinning, disorganization, and co-localization of fast and slow fibers.2 These data are consistent with those observed in rectus abdominis muscles tissue collected from pregnant women with GDM during C-section, which suggests that GDM is indeed capable of damaging the muscular tissue causing a myopathic process.[2] Due to the invasive nature of PFM biopsy, functional tests have been employed to evaluate the impact of GDM on its function. The aim of this longitudinal study was to compare PFM activation pattern between GDM and non-GDM women from 24-30 gestational weeks to 18-24 months postpartum during a standard clinical test during gestation and postpartum.

STUDY DESIGN, MATERIALS AND METHODS

This was prospective cohort study approved by the Institutional Ethical Committee (Protocol Number CAAE 82225617.0.0000.5411). The main inclusion criteria were: pregnant women between 24-30 weeks of gestation in the first assessment; singleton pregnancy; 18–40 years of age; primigravida or primiparous with previous c-section. The participants were allocated in GDM group if they presented fasting glycemic levels ≥92 mg/dL or 1 hour ≥180 mg/dL or 2 hours ≥153 mg/dL. In addition, participants who had lower levels composed the Non-GDM group. Participants were evaluated at three time points: 24–30 weeks of gestation (T1), at 36–38 weeks of gestation (T2) and 18-24 months postpartum (T3). The same procedures were followed at each time point. During first step of the investigation the participants answered a questionnaire, followed by instructions about pelvic floor contraction and vaginal palpation to confirm if they were able to isolate the contraction. After the confirmation that they were prepared to perform the main acquisition, the EMG data collection were performed. The PFM EMG assessment were done according to the Glazer protocol of clinical evaluation. The EMG signal were captured by two-channel EMG device (Miotool 200 Uro; Porto Alegre, Brazil). A water-soluble gel was applied before introducing the probe into the vaginal canal. The EMG signals were processed offline using custom programs implemented in MATLAB (2014b, The MathWorks, Inc., Natick, MA, USA). The EMG profiles were obtained by applying the root mean square (RMS) the entire signal using a sliding window of 200 msec. Consistent with previous studies using the same protocol, the RMS EMG profiles were then normalized by the highest peak detected across the 5 repetitions of the Flick task. To identify the PFM pattern during the entire contraction, the full RMS EMG waveforms from the Flick and Hold tasks were compared between groups using the technique of wavelet-functional ANOVA (wfANOVA).[3] As we were interested in both the phasic activation patterns and the rest amplitudes before and after each contraction, we selected time windows that included 3 seconds before and after each contraction.

RESULTS

The EMG analysis were proceeded with participants who had all time-points completed and with good EMG signal quality (19 non-GDM and 14 GDM). No significant group differences related to demographic and personal data were found in participant characteristics during gestation or postpartum (Table 1). The glucose tolerance test values, as expected, showed marked group differences on fasting, 1 and 2 hours after oral glucose tolerance test (OGTT).

Figure 1 shows the results of the wf-ANOVA analysis, with the average EMG patterns of each group and the significant Group contrasts during the Flick and Hold PFM contraction tasks at each time point. The significant contrasts indicate that, during the Flick contractions, the GDM group generally had smaller PFM EMG amplitude than non-GDM after ~1 second of contraction, suggesting shorter contractions. During the 10-sec Hold contractions, the non-GDM group activated the PFM at higher contraction intensities than the GDM group at both time points T2 and T3, although the timing of the contrasts differed between time points: At T2, the GDM group had lower initial peak amplitude during Hold, but similar amplitudes after ~2 seconds of contraction; at T3, the initial peaks from both groups had similar (normalized) amplitudes, after which the levels of PFM activation decreased faster for the GDM group, remaining lower than the non-GDM group until near the end of the contraction.

INTERPRETATION OF RESULTS

This is an unprecedented study which assessed PFM EMG patterns from pregnancy to long-term post-partum (18-24 months) in women with and without GDM. Using a well-stablished protocol for pelvic floor assessment, we reproduced a similar sequence of PFM contractions requested in clinical consultations, commonly used to identify the motor strategy during brief and sustained PFM tasks. Wavelet analysis showed that, although the GDM group achieve peak PFM EMG amplitudes similar to the non-GDM, they took longer to return to baseline levels. During 10-sec Hold contractions, the GDM group sustained lower levels of PFM activation than the non-GDM group at both T2 and T3. The impairments in PFM function observed in women with GDM have been attributed to physiological and anatomical changes to the musculoskeletal system, namely reduced cross-sectional area and reduced number of fast fiber type, in addition to impairments in ionic channels, as well as fat infiltration and proliferation of connective tissue in the PFM.

CONCLUDING MESSAGE

This novel cohort study evaluated PFM activity in pregnant women with and without GDM at three distinct time points during and after delivery. Taken together, these results suggest that differences on motor behaviour of GDM women arises in late pregnancy and exacerbate on postpartum.

FIGURE 1

Table 1. Average participant characteristics for non-GDM and GDM groups along time-points.

Variable		non-GDM (n=19)	GDM (n=14)	p*
Ethnicity	Caucasian	13 (68.4%)	7 (50%)	.472
	Other	6 (31.6%)	7 (50%)	
Smoking in pregnancy		0 (0.0)	0 (0.0)	1.000
Smoking postpartum		0 (0.0)	0 (0.0)	1.000
Education level–min. High School		7 (36.8%)	4 (28.6%)	.453
Diabetes postpartum		0 (0.0)	0 (0.0)	1.000
Age (years)[1]		26 (18-39)	29 (18-40)	.529
BMI (kg/T2) pre-pregnancy		23.6 (19.1-30.7)	25.2 (18.5-34.7)	.900
BMI (kg/T2) at 24-30 weeks		26.4 (19.1-32.9)	25.9 (21.6-37.4)	.843
BMI (kg/T2) at 36-38 weeks		28.4 (21.2-34.0)	27.7 (22.8-38.7)	.928
BMI (kg/T2) post-partum		24.6 (17.1-35.2)	24.2 (18.3-36.6)	.957
Weeks of Gestational[1]		26.0 (24.2-29.0)	27.0 (24.0-29.0)	.506
Weeks of Gestational[2]		36.0 (35.3-38.0)	36.0 (35.0-38.0)	.843
Postpartum time		24.0 (18.1-24.0)	19.5 (18.0-24.0)	.123
Delivery Mode	C-Section	14 (73,3%)	11 (78,6%)	.746
	Vaginal	5 (26,3%)	3 (21,4%)	
Newborn weight at birth (grams)		3100 (2205-4100)	3150 (2560-3935)	.577
Blood glucose (mg/dL) [1]		84 (65-90)	88 (76-98)	.077
OGTT (mg/dL) – fasting[1]		76.0 (71.7-90.0)	92.0 (76.0-124.0)	.000
OGTT – 1h (mg/dL) [1]		122.0 (76.7-163.0)	152.0 (82.0-211.0)	.012
OGTT – 2h (mg/dL) [1]		110.0 (64.6-148.0)	138.5 (72.0-179.0)	.019

Non-GDM, non-gestational diabetes mellitus group; GDM, gestational diabetes mellitus group; BMI, body mass index; OGTT, oral glucose tolerance test. [1]evaluation at 24–30 weeks of gestation; [2]evaluation at 36–38 weeks of gestation. [3]Evaluation at 18-24 months postpartum. Data are presented in median (minimum - maximum) or absolute frequency (n) and percentage (%). *Based on Mann–Whitney U, Chi-square and Fischer's exact. significance p <0.05. P-values represent the results from the relevant statistical tests.

Average participant characteristics for non-GDM and GDM groups along time-points.

FIGURE 2

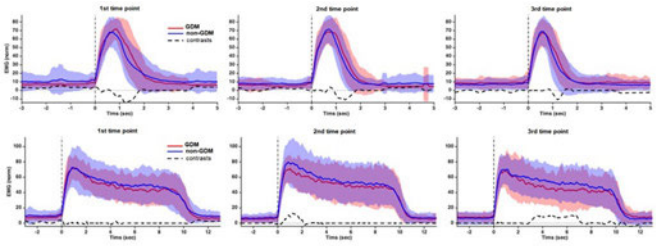

Figure 1. Group average and SD of the RMS EMG during the 1-sec Flick and 10-sec Hold PFM contraction tasks from Glazer protocol. Before averaging, the EMG patterns from each subject was expressed as percentage of the peak recorded during the 1-sec Flick contractions. Positive contrasts indicate that GDM < non-GDM. Source: Diamater Study Group.

Group average and SD of the RMS EMG during the 1-sec Flick and 10-sec Hold PFM contraction tasks from Glazer protocol. Before averaging, the EMG patterns from each subject was expressed as percentage of the peak recorded during the 1-sec Flick contraction

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ADDING KNACK MANOEUVRE AND LIFESTYLE RECOMMENDATIONS TO PELVIC FLOOR MUSCLE TRAINING FOR POST-PROSTATECTOMY URINARY INCONTINENCE: A RANDOMIZED CONTROLLED TRIAL

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HYPOTHESIS / AIMS OF STUDY
A majority of patients (up to 87%) experience moderate-to-severe urinary incontinence (UI) after early radical prostatectomy (1). Pelvic floor muscle training (PFMT) is the most commonly recommended conservative treatment for post-prostatectomy UI (PP-UI) (1). In addition to strength and endurance training, conscious precontraction of the pelvic floor muscles (Knack maneuver) can also be taught in PFMT (2). Another widely recommended approach in the management of UI is lifestyle recommendations (3). However, the evidence for these recommendations is quite limited (3). The aim of this study was to reveal the additional effects of the Knack maneuver and lifestyle recommendations to PFMT in PP-UI in a randomized controlled design.

STUDY DESIGN, MATERIALS AND METHODS
The present study was designed as a prospective randomized-controlled study and included three parallel arms (Group I: PFMT with knack maneuver and lifestyle recommendations, Group II: PFMT with knack maneuver, and Group III: PFMT alone). After the detailed screening, individuals with PP-UI and those having no cooperation problems were included in the study. Exclusion criteria were the presence of acute disease, acute prostatectomy surgery (within the first 3 weeks after prostatectomy), neurological disease or neurogenic bladder, pure urgency UI, pre-operative incontinence, and previous bladder or other prostate surgeries. A computer-based block randomization procedure was used to assign blocks of six participants to each study arm.

Firstly, standardized home-based PFMT protocols were performed in all study groups. Anal palpation was used to teach different types of PFM contractions. A total of 40 contractions (10 fast, 10 sustained, and 20 submaximal) were performed in 3 sessions per day for 8 weeks. All individuals were asked to come for clinical visit every 2 weeks, to monitor exercise accuracy and compliance. The exercise program was intensified by increasing the number of contractions. In Group I and II, the Knack maneuver was instructed to be performed during daily activities that cause UI episodes. Lastly, within the scope of comprehensive lifestyle recommendations, information about UI-related medical conditions, possible factors contributing to UI (diet, fluid intake, constipation, smoking, medications, and exercise), and implications and coping strategies were provided. A written document containing all of the information was provided to the individuals in Group I.

The primary outcome measure was the International Consultation on Incontinence Questionnaire-Short Form (ICIQ-UI SF) score. Secondary outcome measures included the 1-hour pad test, King's Health Questionnaire (KHQ), and the assessments of the Patient Global Impression of Severity and Improvement (PGI-S and PGI-I). Exercise diaries were given to all individuals to increase and monitor exercise compliance.

Kruskal Wallis test was used to compare the data of the 3 study groups. When the difference between the groups was revealed, the Mann Whitney-U test and Bonferroni correction were used for pairwise group comparisons ($p < 0.017$). Wilcoxon test was used in the analysis of within-group changes. Alpha was set at 0.05.

RESULTS
A total of 52 men who had PP-UI symptoms (age: 64.04 ± 6.98 years, BMI: 27.29 ± 3.56 kg/m2) were included in this study. There were no statistically significant differences between groups in terms of the descriptive characteristics and baseline outcome measures ($p > 0.05$). Adherences to PFMT were also similar between groups ($p > 0.05$).

At the end of the 8th week, the effect sizes of the changes in the primary outcome (ICIQ-UI SF) within study groups were 1.9, 1.1, and 1.2, respectively. According to the two-way hypothesis design, the post-hoc power rates were 99%, 95%, and 99%, respectively, with a type I error rate of 5%.

At the end of week 8, there were statistically significant improvements in all outcome measures compared to baseline in all study groups, except for some KHQ subdomain scores and PGI-I scores ($p < 0.05$). However, Group I had significant improvements in all of the KHQ subdomain scores (Table 1).

In the inter-group comparisons of the changes, there was a difference in terms of improvement in ICIQ-UI SF, KHQ role limitations, physical limitations, emotional problems subdomains, and PGI-S scores ($p < 0.05$), while there was no difference between the groups in the 1-hour pad test, other KHQ subdomain scores, and PGI-I scores ($p > 0.05$). According to pairwise comparisons, Group I (PFMT + Knack maneuver + lifestyle recommendations) showed greater improvement in the specified parameters (ICIQ-UI SF, KHQ role limitations, physical limitations, emotional problems subdomains, and PGI-S score) than the other groups.

INTERPRETATION OF RESULTS
This is the first RCT comparing the effect of PFMT, in combination with the Knack maneuver and lifestyle recommendations in the management of PP-UI. The findings from the present study showed that adding the Knack maneuver alone to PFMT did not provide any additional effect on the management of PP-UI. On the other hand, triple combination of PFMT with a Knack maneuver and comprehensive lifestyle recommendations seems to be more effective than PFMT alone and a dual approach combination (PFMT + Knack maneuver) in reducing the subjective severity of urinary loss and improving quality of life. The fact that there was no difference between the groups in the objective incontinence severity measured by the 1-hour pad test may be related to the relatively short duration of the test (compared to the 24-hour pad test). Although the 1-hour pad test is time-saving and cost-effective for the measurement of urinary leakage, the major disadvantage of this test is considered that it gives limited information on leakage conditions during the routine daily activities of individuals.

CONCLUDING MESSAGE
In the treatment of PP-UI, better results can be obtained if PFMT is combined with training on the knack maneuver and comprehensive lifestyle recommendations. In future studies, the objective severity of UI can be evaluated over a wider period of time. Long-term follow-up is also needed in further studies.

FIGURE 1

Table 1. Comparisons of symptoms and objective incontinence severity within and between groups

	Groups	Outcome categories	Baseline n (%)	8th week n (%)	p_1
ICIQ-UI SF	PFMT+Knack+ Lifestyle Recommendations	No UI	0 (0)	1 (5.6)	**0,001***
		Mild UI	0 (0)	9 (50)	
		Moderate UI	4 (22.2)	7 (38.9)	
		Severe UI	11 (61.1)	1 (5.6)	
		Very severe UI	3 (16.7)	0 (0)	
	PFMT+Knack	No UI	0 (0)	0 (0)	**0,006***
		Mild UI	0 (0)	2 (12.5)	
		Moderate UI	6 (37.5)	12 (75)	
		Severe UI	8 (50)	2 (12.5)	
		Very severe UI	2 (12.5)	0 (0)	
	PFMT	No UI	0 (0)	0 (0)	**0,006***
		Mild UI	0 (0)	5 (27.8)	
		Moderate UI	5 (27.8)	10 (55.6)	
		Severe UI	11 (61.1)	2 (11.1)	
		Very severe UI	2 (11.1)	1 (5.6)	
	p_2		0,660	**0,035**	
1-Hour Pad Test	PFMT+Knack+ Lifestyle Recommendations	No UI	0 (0)	10 (55.6)	**<0.001***
		Mild UI	5 (27.8)	8 (44.4)	
		Moderate UI	5 (27.8)	0 (0)	
		Severe UI	8 (44.4)	0 (0)	
	PFMT+Knack	No UI	0 (0)	7 (43.8)	**0.001***
		Mild UI	4 (25)	2 (18.8)	
		Moderate UI	9 (56.3)	5 (31.3)	
		Severe UI	3 (18.8)	1 (6.3)	
	PFMT	No UI	0 (0)	9 (52.9)	**0.003***
		Mild UI	3 (17.6)	3 (17.6)	
		Moderate UI	9 (52.9)	3 (17.6)	
		Severe UI	5 (29.4)	3 (17.6)	
	p_2		0,620	0,300	

UI: Urinary incontinence, ICIQ-UI SF: International Consultation on Incontinence Questionnaire-Short Form, PFMT: Pelvic floor muscle training. Data are presented as number (percentage). p_1: Comparison of changes in outcome variables between baseline and 8th week, Mann-Whitney U test, p_2: Comparison of changes between groups, Kruskal Wallis test * $p<0.05$
No UI: 0, Mild UI: 1–5, Moderate UI: 6–12, Severe UI: 13–18, Very severe UI: 19–21 for ICIQ-UI SF; No UI: <1 g, Mild UI: 1-10 g, Moderate UI: 11-50 g, Severe UI: >50 g for 1-hour pad test

Table 1. Comparisons of symptoms and objective incontinence severity within and between groups

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A QUALITATIVE STUDY OF WOMEN'S VIEWS AND EXPERIENCES OF MULTIMODAL PELVIC FLOOR PHYSIOTHERAPY FOR TREATING DYSPAREUNIA AFTER GYNECOLOGICAL CANCER: AN INSIGHT INTO THIS TREATMENT'S ACCEPTABILITY

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HYPOTHESIS / AIMS OF STUDY

Women treated for gynecological cancer are often affected by pain during sexual intercourse, namely dyspareunia. Despite the negative impact of this condition on women's quality of life, only a few treatments with limited supporting evidence have been proposed in clinical practice guidelines [1]. A recent prospective interventional study has investigated a multimodal pelvic floor physiotherapy (PFPT) treatment in a cohort of women affected by dyspareunia following gynecological cancer [2]. The results suggested significant improvements following treatment, such as a reduction in pain as well as an improvement in sexual function, pelvic floor muscle function (i.e., reduction in muscle tone and increase in tissue flexibility and contractile properties) and psychosexual outcomes (e.g., increase in self-efficacy) at post-treatment, which were maintained at 12-month follow-up [3]. These promising effects indicate that women could benefit from this treatment as part of cancer survivorship care. However, data informing us on whether multimodal PFPT could be implemented in healthcare settings are scarce. Acceptability is a key component in the development and implementation phases of complex treatments. This multifaceted construct reflects the extent to which patients consider a treatment to be appropriate. Data relating to the acceptability of multimodal PFPT treatment in gynecological cancer survivors with dyspareunia are limited to women's adherence to home exercises (88%), the attendance rate at treatment sessions (93%), and the average satisfaction rate (93%) assessed at post-treatment [2]. Careful consideration of patients' views and experiences provides the best opportunity to deepen our understanding of treatment acceptability and to optimize the treatment in healthcare settings. Therefore, the aim of this study was to explore the views and experiences of gynecological cancer survivors with dyspareunia regarding the acceptability of a multimodal PFPT treatment.

STUDY DESIGN, MATERIALS AND METHODS

This qualitative study followed the study that investigated a 12-week multimodal PFPT treatment in a cohort of gynecological cancer survivors with dyspareunia. The multimodal PFPT treatment consisted of 12 weekly individual 60-min sessions, free of charge. The treatment was delivered in person by a physiotherapist with expertise in pelvic and women's health. The treatment comprised education, myofascial release techniques, pelvic floor muscle exercises with biofeedback, and home exercises, including the use of a vaginal dilator. The treating physiotherapist also provided support to women for resuming pain-free sexual intercourse. After completing their participation, women were invited to take part in an individual telephone interview conducted by a physiotherapist not involved in the treatments. Interviews were carried out at 12-month follow-up, allowing the participants to take a step back from the treatment and provide critical insight on treatment acceptability in the long term. The interview guide was constructed based on the framework of acceptability proposed by Sekhon et al. (2017). All interviews were recorded and transcribed for analysis. An inductive approach was adopted where codes are applied to key ideas which give form to emerging themes. The research team members responsible for interviewing and coding the transcriptions were blinded to the participants' treatment response. Coding disagreements were discussed until a consensus was achieved. The research team reviewed the codes during meetings.

RESULTS

Of the 31 women who participated in the multimodal PFPT treatment, 28 (90%) accepted to take part in the interviews at 12-month follow-up. One woman withdrew for family reasons, one was lost at follow-up, and one woman was not available. No significant difference in participant characteristics or treatment response was found between those who participated and those who did not participate in the interviews. At baseline, the mean age of our cohort was 55.9 (SD 10.8) years and the mean body mass index was 28.5 (SD 5.3) kg/m2. Women were diagnosed at various cancer stages and received different oncological treatments: 24 (77%) had surgery, 19 (61%) had brachytherapy, 15 (48%) had external beam radiation therapy, and 16 (52%) had chemotherapy. At 12-month follow-up, three women indicated that they had cancer recurrence or another cancer, and one woman had a severe upper urinary tract infection. Participants confirmed that they did not undertake other treatments during the 12-month follow-up period.

Our cohort described the acceptability of multimodal PFPT according to three main themes. Figure 1 shows the relationship between the themes. Theme 1: Appropriateness of treatment characteristics. The participants reported that the treatment was acceptable given the relevance of the multimodal PFPT treatment characteristics for reducing dyspareunia. They indicated that the choices in treatment modalities, healthcare provider (physiotherapist), care delivery (in person), and treatment intensity were appropriate. Theme 2: Balance between participation and treatment effects. Women explained how the treatment characteristics, along with their beliefs, attitudes, and awareness of the treatment effects, motivated their participation and their efforts to fully adhere to the treatment. Although a few women perceived the treatment intensity as demanding in terms of participation, they all emphasized that it was crucial in achieving significant improvements. Theme 3: Satisfaction. Given their positive experiences with the treatment characteristics and the balance between their efforts and the results they obtained, all women expressed being highly satisfied with the treatment. As a result, all participants recommended this treatment.

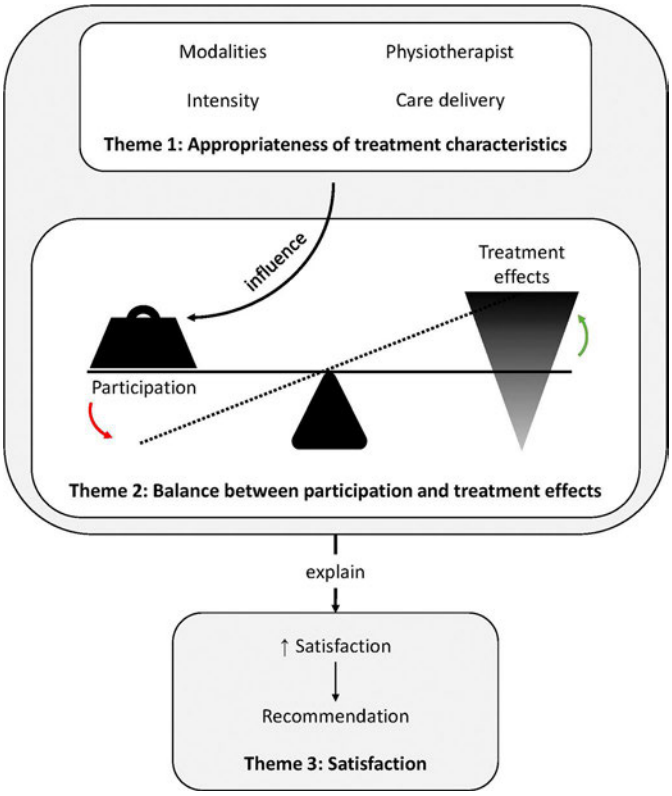
INTERPRETATION OF RESULTS

This is the first study to examine the acceptability of multimodal PFPT for treating women affected by dyspareunia after gynecological cancer. The findings of this qualitative study suggest that multimodal PFPT is acceptable according to gynecological cancer survivors with dyspareunia. The results highlight the importance of selecting the appropriate treatment modalities, healthcare provider, care delivery, and treatment intensity in healthcare settings. Interestingly, although the participants described the intensity as being the principal inconvenience of multimodal PFPT, all women stressed that it was crucial in obtaining satisfying outcomes. The participants also reported that the effects they perceived were related to their participation in the multimodal PFPT treatment. Efforts could therefore be made to alleviate women's perception of burden related to the treatment intensity and to increase their participation. For instance, the underlying mechanisms of dyspareunia related to cancer and oncological treatments and how multimodal PFPT is relevant could be described to women. Explaining how their participation is important in reaching satisfying outcomes could be emphasized. Highlighting the changes throughout the treatment could also encourage women's participation. Given our cohort's positive views and experiences of multimodal PFPT, it is not surprising that all participants recommended this treatment.

CONCLUDING MESSAGE

Multimodal PFPT treatment was deemed acceptable by women affected by dyspareunia after gynecological cancer. The results provide a deeper understanding of what makes this treatment acceptable to women, namely the appropriateness of treatment characteristics, the balance between participation and treatment effects, and satisfaction. Our work also identified several aspects that should be considered in the implementation stage. The findings of this study can serve as a basis for multidisciplinary teams and decision-makers to successfully implement multimodal PFPT to improve the pelvic health of women in gynecological cancer survivorship care.

FIGURE 1



Acceptability of multimodal PFPT treatment.

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HYDROPHILIC VERSUS NON-HYDROPHILIC CATHETERS FOR CLEAN INTERMITTENT CATHETERIZATION: A METANALYSIS TO DETERMINE THEIR CAPACITY IN REDUCING URINARY TRACT INFECTIONS.

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HYPOTHESIS / AIMS OF STUDY
Clean intermittent catheterization (CIC) is associated with increased risk of urinary tract infections (UTI), urethral trauma, urethral stenosis, hematuria and pain. The first catheters developed were made of polyvinyl carbon (PVC). Different types of catheters have been developed to reduce these complications, such as those with hydrophilic coating. The aim of the present study is to determine the rate of urinary tract infections in patients on CIC , who use hydrophilic coated versus uncoated catheters.

STUDY DESIGN, MATERIALS AND METHODS
A systematic literature search was performed in OVID, Embase, Scopus, Web of Science, PubMed, and CENTRAL databases, to identify randomized controlled trials (RCTs) or randomized crossover trials, comparing UTI and hematuria rates in patients using hydrophilic vs. non-hydrophilic catheters for CIC. Literature search was performed using a combination of keywords (MeSH terms and free text words) including ("Intermittent Urethral Catheterization" OR "Intermittent Urethral Catheterization" AND "Urinary Tract Infection" OR "Urinary Tract Infections" OR "Catheter-Related Infections", "Urinary Catheters"). The search aimed to identify all the papers reporting the results of RCTs and randomized crossover trials in full-length articles published in English and Spanish, with no time period limit.

Two independent reviewers carried out the screening process for full-text articles. Once selected, information about study design, inclusion criteria, baseline patient characteristics, and outcomes was recorded. Boths reviewers analyzed the studies, and decided if they should be included. Whenever there was no agreement, a third reviewer determined the inclusion of the study.

The selected RCTs were evaluated for risk of bias by two reviewers individually, using the "Revised Cochrane risk-of-bias tool for randomized trials (RoB 2)", according to the Cochrane Handbook for Systematic Reviews of Interventions (The Cochrane Collaboration, 2018). When discrepancies were found in the risk-of-bias judgment, they were reviewed by a third author. The results were expressed as risk ratio (RR) with 95% confidence interval (CI), under a random-effects model. Data were analyzed using Review Manager 5.4 software.

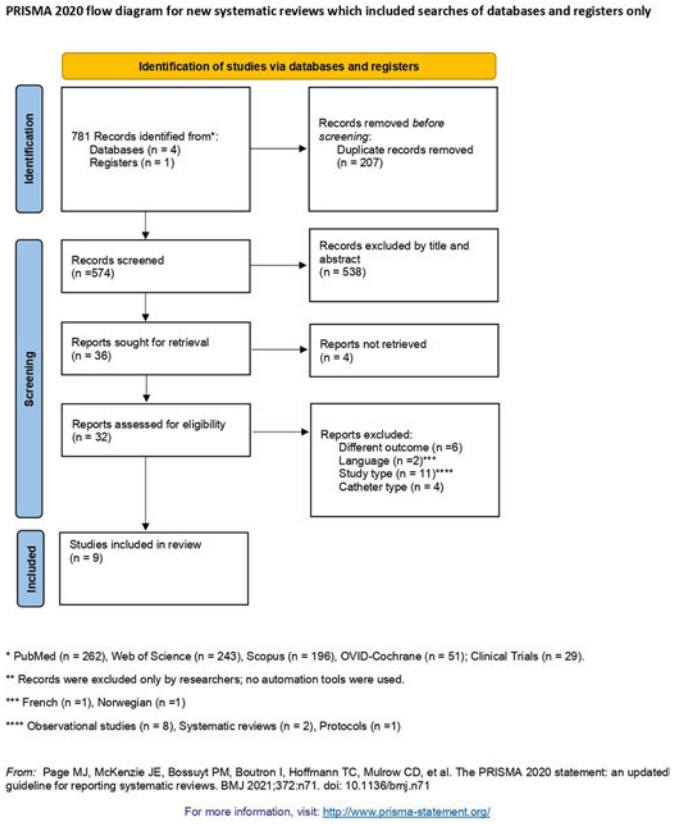
RESULTS
A total of 781 articles were found. After removing the duplicates, 574 articles were left for analysis. We carried out an initial screening by title and abstract, identifying 36 articles for complete review. After applying the inclusion criteria, nine articles were selected to continue with the quality assessment. The Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) flow diagram is shown in Fig. 1.

We identified seven RTCs and two cross-over studies that evaluated urinary tract infection or hematuria in hydrophilic or uncoated catheters users. Nine studies with a total of 525 patients in CIC were analyzed. Overall, the use of hydrophilic catheters had a lower risk of UTIs compared to uncoated catheters (RR = 0.78; 95% CI: 0.62 – 0.97; I2: 37%).(Figure 2) Five of the studies included patients > 18 years showing a reduction of UTIs with the use of hydrophilic catheters (RR= 0.83; 95% CI: 0.74 - 0.93; I 2: 0%). There was no difference in UTI development when comparing single use uncoated vs hydrophilic catheter. However heterogeneity was high (RR = 0.77; 95% CI: 0.59 - 1.00; I2=57%).

INTERPRETATION OF RESULTS
Hydrophilic catheters had a UTI risk reduction of 17% when were compared to uncoated catheters (RR= 0.83; 95% CI: 0.74 - 0.93; I 2: 0%) in adults patients in CIC. We did no find difference in UTI development when comparing single use uncoated vs hydrophilic catheter. However, in this analysis heterogeneity was high.

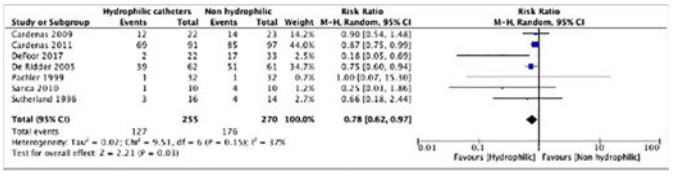
CONCLUDING MESSAGE
This meta-analysis verified a risk reduction of UTIs associated with the use of hydrophilic catheters for IC in adults. Significative differences were not probe in terms of UTI in pediatrics population o hematuria overall. Urethral trauma presence could not be meta-analyzed due to lack of information reported. These result must be interpreted considering that heterogeneity was high between included studies, specially when we assessed hematuria.

FIGURE 1



The Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) flow diagram is shown in Fig. 1

FIGURE 2



Metanalysis of UTIs frequency in patients with IC using hydrophilic catheters compared to non – hydrophilic catheters.

Funding Private funding for research was obtained as an independent research initiative, granted by Coloplast. **Clinical Trial** No **Subjects** Human **Ethics Committee** The current study was approved by the institutional ethics committee **Helsinki** Yes **Informed Consent** No

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SESSION 21 - OVERACTIVE BLADDER

Abstracts 291-302
11:30 - 13:00, Hall G
Chair: Mr Marcus John Drake (United Kingdom)

291 | www.ics.org/2022/abstract/291

A SINGLE-BLIND, RANDOMIZED, PLACEBO CONTROLLED, PROSPECTIVE TRIAL FOR PATIENTS WITH NON-NEUROGENIC OVERACTIVE BLADDER SYNDROME TREATED WITH TRANSCUTANEOUS TIBIAL NERVE STIMULATION

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HYPOTHESIS / AIMS OF STUDY
The idiopathic overactive bladder syndrome is a bothersome medical issue for patients. Unfortunately, the treatment options mostly go along with bothersome side effects as well. Many patients' withdrawal their treatment due to these side effects. Central neuromodulation is a well-established treatment option despite being an invasive procedure. In the past years peripheral neurostimulation has evolved as viable alternative. The percutaneous tibial nerve stimulation (PTNS) is a potential treatment option as first line treatment. The need for medical advice during this treatment and the placement of needles make it a complex procedure even in an outpatient clinic. The transcutaneous tibial nerve stimulation (TTNS) which use adhesive electrodes is less time consuming and can be used by the patients being at home.

We investigate the TTNS as potential conservative management in the treatment of overactive bladder syndrome in this clinical trial.

STUDY DESIGN, MATERIALS AND METHODS
Our trial was designed as single-blind, randomized, prospective trial for patients with overactive bladder syndrome (OAB). We included patients, female, and male, with a non-neurogenic overactive bladder syndrome with no anatomical abnormalities of the lower urinary tract (eg. bladder outlet obstruction, pelvic organ prolapse). Improvement of symptoms reported by the patients and documented by questionnaires (PGI-I) were set as primary endpoint. Adhesive electrodes were attached to the N. tibialis posterior at the medial ankle. A stimulation of the N. fibularis superficialis (lateral ankle) was used as sham stimulation (placebo). The patient side was blinded. The patients were counseled to use the device 15 minutes each day of the week (20 Hz). There were trained by an expert for medical functional electrostimulation.

The statistical analyses were made by SPSS version 27. We used a chi-squared test for non-normal distribution or a two-sided t-test for normal distribution. For an estimated power of 95% in this setting a sample of 58 patients in each arm were calculated. We scheduled 18 months for recruitment.

RESULTS
Overall, we included 82 patients (68 women, 14 men) in 18 months. There were no significant differences neither in the clinical meaningful endpoints of 24-hour frequency (placebo -1.94 vs. verum -1.27, ChiQuadrat $p = 0.2$) , urgency urinary incontinence episodes in 24-hour (0.22 vs 0.22 , $p = 0.32$) and nocturia (-0.27 vs. -0.16, $p = 0.76$), nor in the validated questionnaires overactive bladder symptom score (OAB-SS) (-0.76 vs. 1.33 , $p = 0.18$) ; International Consultation on Incontinence Questionnaire-Urinary Incontinence Short Form ICIQ-UI SF (-1.13 vs. -0.74 , $p = 0.48$) or Patient Global Impression scale disease improvement (PIG-I) (2.47 vs. 2.54 , t-test $p = 0.72$).

There were no side effects of the treatment reported by the patients.

INTERPRETATION OF RESULTS
To our knowledge this was the first single-blind, randomized and placebo-controlled trial to examine the efficiency of a transcutaneous tibial nerve stimulation contributed by an external stimulator. The TTNS were non superior to placebo. Despite this low efficiency patients did not regret the treatment because of its noninvasive with nearly no side effects. We missed the calculated sample size because of a high number of ineligible patients despite a great response with a big number of screened patients.

It should be mentioned that the improvement under sham stimulation was unexpected strong.

CONCLUDING MESSAGE
The TTNS showed no significant improvement for the treatment of overactive bladder syndrome in comparison to a sham stimulation.

As clinicians we should discuss wether a treatment option with nearly no side effects would be worth a try despite being no more effective than placebo.

Funding The trial was funded by TIC-Medizintechnik GmbH, Germany. **Clinical Trial** Yes **Public Registry** No **RCT** Yes **Subjects** Human **Ethics Committee** Ethics committee of the University of Muenster, North Rhine Westphalia, Germany **Helsinki** Yes **Informed Consent** Yes

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PERONEAL ELECTRIC TRANSCUTANEOUS NEUROMODULATION (PERONEAL ETNM®) IS SAFE AND EFFECTIVE IN THE TREATMENT OF THE REFRACTORY OVERACTIVE BLADDER IN HOME-BASED SETTINGS

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HYPOTHESIS / AIMS OF STUDY

Idiopathic overactive bladder symptoms (OAB) have a profound impact on the quality of life of the affected individuals. Although several treatment options are available, each of them is associated with significant drawbacks, which limit their wide use in clinical practice [1].

The Peroneal electric Transcutaneous NeuroModulation (Peroneal eTNM®) is a new fully noninvasive neuromodulation method based on selective stimulation of the peroneal nerve. The URIS® neuromodulation system, engineered to deliver Peroneal eTNM®, consists of the URIS® device, URIS® active electrodes, and the biofeedback foot sensor (BFS). The unique design of the URIS® device and URIS® active electrodes allows for the use of a low voltage during neuromodulation, which significantly reduces the unpleasant sensations. The BFS allows for precise localization of the active electrodes and for continuous adjustment of the stimulation parameters during the stimulation session to achieve the optimal therapeutic effect.

In the initial pilot study, peroneal eTNM® showed excellent efficacy and tolerability in the out-patient office setting [2]. The aim of the present study was to evaluate the efficacy and safety of peroneal eTNM® using URIS® neuromodulation system performed by patients with refractory OAB themselves in home-based setting.

STUDY DESIGN, MATERIALS AND METHODS

This study was designed as a prospective open-label, multicenter trial. The study protocol was approved by independent Institutional Review Board at each study center and all participants provided informed consent.

The study enrolled adult female patients with a clinical diagnosis of refractory idiopathic OAB. The inclusion criteria at baseline included failure of at least one therapeutic attempt during one-year prior to enrollment and ≥ one urgency episode grade 3 or grade 4 according to Patients Perception of Intensity of Urgency Scale (PPIUS) in course of 24 hours and frequency ≥ 8 times/24 hours as documented using the 7-day bladder diary. The exclusion criteria included urinary tract infection, significant prolapse of the pelvic organs, history of previous malignant disease in the pelvic area and any neurological disease that may affect urinary bladder function, among others.

Enrolled patients were treated with peroneal eTNM® using the URIS® neuromodulation system (STIMVIA®, Ostrava, Czech Republic) in their homes for 30 minutes daily for 6 weeks.

The 7-day bladder diary, OAB V8 questionnaire, Treatment satisfaction visual analogue scale (TS VAS) and Pain perception visual analogue scale (PP VAS) were used to assess treatment efficacy and tolerability. The safety assessments included monitoring of the incidence and severity of adverse events (AEs).

The primary endpoint was defined as proportion of subjects with ≥ 50% reduction in average daily number of severe urgency episodes after six weeks of therapy.

Statistical analyses were performed with GraphPad Prism 9.0.0 (GraphPad Software, Inc., San Diego, CA). A non-parametric one-way ANOVA Friedman test was used to compare the changes of categorical variables, while Wilcoxon rank-sum tests were used to assess the changes of the non-categorical variables. P-value < 0.05 was considered statistically significant. No correction for multiple testing was applied.

RESULTS

In total, 40 subjects were screened for the study, 29 of them met the inclusion criteria at BL and were enrolled and ultimately included into the Full Analysis Set. Key participant demographics include: age (median [min.-max.]) 62 [42-77] years, BMI (mean [±SD]) 28 [5.6] and duration of OAB symptoms (median [95%CI]) 6 [4-10] years. Twenty-five out of 29(86%) and 23/29 (79%) of patients were classified as responders at week 4 and at End of Treatment (EoT) visit, respectively. Changes in absolute number of severe urgency episodes are shown in Figure 2. There was significant reduction in urinary frequency from baseline to EoT ($p < 0.001$), number of grade 3 urgency episodes ($p < 0.001$), number of grade 4 urgency episodes ($p = 0.001$) and number of nocturia episodes ($p = 0.002$). The OAB V-8 score also showed significant improvement ($p < 0.001$), reducing the baseline OAB-V8 score by a median of -38% (-51% to -17%, 95% CI). There was a significant improvement in the TS VAS by 230% from 20 (15 to 29, 95% CI) to 66 (30 to 86, 95% CI) ($p < 0.001$).

Overall, the therapy was very well tolerated. Pain perceived during peroneal eTNM® sessions as rated using PP VAS was 0 (0 to 1.5, IQR) at week 1 and 0 (0 to 3.5, IQR) at EoT.

There were 24 AEs recorded, two of them were considered treatment-related. One participant reported light superficial skin abrasion at the contact point with the active electrode and another participant noted limited ability to move the toes of the left foot for several minutes after a session was completed. Both events were considered mild and did not require any intervention. Both patients recovered with no sequelae and completed the study according to the protocol.

INTERPRETATION OF RESULTS

This study documented a significant reduction in all OAB symptoms and an improvement in all patient-reported outcomes in a cohort of female patients with refractory OAB, treated with peroneal eTNM® using the URIS® neuromodulation system. The peroneal eTNM® showed favorable safety profile with very low incidence of treatment-related adverse events. Recording of patients' perception of pain/discomfort during treatment confirmed excellent tolerability of the peroneal eTNM®. Based on PP-VAS scores reported in this study, the method can be considered very close to painless. The data document that peroneal eTNM® can be performed by patients themselves after minimal training at home.

CONCLUDING MESSAGE

The data collected in this study provide the initial evidence that peroneal eTNM® using the URIS® neuromodulation system is effective and safe method for the home-based treatment of OAB. Further research is required to confirm its long-term efficacy and safety and to assess the optimal neuromodulation schedule.

FIGURE 1

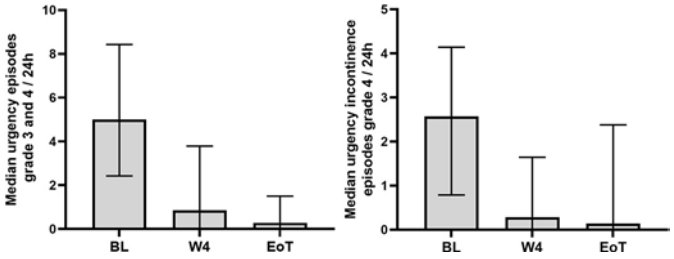

Figure 1: Changes in number of severe urgency episodes and urgency incontinence episodes during the study

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Funding This study was funded by STIMVIA®, Ostrava, Czech Republic **Clinical Trial** Yes **Registration Number** ClinicalTrials.gov database (reg. Nr. NCT 05211193) **RCT** No **Subjects** Human **Ethics Committee** Institutional Review Board at each study center **Helsinki** Yes **Informed Consent** Yes

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TRANSCUTANEOUS ELECTRICAL TIBIAL NERVE STIMULATION IN TREATMENT OF OVERACTIVE BLADDER SYNDROME IN OLDER WOMEN – RANDOMIZED CONTROLLED CLINICAL TRIAL

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HYPOTHESIS / AIMS OF STUDY

Transcutaneous electrical tibial nerve stimulation (TTNS) is being studied for the management of Overactive Bladder Syndrome (OAB). It is a non-invasive, effective, safe, and tolerable treatment to reduce voiding symptoms in adults and the elderly with idiopathic and neurogenic OAB (1). Schreiner et al suggested the use of TTNS associated with behavioral therapy (BT) as a first-line intervention for the treatment of OAB symptoms in older women (2). The overactive bladder has a global prevalence in both sexes and tends to increase with advancing age, in addition, to having a negative impact on quality of life (QoL) (1). Among the treatment options, Guidelines (3) suggest, as a gold standard, initially, conservative treatment with behavioral therapy (BT), which includes bladder training, pelvic floor muscle training (PFM), and fluid intake control. Considering the prevalence and impact on QoL, in addition to the option of non-invasive treatments and vaginal manipulation in this population, further research is needed regarding TTNS in elderly women as a safe and tolerable form of treatment, non-medicated, with the use of superficial electrodes to reduce the symptoms of OAB. Therefore, the objective of this study was to evaluate the effects of transcutaneous electrical tibial nerve stimulation associated with behavioral therapy in the treatment of OAB in older women, comparing the effects of exclusive behavioral therapy, a treatment recommended as the first line by the Guidelines in adults.

STUDY DESIGN, MATERIALS AND METHODS

A randomized controlled clinical trial was conducted with a blinded evaluator and a comparison between control and intervention groups. The sample was selected for convenience and the screening of patients was performed through the indication of doctors, and partner groups and the dissemination of the service in groups of older women in the city. The inclusion criteria were female gender, age between 60 and 80 years, with the presence of urinary dysfunction identified by the score greater than or equal to 8 points in the OAB-V8 (Overactive Bladder Awareness Tool) questionnaire. Were excluded women with lower urinary tract infection, identified by a urine test, history of treatment for OAB in the last 6 months, baseline neurological diseases, history of genitourinary neoplasia, previous pelvic irradiation, genital prolapse that exceeds the vaginal ostium, cardiac pacemaker, or use of medicine for OAB. The analyzed variables of the study were symptoms and degree of discomfort of the OAB through the ICIQ-OAB (International Consultation on Incontinence Questionnaire Overactive Bladder). The treatment of the G1 consisted of 2 sessions of BT, which were passed orientations concerning the proper positioning for urination, always seated, with legs apart, trunk forward, elbows supported on the knees, and use of foot support to maintain greater hip flexion; programmed urination, patients should try to postpone the urination to the maximum, trying to reach an interval of 2 hours; avoid the ingestion of liquid 2 hours before bedtime to avoid episodes of nocturia and avoid the consumption of irritants food and beverages to the bladder. The G2 performed 8 sessions (2x per week) of TTNS associated with 2 sessions of BT. The following parameters were fixed for electrical nerve stimulation F = 10 Hz, T = 200 μs, t = 30 min, and maximum intensity tolerated by the patient. The sample size calculation was performed from a pilot study with 19 participants (8 in G1 and 11 in G2), using the G-Power 3.1.9.2 program, with a significance level of 5% and an error of 20%. Based on the main outcome of the impact of OAB symptoms in QoL, a sample size of 17 participants was obtained in each group. Data analysis was performed using SPSS 26 software. Data normality was verified using the Shapiro-Wilk test. The comparison of OAB symptoms before and after the intragroup intervention was analyzed using the Wilcoxon test and the analysis between the groups was using the Mann-Whitney U test. The significance level adopted was 5% ($p < 0,05$). Intention-to-treat analysis was performed to preserve randomization. To evaluate the power of the test used in the study was applied the post hoc analysis demonstrated power of 0.94 with an effect size of 0.81.

RESULTS

Were considered eligible for the study, 75 older women with OAB. After the initial interview, 37 patients were excluded by: of neurological disease (12), lower urinary tract infection (1), previous pelvic irradiation (1), cardiac pacemaker (1), severe genital prolapse (8), history of physiotherapeutic treatment for OAB (7) and drug treatment for OAB (7). Thus, 38 patients were randomized to compose the final study sample, 19 in G1 (BT) and 19 in G2 (BT + TTNS).

INTERPRETATION OF RESULTS

Both groups were homogeneous for the characteristics and clinical complaints analyzed pre-treatment. In the intragroup comparison, there was a significant improvement in QoL in both groups (G1 - BT and G2 - BT + T-TNS). Group 1 (BT) also showed a significant reduction in the discomfort of urgeincontinence and nocturia symptoms. In G2 (BT + TTNS), only the daytime frequency variable showed no significant reduction evaluated by the ICIQ-OAB. No significant differences were found in the analysis between groups (Table I).

CONCLUDING MESSAGE

If we consider the reduction in the discomfort of OAB symptoms, other than the discomfort daytime urinary frequency, evaluated by the ICIQ-OAB, transcutaneous electrical tibial nerve stimulation can be used as initial therapy associated with behavioral therapy in older women with overactive bladder. However, we emphasize that the aspects related to the improvement of quality of life, both combined therapy and isolated behavioral therapy were effective.

FIGURE 1

Table 1 – Comparison of quality of life and urinary symptom inter and intra-group (before and after intervention)

Variable Mean ± SD	G1 (n = 19)	G2 (n = 19)	*p*	*p*[a]
ICIQ-OAB (total score)				
Before	9,58 ± 3,91	8,74 ± 3,25		
After	7,26 ± 4,54	4,99 ± 2,27	0,47	0,12
p[b]	**0,01**	**<0,001**		
Mean – CI 95%	-2,32 (-3,93 a -0,70)	-3,75 (-5,20 a -2,29)		
ICIQ-OAB (bother)				
Bother of Daytime frequency				
Before	5,74 ± 4,39	6,95 ± 3,81		
After	4,53 ± 3,92	4,96 ± 3,21	0,40	0,40
p[b]	0,10	0,10		
Mean – CI 95%	-1,20 (-2,73 a 0,33)	-1,98 (-4,23 a 0,27)		
Bother of Nocturia				
Before	7,47 ± 4,14	6,00 ± 4,29		
After	4,49 ± 3,59	2,93 ± 3,23	0,17	0,92
p[b]	**0,01**	**0,004**		
Mean – CI 95%	-2,98 (-5,17 a -0,79)	-3,07 (-4,77 a -1,37)		
Bother of Urgency				
Before	8,11 ± 2,87	8,26 ± 2,60		
After	6,56 ± 3,94	4,42 ± 3,49	0,98	0,06
p[b]	0,18	**0,002**		
Mean – CI 95%	-1,54 (-3,47 a 0,38)	-3,84 (-5,80 a -1,88)		
Bother of Urgency urinary incontinence				
Before	7,95 ± 3,26	7,58 ± 3,53	0,76	0,39
After	5,85 ± 4,00	4,60 ± 3,16		
p[b]	**0,03**	**0,03**		
Mean – CI 95%	-2,10 (-3,95 a -0,25)	-2,98 (-5,63 a -0,33)		

p Mann-Whitney U test for analyze homogeneity between groups; *p*[a] Mann Whitney U test for intergroup comparison; *p*[b] Wilcoxon test for intragroup comparison; ICIQ-OAB *International Consultation on Incontinence Questionnaire Overactive Bladder*; G1 behavioral therapy; G2 transcutaneous electrical tibial nerve stimulation and behavioral therapy; x±SD mean ± standard deviation; CI confidence interval

Table I - Comparison of quality of life and urinary symptom inter and intra-group (before and after intervention)

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Funding None **Clinical Trial** Yes **Registration Number** REBEC: RBR-9q7j7y **RCT** Yes **Subjects** Human **Ethics Committee** College of Medicine of University of Brasilia – UnB **Helsinki** Yes **Informed Consent** Yes

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ACUPUNCTURE FOR OVERACTIVE BLADDER IN ADULTS: A COCHRANE REVIEW

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1. Newcastle upon Tyne Hospitals NHS Foundation Trust, 2. Centre for Evidence-Based Chinese Medicine, Beijing University of Chinese Medicine, 3. Northumbria University, 4. Warwick University, 5. Breeze Academy

HYPOTHESIS / AIMS OF STUDY
This is the first Cochrane Review to address the use of acupuncture to treat symptoms of overactive bladder in adults. The abstract is based on a post-editorial review version of the review. Upon completion and approval, the final version is expected to be published in the Cochrane Database of Systematic Reviews (www.cochranelibrary.com)."

Overactive bladder (OAB) is a symptom complex including frequency of micturition, urgency with or without associated incontinence, and nocturia (1). It is a common, long-term complaint with around 11% of the population having symptoms; this figure increases with age. Symptoms can be linked to social anxiety and adaptive behavioural change. The cost of treating OAB is considerable. Medication for OAB is poorly tolerated or ineffectual in many cases (2). Botox injections and sacral nerve stimulation are invasive treatments and are associated with side effects. Therefore, it is imperative that alternative strategies are tested. Researchers have studied the effect of acupuncture as a treatment for OAB, and it is postulated to influence afferent and efferent nerve signalling to the bladder and central nervous system.

The aims of the review were to assess the effects and safety of acupuncture for treating OAB in adults; and to summarise the priorities for further research.

STUDY DESIGN, MATERIALS AND METHODS
This review drew on the search strategy developed for Cochrane Incontinence. We identified relevant trials from the Cochrane Incontinence Specialised Register. We also searched the Allied and Complementary Medicine database (AMED) on OvidSP. In addition, electronic bibliographic databases where knowledge of the Chinese language was necessary were searched, China National Knowledge Infrastructure (CNKI); Chinese Medical Literature Database (CBM); Chinese Medical Current Content (CMCC)VIP, and WANFANG (China Online Journals). The date of the most recent search of the Cochrane Incontinence Specialised Register for this review is 1 March 2021

We included randomised controlled trials (RCTs), quasi-RCTs, and cross-over studies of acupuncture for treating OAB in adults. Four review authors formed pairs to review studies and extract data (two for English-language studies; two for Chinese-language studies). Both pairs of review authors used Covidence software (3) and the same screening and data extraction processes. Risk of bias was assessed using Cochrane's 'Risk of bias' tool and heterogeneity was assessed using the Chi2 and I2 statistics generated in the meta-analyses. A fixed effects model was used unless there was a moderate or high level of heterogeneity when a random effects model was employed. The GRADE approach was used to assess the certainty of evidence.

RESULTS
We included 15 studies involving 1395 participants in the review. Of these, 14 were RCTs and 1 was a quasi-RCT.

Acupuncture versus no treatment

One study compared acupuncture to no treatment to establish feasibility for a larger study. The evidence is very uncertain regarding the effect of acupuncture compared to no treatment in terms of cure or improvement in OAB symptoms.

Acupuncture versus sham acupuncture

Five studies compared acupuncture with sham acupuncture. The evidence is uncertain about the effect of acupuncture on cure or improvement in OAB symptoms compared to sham acupuncture (SMD -0.36, 95%CI -1.03 to 0.31; 3 studies; 151 participants; I2 = 65%; very low-certainty evidence).

Acupuncture versus medication

Eleven studies compared acupuncture with medication for OAB symptoms. Low certainty evidence suggests that acupuncture may slightly increase cure or improvement in OAB symptoms compared to medication for OAB (RR 1.25; 95% CI 1.10 to 1.43; 5 studies; 258 participants; I2 =19%; low certainty evidence).

Safety of acupuncture for OAB

There were no incidences of major adverse events in any of the included studies. However, major adverse events are rare in acupuncture trials and the numbers included in this review may be insufficient to detect these events.

There is no evidence of a difference between true and sham acupuncture in terms of minor adverse events. There is low-certainty evidence that acupuncture may slightly reduce the incidence of minor adverse events when compared to medication for OAB (OR 0.25; 95% CI 0.18 to 0.35; 8 studies; 1004 participants; I^2 = 73%; low certainty evidence).

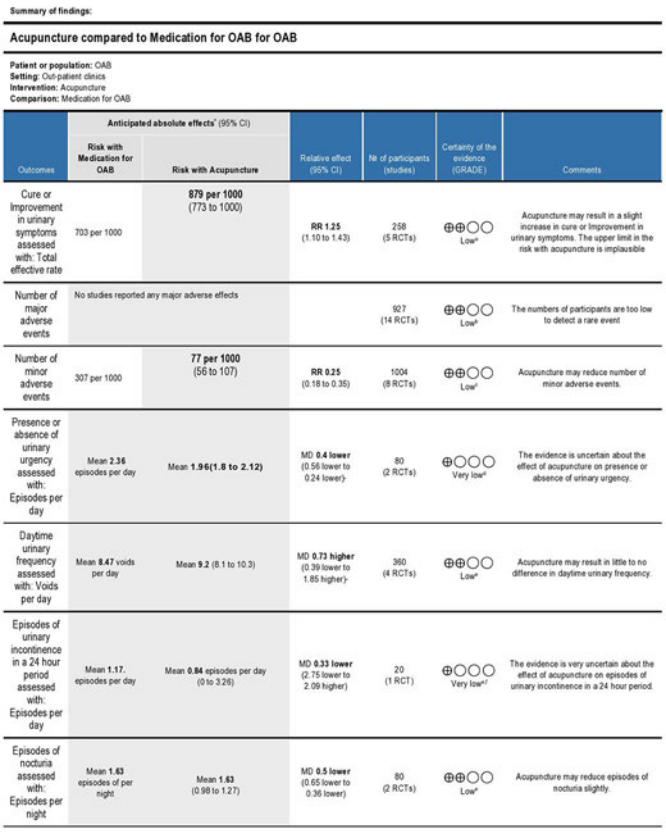
INTERPRETATION OF RESULTS
This review provides low-certainty evidence that acupuncture may result in a slight increase in cure or improvement of OAB symptoms when compared with medication for OAB. In addition, it may reduce the incidence of minor adverse effects compared to medication.

It is uncertain if there is any difference between acupuncture and sham acupuncture for cure or improvement in OAB symptoms.

The evidence is very uncertain about the effect acupuncture has on cure or improvement in OAB symptoms compared to no treatment.

CONCLUDING MESSAGE
The conclusions of this review were limited by the certainty of the current evidence. The review team identified that many of the included studies recruited small numbers of participants, had design flaws, and were conducted over a short time-period. The evidence does suggest that acupuncture may have similar outcomes to medication for OAB but with a lower side effect profile. This finding must remain tentative until larger, high-quality studies, that use comparable and relevant outcomes, are completed. Timing and frequency of treatment, point selection, application and long- term follow up are all relevant topics for research. Acupuncture could be offered as a treatment option to OAB sufferers who are not suitable for, or do not wish to consider more invasive treatments or those who wish to avoid the use of medication.

FIGURE 1



Summary of findings:

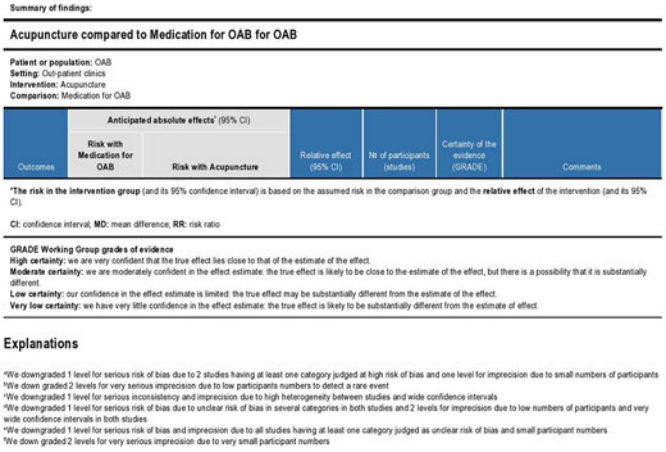
Acupuncture compared to Medication for OAB for OAB

Patient or population: OAB
Setting: Out-patient clinics
Intervention: Acupuncture
Comparison: Medication for OAB

Outcomes	Anticipated absolute effects* (95% CI) Risk with Medication for OAB	Risk with Acupuncture	Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
Cure or Improvement in urinary symptoms assessed with: Total effective rate	703 per 1000	**879 per 1000** (773 to 1000)	**RR 1.25** (1.10 to 1.43)	258 (5 RCTs)	⊕⊕◯◯ Low[a]	Acupuncture may result in a slight increase in cure or Improvement in urinary symptoms. The upper limit in the risk with acupuncture is implausible
Number of major adverse events	No studies reported any major adverse effects			927 (14 RCTs)	⊕⊕◯◯ Low[b]	The numbers of participants are too low to detect a rare event
Number of minor adverse events	307 per 1000	**77 per 1000** (56 to 107)	**RR 0.25** (0.18 to 0.35)	1004 (8 RCTs)	⊕⊕◯◯ Low[c]	Acupuncture may reduce number of minor adverse events.
Presence or absence of urinary urgency assessed with: Episodes per day	Mean **2.36** episodes per day	Mean **1.96(1.8 to 2.12)**	MD **0.4 lower** (0.56 lower to 0.24 lower)	80 (2 RCTs)	⊕◯◯◯ Very low[a]	The evidence is uncertain about the effect of acupuncture on presence or absence of urinary urgency.
Daytime urinary frequency assessed with: Voids per day	Mean **8.47** voids per day	Mean **9.2** (8.1 to 10.3)	MD **0.73 higher** (0.39 lower to 1.85 higher)	360 (4 RCTs)	⊕⊕◯◯ Low[a]	Acupuncture may result in little to no difference in daytime urinary frequency.
Episodes of urinary incontinence in a 24 hour period assessed with: Episodes per day	Mean **1.17.** episodes per day	Mean **0.84** episodes per day (0 to 3.26)	MD **0.33 lower** (2.75 lower to 2.09 higher)	20 (1 RCT)	⊕◯◯◯ Very low[a,c]	The evidence is very uncertain about the effect of acupuncture on episodes of urinary incontinence in a 24 hour period.
Episodes of nocturia assessed with: Episodes per night	Mean **1.63** episodes of per night	Mean **1.63** (0.98 to 1.27)	MD **0.5 lower** (0.65 lower to 0.36 lower)	80 (2 RCTs)	⊕⊕◯◯ Low[a]	Acupuncture may reduce episodes of nocturia slightly.

Acupuncture v Medication for OAB summary of findings table

FIGURE 2



Summary of findings:

Acupuncture compared to Medication for OAB for OAB

Patient or population: OAB
Setting: Out-patient clinics
Intervention: Acupuncture
Comparison: Medication for OAB

Outcomes	Anticipated absolute effects* (95% CI) Risk with Medication for OAB	Risk with Acupuncture	Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments

*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: confidence interval; **MD:** mean difference; **RR:** risk ratio

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

Explanations

[a]We downgraded 1 level for serious risk of bias due to 2 studies having at least one category judged at high risk of bias and one level for imprecision due to small numbers of participants
[b]We down graded 2 levels for very serious imprecision due to low participants numbers to detect a rare event
[c]We downgraded 1 level for serious inconsistency and imprecision due to high heterogeneity between studies and wide confidence intervals
[d]We downgraded 1 level for serious risk of bias due to unclear risk of bias in several categories in both studies and 2 levels for imprecision due to low numbers of participants and very wide confidence intervals in both studies
[e]We downgraded 1 level for serious risk of bias and imprecision due to all studies having at least one category judged as unclear risk of bias and small participant numbers
[f]We down graded 2 levels for very serious imprecision due to very small participant numbers

Acupuncture v Medication for OAB Summary of findings tables notes

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BIOFEEDBACK-ASSISTED PELVIC FLOOR MUSCLE TRAINING AND PELVIC ELECTRICAL STIMULATION IN WOMEN WITH OVERACTIVE BLADDER: A SYSTEMATIC REVIEW AND META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS

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HYPOTHESIS / AIMS OF STUDY
This meta-analysis aims to compare biofeedback-assisted pelvic muscle floor training (PFMT) and low-frequency pelvic electrical stimulation (ES) as an intervention group, with PFMT or bladder training (BT) as the control group, in women with an overactive bladder (OAB). The major goal of this study is to examine the role and efficacy of interventions in terms of improving QoL and reducing symptoms following therapy.

STUDY DESIGN, MATERIALS AND METHODS
PubMed, Cochrane, CINAHL, EMBASE, and Scopus were systematically searched for randomized controlled trials (RCTs) published up to November 2021. The RCTs were screened for our eligibility criteria and quality was evaluated using the Cochrane Risk Index of Bias tools. The outcomes were changes in quality of life (QoL), episodes of incontinence, and the number of participants cured/improved.

RESULTS
Eight studies involving 562 patients (comprising of 204 patients with biofeedback-assisted PFMT, 108 patients with pelvic ES, and 250 patients who received PFMT alone or BT and lifestyle recommendations only, as the control group) were included. The ES group showed significant differences in terms of changes in QoL (MD 7.41, 95% CI 7.90 to 12.92, $p = 0.008$), episodes of incontinence (MD -1.33, 95% CI -2.50 to -0.17, $p = 0.02$), and the number of participants cured or improved (RR 1.46, 95% CI 1.14 to 1.87, $p = 0.003$), while the biofeedback group resulted in non-significant changes in QoL (MD 0.13, 95% CI -7.87 to 8.12, $p = 0.98$), episodes of incontinence (MD 0.01, 95% CI -0.89 to 0.90, $p = 0.99$), and the number of participants cured or improved (RR 1.15, 95% CI 0.99 to 1.33, $p = 0.08$), both compared to the control group respectively.

INTERPRETATION OF RESULTS
The main purpose of treatment is to reduce OAB symptoms and thus improve the patients' QoL. Significant results in term of change in QoL, incontinence episodes, and cure/improvement rate are shown in patients undergoing low-frequency electrical stimulation as an adjuvant therapy when compared to PFMT alone or BT with lifestyle recommendations. These data suggest that pelvic ES may help with OAB treatment, as seen by a decrease in incontinence episodes and a higher improvement in QoL. Evidence of which parameters in the training protocol for ES are the most effective remains open for future investigation. In contrast, the biofeedback-assisted PFMT group revealed a non-statistically significant difference in those outcomes. These results show the benefits of biofeedback-assisted PFMT appear to be minimal for women with OAB.

CONCLUDING MESSAGE
This meta-analysis shows that low-frequency pelvic ES appears to be sufficient and effective as an additional intervention for women with OAB in clinical practice according to improvements in the subjects' QoL and reduction of symptoms. Meanwhile, biofeedback-assisted PFMT does not appear to be a significant adjuvant for conservative OAB therapy.

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COGNITIVE IMPAIRMENT DOES NOT IMPACT SACRAL NEUROMODULATION IMPLANT RATES FOR OVERACTIVE BLADDER

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HYPOTHESIS / AIMS OF STUDY

Overactive bladder (OAB) and cognitive impairment (CI) are both increasingly prevalent with age. Given the known association between anticholinergics and dementia risk, there is a need to optimize other therapies. [1]

Sacral neuromodulation (SNM), a current third-line therapy for OAB, offers an attractive potential non-anticholinergic therapy for older adults. It can be placed under light sedation or local, has been shown to reduce or eliminate anticholinergic use for refractory OAB, and compared to other third-line therapies, intradetrusor onabotulinumtoxinA and percutaneous tibial nerve stimulation, SNM does not require indefinite, ongoing office and procedural visits. [2]

Though American Urologic Association (AUA) and Society for Urodynamics, Female Pelvic Medicine and Urogenital Reconstruction (SUFU) guidelines on OAB cite intact cognitive ability as necessary to maintain OAB therapy, cognitive assessment is not a formal part of perioperative evaluation and there is no data to guide cognitive thresholds for therapy. [3] This study aimed to assess the impact of CI diagnosis on SNM implant rates and device related outcomes in an older OAB population.

STUDY DESIGN, MATERIALS AND METHODS

Following institutional review board (IRB 20-1141) approval, a retrospective chart review was performed of patients aged 55 years or older who underwent test-phase SNM (peripheral nerve evaluation (PNE) or stage 1) for OAB or urgency urinary incontinence between January, 2014 and March, 2021 within a large multi-regional health system. The electronic medical record was queried for all SNM test-phase procedures performed during the study period using the appropriate CPT codes (64561, 64581).

Patient demographics and comorbidities, CI diagnoses (dementia or mild cognitive impairment (MCI)), OAB medication and/or botulinum toxin use, and SNM procedures were recorded. Patients were considered to have cognitive impairment if they had any dementia or MCI diagnosis code assigned or had an active dementia medication (donepezil, galantamine, rivastigmine or memantine). SNM procedure outcomes were categorized as implant (Stage 2 or combined Stage1 + 2), explant, and/or revision of the lead and/or implantable pulse generator (IPG). Manual chart review was performed to confirm all SNM outcomes. Test-phase success was defined as 50% or greater reduction in symptoms documented in the chart. For device revisions and explants, indication was also recorded.

Logistic regression modeling was performed to assess the impact of CI on SNM implantation rate. To do so, a backward-elimination method an $\alpha < 0.20$ criterion was employed. All statistical analyses were performed using R programming language (version 3.6.1).

RESULTS

510 patients underwent SNM test-phase (161 PNE, 349 Stage 1). Mean age was 71.0(8.5) years and 80.6% were female. Overall, 52(10.1%) patients had a CI diagnosis at time of SNM, and 30(5.8%) were diagnosed a median 18.5[9.25, 39.5] months after SNM. Most common CI diagnosis at time of SNM test-phase was MCI (n = 17). Patients with CI were older, with more comorbidities and were more likely to undergo PNE (Figure 1). Univariable comparison found no difference in implantation rate based on pre-SNM CI (85.4% vs 76.9%, p = 0.16).

Multivariable analysis identified PNE, age, and prior beta-3 agonist use but not CI or dementia as independent negative predictors of implantation (Figure 2). Implanted patients had median urologic follow-up of 17[6.0, 44.0] months. Explant (12.1%), revision (10.4%), and battery replacement (3.4%) rates did not differ according to CI.

Rates of OAB medication cessation with SNM varied by medication across the study sample (Anticholinergic, N = 237 (64.6%); B3 agonist, N = 137 (77.4%)). However, patients with any CI diagnosis were more likely than those without CI to continue or restart a B3 agonist (37.1% vs 19.0%, p = 0.038) after SNM implantation. Treatment with onabotulinumtoxinA after SNM was uncommon (8.3%) and did not differ based on CI.

INTERPRETATION OF RESULTS

This retrospective study is the first to our knowledge to assess the impact of cognition on SNM outcomes. It identified a high rate of CI in an older OAB cohort pursuing SNM, finding 10% of patients had an active CI diagnosis or dementia medication prescription at the time of their SNM test-phase. Consistent with expectations of SNM, most patients proceeded to permanent implantation, while implant rates did not differ based upon CI. On longer term follow-up, most implanted patients did not continue or restart anticholinergic medications, and device explant and revision rates did not differ based upon CI.

While the AUA/SUFU OAB guidelines note that adequate cognitive ability is necessary for patients to engage with OAB treatment, there is no data to inform a specific cognitive threshold. The cohort of patients in this study present an older refractory OAB population who were offered SNM by experience subspecialist urologists. Thus, patients were presumably deemed appropriate procedural and SNM candidates. Further study is necessary to determine what an appropriate cognitive function threshold may be for successful SNM therapy.

CONCLUDING MESSAGE

Patients with CI and OAB proceed to SNM implant at rates that do not differ from patients without cognitive deficits. Diagnoses of CI should not preclude physicians from offering SNM for refractory OAB management.

FIGURE 1

	No Cognitive Impairment n=428	Cognitive Impairment n=82	p-value
PNE	136 (29.7%)	25 (48.1)	0.011
Age (yr)	70.0 (8.4)	76.1 (7.4)	<0.001
Male	76 (17.8%)	23 (28.0%)	0.045
Race			0.99
White	380 (88.9%)	72 (87.8%)	
Black	24 (5.6%)	5 (6.1%)	
Hispanic	11 (2.6%)	2 (2.4%)	
Other	13 (3.0%)	3 (3.7%)	
BMI (kg/m²)	31.2 (7.2)	29.2 (6.6)	0.02
Smoking			0.80
Former	170 (40.2%)	37 (45.1%)	
Current	27 (6.4%)	4 (4.9%)	
Comorbidities			
Diabetes	124 (29.0%)	32 (39.0%)	0.09
COPD	80 (18.7%)	27 (32.9%)	0.006
CHF	34 (7.9%)	10 (12.2%)	0.30
CAD	71 (16.6%)	32 (39.0%)	<0.001
Myocardial infarct	11 (2.6%)	10 (12.2%)	<0.001
Hypertension	264 (61.7%)	61 (74.7%)	0.039
Stroke	47 (11.0%)	29 (35.4%)	<0.001
Multiple sclerosis	9 (2.1%)	2 (2.4%)	1.00
Parkinson's disease	14 (3.3%)	17 (20.7%)	<0.001
Prior OAB Treatments			
Anticholinergic	354 (82.7%)	80 (97.6%)	<0.001
Beta-3 agonist	173 (40.5%)	48 (58.5%)	0.004
BTX-A	56 (13.1%)	11 (13.4%)	1.00

Data presented as n (%) or mean (SD).
PNE, peripheral nerve evaluation; BMI, body mass index; COPD, chronic obstructive pulmonary disease; CHF, chronic heart failure; CAD, coronary artery disease; BTX-A, onbotulinumtoxinA

Patient characteristics and demographics based on cognitive impairment diagnosis

FIGURE 2

	Unadjusted		Adjusted	
	OR (95% CI)	p-value	OR (95%)	p-value
Age (per 1 year)	0.95 (0.92-0.98)	p<0.001	0.95 (0.93-0.98)	p=0.003
Male	0.61 (0.35-1.08)	p=0.08	0.64 (0.36-1.17)	p=0.14
PNE	0.43 (0.26-0.70)	p<0.001	0.42 (0.26-0.70)	p<0.001
Cognitive impairment*	0.57 (0.29-1.19)	p=0.11		
Hypertension	0.68 (0.40-1.14)	p=0.15		

**Cognitive impairment diagnosis at time of SNM test-phase*
Abbreviations: SNM, sacral neuromodulation; PNE, peripheral nerve evaluation (vs Stage 1)

Multivariable logistic regression analysis - Odds of permanent implant following SNM test-phase

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Funding N/A **Clinical Trial** No **Subjects** Human **Ethics Committee** Institutional Review Board (protocol #20-1141) **Helsinki** Yes **Informed Consent** No

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LONG-TERM EFFICACY AND SAFETY OF VIBEGRON FOR OVERACTIVE BLADDER SYNDROME IN PATIENTS ≥65 YEARS OLD: ANALYSIS FROM THE EMPOWUR EXTENSION TRIAL

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HYPOTHESIS / AIMS OF STUDY

Overactive bladder (OAB) syndrome prevalence increases with age. Vibegron is a β3-adrenergic agonist approved for adults with OAB. In the phase 3 EMPOWUR extension trial [1], once-daily vibegron 75 mg showed long-term safety and efficacy in patients with OAB, consistent with results of the 12-week study [2]. These post hoc analyses of the extension trial assessed safety and efficacy in patients ≥65 years old.

STUDY DESIGN, MATERIALS AND METHODS

Patients completing the EMPOWUR trial could enter the 40-week extension trial (NCT03583372). Patients previously receiving vibegron or tolterodine 4 mg extended release continued active treatment; patients previously receiving placebo were randomly assigned 1:1 to vibegron or tolterodine. The primary outcome was safety, assessed by adverse events (AEs). Key efficacy endpoints were change from EMPOWUR baseline at week 52 in average daily micturitions, urgency urinary incontinence (UUI) episodes, and urgency episodes. Outcomes were assessed in patients ≥65 years old. No formal sample size calculation was performed; it was determined that rolling 500 patients over from the EMPOWUR trial was sufficient to characterize the long-term safety profile of vibegron. The study was approved by an institutional review board, research ethics board, or independent ethics committee prior to study initiation; all patients provided written informed consent.

RESULTS

Of 505 patients receiving ≥1 dose of study drug in the extension (n = 273, vibegron; n = 232, tolterodine), 235 patients (46.5%) were ≥65 years old, and 60 patients (11.9%) were ≥75 years old. Of the patients ≥65 years old, 71.1% were women, and 75.7% had OAB wet (ie, with incontinence). Of the patients ≥75 years old, 55.0% were women, and 68.3% had OAB wet. After 40–52 weeks of treatment, the rate of treatment-related AEs was similar between vibegron (33.3%) and tolterodine (25.5%) (Table 1). The most commonly occurring AEs were hypertension (10.9% with vibegron vs 9.4% with tolterodine), urinary tract infection (7.8% vs 12.3%, respectively), and headache (7.0% vs 4.7%, respectively). Patients who received 52 weeks of active treatment showed improvement in least squares mean change from baseline at week 52 in average daily number of micturitions (vibegron, −2.3; tolterodine, −1.7), UUI episodes (−1.8; −1.2, respectively), and urgency episodes (−3.3; −2.4, respectively) (Table 2). Safety and efficacy outcomes were generally similar in patients ≥75 years old.

INTERPRETATION OF RESULTS

In this subgroup analysis of the EMPOWUR extension trial, once-daily vibegron 75 mg was associated with sustained reductions from baseline in micturitions, UUI episodes, and urgency episodes and was safe in older adults (≥65 years) with OAB.

CONCLUDING MESSAGE

The safety and efficacy of vibegron in older adults was consistent with that observed in the overall population of the EMPOWUR extension trial. These results suggest that vibegron is similarly safe and effective for symptoms of OAB in adult patients.

FIGURE 1

Table 1. Summary of Safety in Patients ≥65 Years Old (Safety Set–Extension*)

AE, n (%)	Vibegron (N=129)	Tolterodine (N=106)
≥1 AE	92 (71.3)	63 (59.4)
≥1 treatment-related AE	43 (33.3)	27 (25.5)
≥1 serious AE	4 (3.1)	3 (2.8)
AEs occurring in ≥2% of patients in either treatment group		
Hypertension	14 (10.9)	10 (9.4)
Urinary tract infection	10 (7.8)	13 (12.3)
Headache	9 (7.0)	5 (4.7)
Constipation	8 (6.2)	6 (5.7)
Diarrhea	8 (6.2)	2 (1.9)
Nasopharyngitis	6 (4.7)	3 (2.8)
Nausea	6 (4.7)	4 (3.8)
Dry mouth	5 (3.9)	6 (5.7)
Hyperglycemia	5 (3.9)	2 (1.9)
Abdominal pain	4 (3.1)	0
Back pain	4 (3.1)	0
Influenza	4 (3.1)	0
Bronchitis	3 (2.3)	3 (2.8)
Peripheral swelling	3 (2.3)	0
Residual urine volume increased	3 (2.3)	2 (1.9)
Anemia	3 (2.3)	0
Musculoskeletal pain	3 (2.3)	0
Upper respiratory tract infection	3 (2.3)	0
Urinary retention	3 (2.3)	1 (0.9)
Arthralgia	2 (1.6)	3 (2.8)
Cataract	0	3 (2.8)
Hyperkalemia	0	3 (2.8)

AE, adverse event.

*All randomized patients who took ≥1 dose of double-blind study treatment and received active treatment for 40 weeks and 52 weeks.

Table 1

FIGURE 2

Table 2. LS Mean Change from Baseline at Week 52 in Efficacy Endpoints in Patients ≥65 Years Old (Full Analysis Set–Extension*)

Outcome	Vibegron (N=89)	Tolterodine (N=62)
Micturitions		
Mean (SD) baseline	10.9 (3.0)	11.1 (3.1)
LS mean (95% CI) change from baseline	−2.3 (−2.8 to −1.7)	−1.7 (−2.4 to −1.1)
UUI episodes†		
Mean (SD) baseline	2.9 (2.6)	2.8 (1.9)
LS mean (95% CI) change from baseline	−1.8 (−2.2 to −1.4)	−1.2 (−1.7 to −0.8)
Urgency episodes		
Mean (SD) baseline	7.9 (4.1)	7.8 (3.6)
LS mean (95% CI) change from baseline	−3.3 (−4.3 to −2.4)	−2.4 (−3.5 to −1.4)

LS, least squares; UUI, urgency urinary incontinence.

*All randomized patients who took ≥1 dose of double-blind study treatment, had ≥1 evaluable change from baseline micturition measurement, and received active treatment for 52 weeks.

†Full analysis set–extension for incontinence (all randomized patients who took ≥1 dose of double-blind study treatment, had OAB wet at baseline, and received active treatment for 52 weeks): vibegron, N=75; tolterodine, N=48.

Table 2

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Funding Urovant Sciences **Clinical Trial** Yes **Registration Number** ClinicalTrials.gov, NCT03583372 **RCT** Yes **Subjects** Human **Ethics Committee** The study was approved by an institutional review board or independent ethics committee at each of the 107 study sites **Helsinki** Yes **Informed Consent** Yes

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THE INCIDENCE OF NEW OR WORSENING OAB SYMPTOMS IN PATIENTS WITH PRIOR SARS COV-2 INFECTION: A COHORT STUDY

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HYPOTHESIS / AIMS OF STUDY

The advent of the SARS CoV-2, or COVID-19, pandemic has spurred great research interest into this viral disease and its clinical implications. Besides the acute phase, long-term symptoms have been reported, with over 50 side effects listed thus far[1]. However, the majority of urological symptoms have been overlooked in these early studies. Given that there is extensive literature on viral etiologies causing urological conditions, such as adenovirus or BK virus in hemorrhagic cystitis, or Epstein-Barr virus in interstitial cystitis, the possibility of SARS CoV-2 causing a novel condition is not outside the realm of possibility[2,3]. Early in the pandemic, investigators from our institution were the first group to identify de novo genitourinary symptoms, such as frequency, urgency, nocturia, and pain/ pressure, in individuals with prior COVID-19 infection. They termed this condition COVID-19 associated cystitis (CAC).

The aims of our study are to establish the incidence of worsening or de-novo CAC, evaluate its short-term natural progression, and to determine its correlation with serology status and antibody levels.

STUDY DESIGN, MATERIALS AND METHODS

After IRB approval, 18,785 individuals from the largest COVID-19 serology study (BLAST COVID Study Group) were invited to participate in a follow-up study, with 1,895 subsequent respondents. Demographics and serology data was obtained from the BLAST COVID Study which used the EUROIMMUN serology assay to obtain SARS-CoV-2 IgG level. An antibody ratio of ≥1.1 is considered significant. Participants were asked to score their OAB symptoms retrospectively at three different time points - prior to the pandemic, 2 months after COVID-19 infection (if applicable), and at the present time - and prospectively at 2- and 4- months. To capture those infected after the serology studies were concluded (April to May 2020), participants were asked "Have you been diagnosed with COVID?" via a nasopharyngeal polymerase chain reaction test. If affirmative, they were prompted to evaluate their symptoms 2 months after COVID infection, and were considered PCR positive. Genitourinary symptoms were assessed using the ICIQ-OAB, a grade A validated questionnaire which assesses both symptom severity and bother. The minimal important difference (MID) of 1 is considered a significant change. Questions evaluated 4 domains: frequency ("How often do you pass urine during the day?" 0 = 1 to 6 times, 1 = 7 to 8 times, 2 = 9 to 10 times, 3 = 11 to 12 times, 4 = 13 or more times), nocturia ("During the night, how many times do you have to get up to urinate, on average? 0 = none, 1 = 1 time, 2 = 2 times, 3 = 3 times, 4 = four or more times), urgency ("Do you have to rush to the toilet to urinate?" 0 = never, 1 = occasionally, 2 = sometimes, 3 = most of the time, 4 = all of the time), and urge incontinence ("Does urine leak before you can get to the toilet?" 0 = never, 1 = occasionally, 2 = sometimes, 3 = most of the time, 4 = all of the time). Bother score for each domain ranged from 0 (not at all) to 10 (a great deal).

Statistical analysis was conducted using IBM SPSS 28·0 and R. Categorical data (e.g. demographics) was analyzed using Pearson's Chi Square test. Continuous data, such as the average values for the ICIQ-OAB individual and total symptoms scores were calculated and the standard deviations provided. Statistical analysis was performed using 1-way ANOVA. A p-value $<0{\cdot}05$ is considered significant. Multivariate analysis was done for co-morbidities and change in ICIQ-OAB scores based on diagnosis using 1-way ANOVA. Sample size of 618 COVID positive individuals was calculated for a power of 80% and α of 0.05 with regards to the primary objective.

Primary objective is the incidence of de novo or worsening OAB symptoms in COVID positive patients. Secondary objectives are the natural progression and the correlation between antibody levels and OAB symptoms.

RESULTS

Of the 1,895 participants, 81.7% (n = 1,548) were female, 16.5% male (n = 312), 1.9% other/unknown (n = 35). Most were Caucasian (85.8%), followed by African American (4.1%), Asian (3.8%), Hispanic (1.4%), and other/unknown (2.1%). A third of participants (n = 605) were COVID-19 positive as defined by positive serology or PCR test. Of these, 492 had 2 months post infection data with 36.4% (n = 179/492) reporting an increase of ≥ 1 unit in OAB symptom score compared to pre-pandemic. Out of these, the OAB symptoms of 22% (n = 40/179) were de novo. Comparing pre-pandemic to present symptoms, 35.7% (n = 219) of participants with prior COVID-19 infection had an increase of ≥1 unit on the ICIQ-OAB, compared to 15.7% (n = 202) of uninfected patients (OR: 2.99, 99.6Cl, 2.21, 4.05, p < 0.001). COVID + patients with baseline diabetes mellitus (p = 0.004), chronic steroid use (p = < 0.001), or on immunosuppression (p < 0.001) were more likely to have an increase in ICIQ-OAB scores than those who were COVID – and without co-morbidities. BMI positively correlated with symptom severity in COVID + patients, so that higher BMI led to worse OAB symptoms (p = 0.213).

Approximately 40% were lost to follow up (n = 740) with 2- and 4-month data available for the remaining cohort (n = 1,155). Both COVID-19 positive (n = 192) and COVID-19 negative (n = 963) groups had significant increases in OAB symptoms from pre-pandemic to the time of study, 2- and 4-months (p < 0.001), but the difference between the two groups was only statistically significant at the time of study (3.72 vs 3.11, p = 0.003) and at 2 months (3.72 vs 3.18, p = 0.007). At 4 months follow-up, the domain with the highest average symptom severity score amongst COVID-19 positive patients was nocturia (1.21 out of 4), followed by urgency (1.04 out of 4), urinary incontinence (0.86 out of 4), and frequency (0.74 out of 4). However, participants were most bothered by urge incontinence (3.26/10), then urgency (3.26/10), nocturia (2.96/10), and frequency (2/10). For participants who received a positive COVID-19 test using PCR, no correlation was found between OAB symptoms and antibody levels (r = -0.10). For participants with COVID-19 positive serology test, symptoms were weakly correlated with antibody levels (r = 0.14).

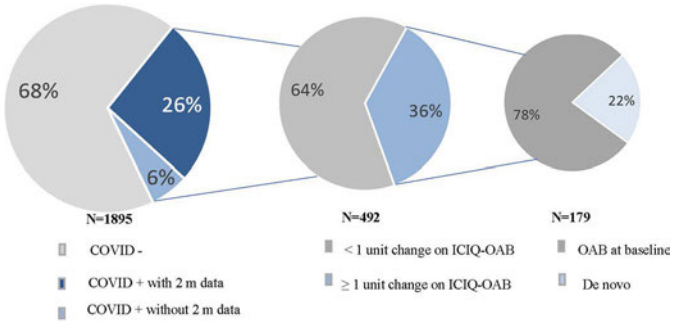
INTERPRETATION OF RESULTS

Infection with COVID-19 portends a significantly higher risk of developing de novo or worsening OAB symptoms at 2-month follow-up while OAB symptoms were increased by all participants at 4- months follow up. Of all domains, nocturia is most strongly affected, though urge incontinence was most bothersome for patients. Immunosuppression, diabetes and obesity are risk factors for CAC, though no correlation was found between antibody levels and OAB symptoms in patients with prior COVID-19 infection.

CONCLUDING MESSAGE

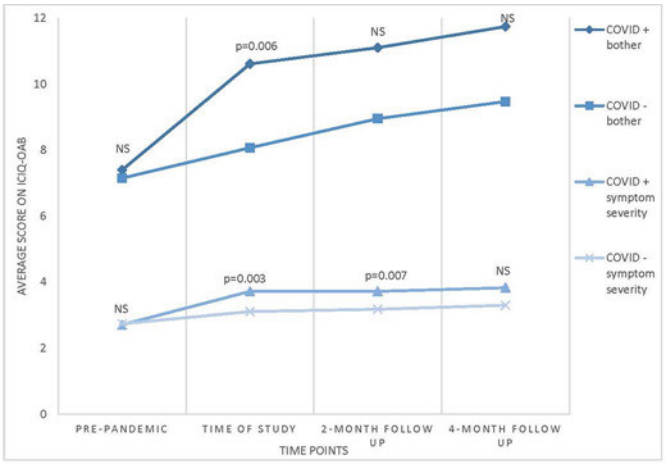
CAC, as a direct result of the COVID-19 pandemic, is a novel condition that may affect millions of patients worldwide. Therefore, it is imperative for practicing clinicians to be aware of this potential diagnosis. Further work evaluating the effects of available OAB treatments on CAC is in progress.

FIGURE 1



Over a third experienced worsening OAB symptoms after COVID infection. Of the total, 32% were COVID+. Out of these, 492 had 2 months post-infection data with 36.4% (n = 179/492) reporting an increase of ≥ 1 unit on the ICIQ-OAB compared to pre-pandemic.

FIGURE 2



Both symptom severity (p = 0.003) and bother scores (p = 0.006) were significantly higher amongst COVID positive patients at time of study than COVID negative. At 2- and 4-months symptoms remain high, but the difference was nonsignificant.

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DIFFERENCES IN THE BLADDER MICROBIOTA BETWEEN MEN AND WOMEN WITH OR WITHOUT OVERACTIVE BLADDER

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HYPOTHESIS / AIMS OF STUDY

Urine specimens have been considered to be sterile in the absence of a clinically identifiable infection. However, recent evidence suggests that the bladder harbours commensal bacteria different among men, pre- and post-menopausal healthy women [Ref.1,2]. Whether the bladder microbiota contributes to lower urinary tract symptoms (LUTS) remains known. The aim of this study is to determine how the bladder microbiota are different between men and women with or without overactive bladder (OAB).

STUDY DESIGN, MATERIALS AND METHODS

Urine specimens were collected from postmenopausal women with OAB (n = 20) and pre-(n = 20) and post- (n = 20) menopausal women without LUTS using a transurethral catheter to avoid bacterial contamination from external tissues. Midstream urine specimens were also collected from age (postmenopause) matched-men with (n = 20) or without (n = 20) OAB. The DNA was extracted from the urine pellet, and bacterial 16S rRNA gene sequencing was performed using Illumina MiSeq. The bladder microbiota at the phylum and genus levels with low relative abundances (< 0.1%) were filtered and the remaining top 50 different types were analysed using Mann Whitney U-test.

RESULTS

At the phylum level, there were no significant differences in the relative abundance of microbiota between the pre-and postmenopausal controls (Fig.1A and 1B). At the genus level, the relative abundance of Lactobacillus and Gardnerella was significantly decreased and that of Peptoniphilus, Anaerococcus, Escherichia and Corynebacterium was significantly increased in the postmenopausal controls compared with the premenopausal controls. Next, the significantly increased abundance of Firmicutes and the significantly decreased abundance of Proteobacteria were seen in the age-matched male controls compared with the postmenopausal controls at the phylum level (Fig.1B and 1C). The relative abundance of Peptoniphilus, Anaerobacillus, Trabulsiella and Escherichia was significantly decreased and that of Streptococcus, Staphylococcus and Corynebacterium was significantly increased in the age-matched male controls compared with the postmenopausal controls at the genus level. On the other hand, there were no significant differences in the relative abundance of bladder microbiota between the postmenopausal controls and OAB patients as well as between the age-matched male controls and OAB patients at the phylum (Fig.1B and Fig.2A, Fig.1C and 2B) and genus levels, respectively.

INTERPRETATION OF RESULTS

The age and sex differences in the bladder microbiota were clearly demonstrated in this study. The significant increases in Peptoniphilus, Anaerococcus and Escherichia and the significant decreases in Lactobacillus and Gardnerella were seen in the postmenopausal controls. In addition, the dominant bacteria in the bladder were Peptoniphilus, Anaerobacillus, Trabulsiella and Escherichia in in the postmenopausal women, and Streptococcus, Staphylococcus and Corynebacterium in the age-matched men.

CONCLUDING MESSAGE

The results of this study suggest that, while there is the significant age and sex differences in bladder microbiota, commensal bacteria in the bladder do not contribute to OAB.

FIGURE 1

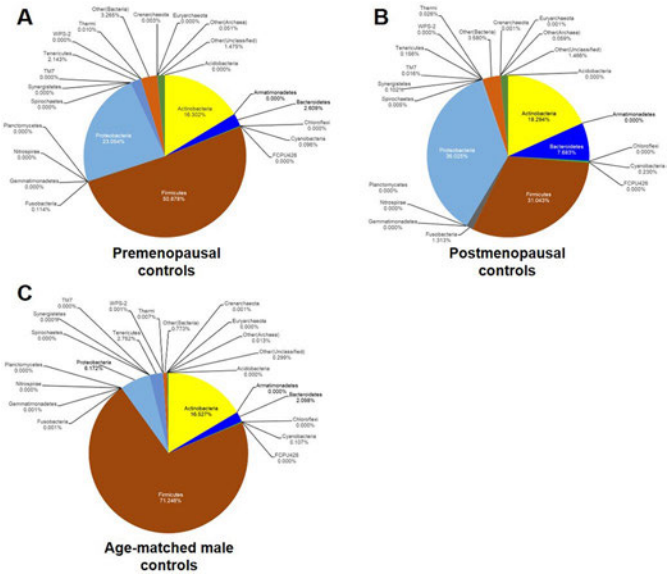

Fig.1 Age and sex differences of bladder microbiota among premenopausal (A), postmenopausal (B) and age-matched male (C) controls at the phylum level

FIGURE 2

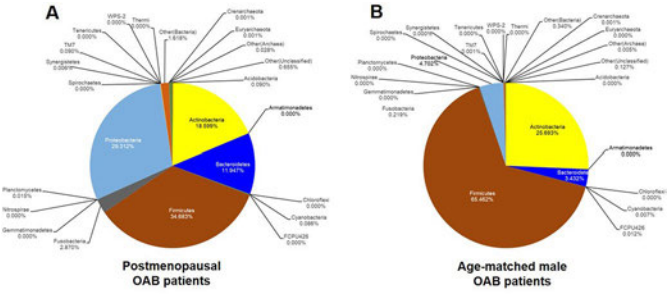

Fig.2 Bladder microbiota in female (A) and male (B) patients with overactive bladder (OAB) at the phylum level

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A TREATMENT PREDICTION STRATEGY FOR OVERACTIVE BLADDER USING A MACHINE LEARNING ALGORITHM THAT UTILISED DATA FROM THE FAITH STUDY

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HYPOTHESIS / AIMS OF STUDY

Overactive bladder (OAB) is a chronic, multifactorial condition characterised by urinary urgency, with or without urgency urinary incontinence, usually with increased daytime frequency and nocturia, if there is no proven infection or other obvious pathology [1]. In patients with OAB, low treatment persistence rates can lead to unreliable symptom control and progression of symptom severity. The syndrome exerts a significant impact on worldwide healthcare systems, with epidemiological estimates indicating that approximately 18% of individuals aged ≥40 years in Taiwan and South Korea have OAB [2]. The objective of this study was to develop a prediction model for assessing response to antimuscarinic and mirabegron treatment in patients with OAB using data from the FAITH study.

STUDY DESIGN, MATERIALS AND METHODS

FAITH was a prospective, longitudinal, observational registry study conducted in Taiwan and South Korea to describe the treatment patterns for OAB therapies and to identify and evaluate factors associated with the effectiveness and persistence of OAB therapies. Adult patients (≥18 years) who had been diagnosed with OAB symptoms at least 3 months prior to study enrolment were eligible for inclusion. Patients were due to initiate monotherapy with mirabegron or any antimuscarinic that had been prescribed as part of routine clinical practice for the treatment of OAB symptoms. Informed consent was required to participate in the study. The objective of this investigation was to use data from the FAITH study to successfully develop an algorithm to predict treatment effectiveness that was based on a composite outcome of safety, efficacy, and treatment change. Safety was defined as no occurrences of moderate or severe adverse events; if this occurred the treatment was deemed "safe" otherwise it was judged to be "less safe". Efficacy was defined as a decrease in Overactive Bladder Symptom Score (OABSS) of ≥3, which has been identified as the minimal threshold for a meaningful change [3]; if this criterion was met the treatment was deemed "successful" otherwise it was "less successful". Treatment change was defined as any treatment discontinuation, interruption, switch, or addition; if any of these were present, a "treatment change" was deemed to have occurred, otherwise "no treatment change" was recorded. Patients within the FAITH study were followed for 183 days to establish occurrences of the above parameters. The composite outcome was defined as "safe", "successful", and "no treatment change"; which meant the treatment was deemed "more effective", otherwise it was "less effective". To explore the composite algorithm, a total of 14 clinical risk factors were included in the initial data set, which included demographic factors (age, sex, body mass index, and Charlson Comorbidity Index), OAB symptoms (frequency, urgency, nocturia, OAB type, and incontinence type), questionnaire data (Baseline OABSS and overactive bladder questionnaire [OAB-q] short form [bother and health-related quality of life scores]), any prior OAB medication, and planned treatment. Using data from the initial data set, a 10-fold cross-validation procedure was performed, and a range of machine learning models were evaluated to determine the most effective algorithm for prediction of treatment effectiveness. In total, six different models were chosen (regularised regression, decision tree [C5.0], boosted tree model, random forest, neural network [multilayer perceptron (MLP)], and support vector machine) and tested using a variety of recipes. Due to the nature of some of the models, it was necessary to format the data in different ways to ensure the optimal performance of each model algorithm. Receiver operating characteristic (ROC) area under the curve (AUC) analyses were used to determine rank performance for each model. The chosen model was optimised to help reduce model error rate and maximise ROC curve stability (method of validation) and model generalisability (minimising overfitting). The parameters used to optimise the model were the input parameters within the model from the original set within the baseline characteristics analysis and the number of patients within each tree "split" or "branch" (min_n). To determine the variables that should be included in the final model, the percentage that each variable appeared following the use of 50 resamples was calculated, as using a single train/test split was considered unstable. The final model performance was evaluated using the chosen variables and with the minimum n parameter set to the optimal level. The model was subsequently fitted over the 50 resamples to enable an average AUC and 95% confidence intervals (CIs) to be calculated. The final algorithm was integrated into an online application for intended use as an educational assessment tool. The online platform was constructed to allow for the prediction of "more effective" or "less effective" treatment results for both mirabegron and antimuscarinics.

RESULTS

In total, 396 patients from the FAITH study were included in this analysis. Of these, 266 (67.2%) initiated treatment with mirabegron and 130 (32.8%) initiated treatment with an antimuscarinic. In terms of the composite outcome, 138 (34.8%) were judged to be in the "more effective" group and 258 (65.2%) were in the "less effective" group (Figure 1). Data from the initial data set showed that incontinence type, OAB type, OAB-q score, and Baseline OABSS were significantly different between the "more effective" and "less effective" groups. The ROC analyses indicated that the best performance was achieved with the random forest (AUC: 0.66) and decision tree (C5.0; AUC: 0.65) models. Given the relative simplicity of the decision tree model and its comparable performance to the more complex random forest algorithm, the decision tree (C5.0) model was chosen as it allows for easier interpretation and implementation. The resample analysis showed that Baseline OABSS, planned treatment, OAB-q health-related quality of life scores, urgency, and incontinence type appeared in the models >75% of the time over the 50 resamples and were therefore included in the final model. For the ROC analysis, an AUC result of 0.70 (95% CI: 0.54, 0.85) was achieved (Figure 2) when the optimal value of 15 was used for the minimum n parameter. The input parameters for the online application were integrated to match the inputs for the final decision tree model, namely the OABSS and OAB-q questionnaires, the urination urgency for the patient, and the presence/absence of urge urinary incontinence or urinary incontinence.

INTERPRETATION OF RESULTS

A tool was developed that effectively predicted more effective and less effective treatment responses following antimuscarinic or mirabegron therapy in patients with OAB. The final algorithm was based on an optimised decision tree (C5.0) model. This machine learning algorithm model is currently designed specifically for research purposes. To be utilised in clinical practice to predict treatment responses, further analysis, validation, inclusion of additional data, adjustment of clinical input, and possibly certification are required.

CONCLUDING MESSAGE

This study used real-world evidence from the FAITH study to successfully develop an algorithm to predict treatment effectiveness for patients with OAB. The algorithm was developed using a composite outcome of safety, efficacy, and treatment change, achieving an AUC of 0.70 with the final model. The design and methodology permitted the integration of the algorithm into a simple, rapid, and easy-to-use interface that could be refined in the future to produce a valuable educational or clinical decision-making aid.

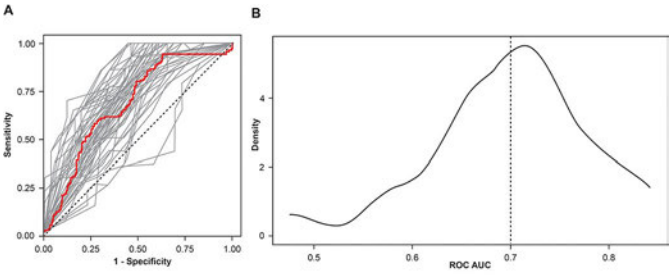
FIGURE 1

	Overall (n = 396)	Mirabegron initiator (n = 266)	Antimuscarinic initiator (n = 130)
Safety outcome			
Less safe	19 (4.8)	12 (4.5)	7 (5.4)
Safe	377 (95.2)	254 (95.5)	123 (94.6)
Efficacy outcome			
Less successful	215 (54.3)	143 (53.8)	72 (55.4)
Successful	181 (45.7)	123 (46.2)	58 (44.6)
Treatment change			
Treatment change	83 (21.0)	50 (18.8)	33 (25.4)
No treatment change	313 (79.0)	216 (81.2)	97 (74.6)
Composite outcome			
More effective	138 (34.8)	98 (36.8)	40 (30.8)
Less effective	258 (65.2)	168 (63.2)	90 (69.2)

Data shown in terms of n (%).

Outcome results using data from the FAITH study

FIGURE 2



The red line on graph A represents the mean ROC curve and the vertical dotted black line on graph B represents the mean AUC.
AUC, area under the curve; ROC, receiver operating characteristic

ROC performance of the final model following 50 resamples

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IDENTIFYING REAL-WORLD PRACTICE PATTERNS IN SECOND-LINE TREATMENTS FOR PATIENTS WITH OVERACTIVE BLADDER RECEIVING NAVIGATED OR ROUTINE CARE FROM A US NATIONAL RETROSPECTIVE DATABASE STUDY

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HYPOTHESIS / AIMS OF STUDY
Overactive bladder (OAB) is a condition based on the development of symptoms of urgency, usually with frequency and nocturia, with or without urge urinary incontinence. Real-world utilization data of second-line pharmacological treatments for OAB and the impact of navigated care through the OAB treatment pathway are limited. The objective was to describe real-world utilization patterns of second-line pharmacological treatments for OAB stratified by those who did or did not receive navigated care.

STUDY DESIGN, MATERIALS AND METHODS
Patients with OAB were randomly and retrospectively identified using the ninth and tenth revisions of the International Classification of Diseases, Clinical Modification and procedure codes from the Precision Point Specialty Analytics Portal for OAB database. This database contains the electronic medical record data for >90 US community-based urology practices for ≈2.4 million OAB patients. Eligible patients were ≥18 years of age, newly diagnosed and treated for OAB between January 1, 2015, and December 31, 2019, and had ≥2 OAB visits ≥30 days apart. A treatment navigator was identified as a health professional focused on individualized patient-centered care by assisting in the guidance of the patient through the OAB clinical pathway. Use of second-line treatment medications during the study period was collected. The date of discontinuation of initial second-line treatment, identified by a physician or navigator, began when a different OAB treatment was used without continuing the prior treatment. A switch in second-line treatment was defined as starting a new treatment within 30 days of discontinuing initial second-line treatment. Proportions were compared using chi-squared tests. Time-to-event data were compared using log-rank tests.

RESULTS
Of 190,697 patients who met all inclusion criteria, 9000 were randomly selected. Overall, 95.8% (n = 8623) of patients received second-line treatment of which 56.2% received an anticholinergic and 41.7% received a beta-3 agonist. Of those patients receiving second-line treatment, 60.2% received 1 medication, 27.3% received 2 medications, and 12.6% received 3+ medications. 9% of patients receiving second-line treatment switched treatment within 30 days with no difference between the navigated or non-navigated patients. Of all patients starting a second-line treatment, 70.2% (n = 6051/8623) discontinued treatment during the study timeframe. Of patients who discontinued their initial second-line treatment, 59.1% discontinued anticholinergics and 39.1% discontinued beta-3 agonists. 62.5% of the patients who discontinued had navigated care compared with 71.3% who were not under navigated care ($P < 0.001$). Discontinuations were lower in patients who received navigated care and follow-up visits (61.4% of patients) compared with navigated patients who did not have follow-up visits (71.1% of patients, $P = 0.042$).

INTERPRETATION OF RESULTS
The present analysis suggests that patients with OAB that had navigator-based care had a lower rate of discontinuation of second-line treatment compared to patients without navigated care. The discontinuation of second-line treatment further decreased in navigated patients who had follow up visits.

CONCLUDING MESSAGE
While having a patient navigator with follow up visits leads to less discontinuation of second-line treatments, this rate is still above 60%. This suggests that advancing to treatment options beyond second-line treatments may be of interest to some patients with OAB seeking symptom management.

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THE PATIENT PATHWAY FOR OVERACTIVE BLADDER MANAGEMENT: A QUALITATIVE ANALYSIS

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1. Isala Clinics Zwolle

HYPOTHESIS / AIMS OF STUDY
Current treatment guidelines for overactive bladder (OAB) advice a linear pathway based on treatment invasiveness (1). Patients often try two or more treatments before satisfaction (2). The current treatment algorithm may not produce a quick reduction in symptom severity for many patients, leading to impaired quality of life and additional costs (3). To better understand the expectations and experiences of patients of their OAB treatment, we performed this qualitative study.

STUDY DESIGN, MATERIALS AND METHODS
We performed an exploratory qualitative study by interviewing female patients with OAB and urge-incontinence. We randomly selected patients from a large database of patients with OAB/urge-incontinence treated in our outpatient clinic between January 1st, 2014, and September 30th, 2016. If approved, patients sent us an informed consent. Patients were interviewed by telephone using a semi-structured interview guide. Recruitment ended when saturation was reached, i.e. there were no new opinions or findings in two consecutive interviews. Interviews were auto-taped and transcribed verbatim. The two researchers separately analyzed the transcripts and added codes to the responses. After the initial coding, we evaluated the codes and organized them into themes, using Atlas.TI 8® (ATLAS.ti Scientifc Software Development GmbH).

RESULTS
We interviewed nine patients with OAB. In total, we labeled 232 codes, resulting in 14 themes, which were categorized in three major themes: expectations of treatment, organization of care and embarrassment.

Expectations of treatment

All responders suffered from OAB for a longer time. They reported a variety of self-management therapies and thought it was a part of normal life. They all started seeking for help, when the symptoms were not manageable anymore. They independently stated that success of treatment was not to be completely free of incontinence, but to be able to manage their OAB-symptoms better.

Quote:

‘Yes, it was there for many years, but it (incontinence) increased over time’

‘I hoped for everything to be normal again, when I go out, I should not worry about were the toilet is and if I will suffer from incontinence’

‘At the start, you think it is nice if all gets over. But manageable is okay for me as well’

Responders lost their trust in successful treatment, after disappointing experiences with earlier therapies. Moreover, with treatments being unsuccessful, they fall back in self-management.

Quote:

‘What I found very difficult, I was in the process for quite some time and had different treatment modalities. Every time I hoped that it helped, but it didn’t.’

‘Yes, you get skeptical’

Organization of care.

Responders mentioned that it was rather unpleasant seeing different nurses/physicians every time. Patients reported lack of guidance with long-term treatments, such as medication, percutaneous tibial nerve stimulation (PTNS) or intravesical BoNT-A injections. They doubted if medication should be continued lifelong, and it was not clear to them who was in charge: the general practitioner or urologist. Many patients experienced long waiting lists after they reported they needed new intravesical BoNT-A injections, which was disappointing

Quote:

‘At the first time I came for Botox injections, it was a different doctor than I spoke to before. I met him all dressed down, I think that is not done, it was so embarrassing.’

‘I think it is quite odd; you keep getting this medication form the pharmacy and no one decides if it is still necessary.’

Embarrassment

During the interviews, all patients told how OAB symptoms affect their daily life. Patients avoid long walks and social events. They all used pads and at work, they needed a toilet close to their desk. Most patients experienced less problems at home, because a toilet is readily available and most family members were aware of their condition. They felt ashamed at work and some responders showed that not themselves, but their environment (e.g. colleagues) pushed them to seek help. Patients reported shame and discomfort during invasive studies like urodynamics, but they also mentioned understanding the purpose of it.

Quote

‘I was sent home from work, my employer said it could (urgency) not be any longer like this.’

‘At home, you are in control and you can go to the bathroom whenever you like. At work, it was different, when you are in meeting at you get the sign you need to go to the bathroom, you cannot just leave every time during a meeting.’

‘I endured it (urodynamics), but it was unpleasant.’

INTERPRETATION OF RESULTS
This study gave us insights in the three major themes that OAB patients experience with their treatment: expectations of treatments, organization of care and embarrassment. An important lesson is that the organization of OAB-care should be personal, because patients feel embarrassed by changing caregivers. Moreover, the organization should be flexible to be able to provide the right care at the right moment and prevent long waiting lists (e.g. with repeat intravesical BoNT-A injections). Finally, some patients become skeptical to try a new treatment after a failed therapy. This is worrisome, since this nocobo-effect negatively affects outcomes and the patient’s motivation to persevere treatment until the moment of evaluation (e.g. in case medication or PTNS).

CONCLUDING MESSAGE
In this qualitative study, we found that expectations of treatment, organization of care and embarrassment were the most important themes for patients in the pathway of OAB treatment. We think awareness of these themes may be helpful for clinicians to provide better care to OAB patients. A personal approach in a flexible organization with clarity over treatment effects and long-term follow up may improve the OAB-patients experience.

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SESSION 24 - BOWEL DYSFUNCTION

Abstracts 395-406
15:30 - 17:00, Hall D
Chair: Mr Alexis M P Schizas (United Kingdom)

395 | www.ics.org/2022/abstract/395

REBOXETINE INCREASES ANAL PRESSURE SUBSTANTIALLY IN HEALTHY WOMEN: A DOUBLE-BLIND, RANDOMIZED, PLACEBO-CONTROLLED CROSSOVER STUDY

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HYPOTHESIS / AIMS OF STUDY
Fecal incontinence, defined as the involuntary discharge of liquid or solid stool, is a prevalent and debilitating condition with limited treatment options. Anal sphincter dysfunction, accompanied by decreased anal pressure, is an important cause of fecal incontinence in women. Therefore, drugs that increase the tone of the anal sphincters constitute potential pharmacological treatments of fecal incontinence. On the other hand, drugs that decrease the anal pressure may contribute to fecal incontinence. While an observational study suggests that selective serotonin reuptake inhibitors (SSRI) are associated with urinary incontinence [1], clinical studies indicate that reboxetine, a noradrenaline reuptake inhibitor (NaRI), increases the urethral pressure and alleviates urinary incontinence symptoms [2,3]. Because the physiology of fecal continence resembles the corresponding urinary continence process, we hypothesized that reboxetine increases and citalopram decreases the anal pressure. This study aimed to evaluate the effect of reboxetine and citalopram on anal opening pressure (AOP) in healthy women.

STUDY DESIGN, MATERIALS AND METHODS
We recruited healthy women (age 18–55 years, body mass index 18.5–30 kg/m2) for this single-site, randomized, double-blind, placebo- and active-controlled crossover study. At three clinic visits, the participants received single oral doses of 40 mg citalopram (and reboxetine-matched placebo), 8 mg reboxetine (and citalopram-matched placebo), and two placebos, respectively. We measured AOP at rest and under voluntary contraction (squeeze) using anal acoustic reflectometry at the reported time of peak plasma drug concentrations (tmax). The administration of study drugs was split into two timepoints due to a one-hour difference in reported tmax. The washout period between clinic visits was a minimum of eight days. Randomization of participants to one of six possible treatment sequences was balanced for period, and sequence allocation was concealed to participants, investigators, and outcome assessors. Adverse events were collected at the end of each visit, by phone one day after each visit, and eight days after last visit.

RESULTS
We screened and randomized 24 women and had no dropouts. Compared to placebo, reboxetine increased AOP with 23.4 cmH2O (95% confidence interval [CI] 16.5-30.2, $p<0.001$) in resting condition and 22.5 cmH2O (95% CI 15.2-29.8, $p<0.001$) in squeezing condition. Citalopram did not change AOP statistically significantly compared to placebo (resting: 4.2 cmH2O [95% CI -2.7-11.1, $p=0.2$]; squeezing: 3.0 cmH2O [95% CI -4.3-10.3, $p=0.4$]) (Figure 1). Adverse drug reactions (ADRs) were more common with reboxetine and citalopram vs. placebo, (nausea: 11% vs. 17% vs. 0%; insomnia: 11% vs. 6% vs. 2%; dizziness: 9% vs. 6% vs. 0%; and headache: 2% vs. 8% vs. 2% of total ADRs). No serious adverse events were reported.

INTERPRETATION OF RESULTS
This is the first randomized, placebo-controlled study evaluating the effect of reboxetine and citalopram on anal pressure in humans using anal acoustic reflectometry. We found that reboxetine induced a substantial increase in both resting and squeezing AOP, suggesting that reboxetine enhances the tone of both the internal and external anal sphincter. An effect of this magnitude is likely to be clinically relevant for the prevention of fecal incontinence, however, clinical studies in women with fecal incontinence are needed to elucidate the potential role of reboxetine in the management of fecal incontinence. Citalopram did not cause any statistically significant change in AOP, suggesting that SSRI treatment will not influence fecal incontinence pathophysiology.

CONCLUDING MESSAGE
Single dose 8 mg reboxetine increased the placebo-corrected AOP significantly, suggesting that reboxetine or other NaRIs may be efficacious in the treatment of fecal incontinence. Clinical trials in patients with fecal incontinence are needed to evaluate the potential clinical benefit of this treatment approach.

FIGURE 1

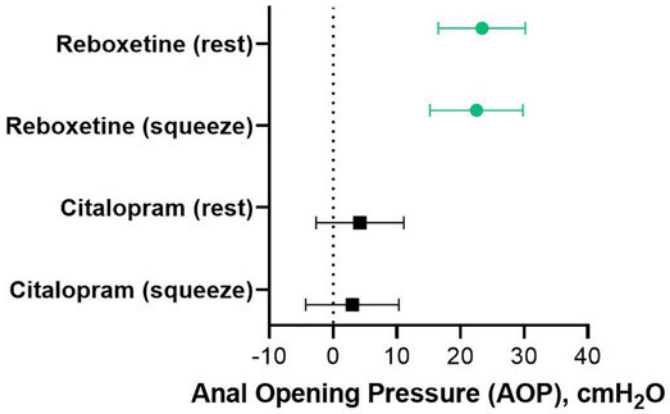

Figure 1. The figure shows the mean opening anal pressure at tmax corrected for the placebo value (mean AOP, cmH2O [95%CI]).

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Funding None **Clinical Trial** Yes **Registration Number** ClinicalTrials.gov (Identifier: NCT04097288), EudraCT (Identifier: 2019-000059-14) **RCT** Yes **Subjects** Human **Ethics Committee** Regional **Ethics Committee** of The Capital Region of Denmark **Helsinki** Yes **Informed Consent** Yes

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SINGLE-DOSE TADALAFIL DECREASES ANAL PRESSURE: A DOUBLE-BLIND, RANDOMIZED, PLACEBO-CONTROLLED, CROSSOVER STUDY IN HEALTHY WOMEN

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HYPOTHESIS / AIMS OF STUDY

Phosphodiesterase type 5 (PDE5) inhibitors induce, via nitric oxide mediated intracellular increases of cyclic GMP, smooth muscle relaxation in tissues containing PDE5. The vascular smooth muscle in the male corpus cavernosum have shown the highest abundance of PDE5 [1], however, PDE5 expression has also been reported in other tissues, including vascular smooth muscle in other tissues and the internal anal sphincter (IAS). Hypertonicity of IAS is a key pathophysiological trait in patients with anal fissure and treatment with topical application of the PDE5 inhibitor sildenafil has, therefore, been evaluated in patients suffering from chronic anal fissure. These studies have shown reduction in anal resting pressure and symptom relief [2,3]. However, the effect of PDE5 inhibition on IAS pressure has not been evaluated in a placebo-controlled setting. This study aimed at investigating the effect of the long-acting PDE5 inhibitor tadalafil on anal pressure in healthy women using anal acoustic reflectometry.

STUDY DESIGN, MATERIALS AND METHODS

For this double-blind, randomized, placebo-controlled crossover study, we recruited healthy female volunteers by advertisement. Participants were randomly assigned to either a single dose of tadalafil (40 mg) or matching placebo at the first visit, and then switched to the opposite treatment at the second visit (50% tadalafil at 1st clinic session). To avoid carry-over effect, the clinic sessions were separated by a washout phase of at least six days. At specified time of peak plasma drug concentration, we assessed anal opening pressure (AOP) under resting and squeezing conditions using anal acoustic reflectometry. Adverse events were collected at the end of each clinic session, and by a phone call six days after the last visit. With a sample size of 24 women we had a power of 99% to detect a 15 cmH2O difference in anal pressure (tadalafil vs. placebo) at a 5% significance level. Endpoints were analysed in multiple regression models with subjects, period, and treatment as covariates (SAS statistical software v. 9.4.6).

RESULTS

From August to December 2021, we screened and included 24 healthy women. The procedures were well tolerated by the participants, and there were no dropouts. Single-dose tadalafil induced a decrease in resting AOP of 12.9 cmH2O (95% confidence interval [CI] 5.0–20.7, $p = 0.003$) compared to placebo. The effect during squeezing condition was not statistically significant (-5.7 cmH2O [95% CI -17.3–6.0, $p = 0.3$]). The participants reported a total of 41 adverse events (36 during tadalafil and 5 during placebo treatment). The most common adverse events were headache (15 related to tadalafil and 3 related to placebo) and flushing (8 related to tadalafil and 0 related to placebo). There were no serious adverse events.

INTERPRETATION OF RESULTS

In this double-blind, randomized, placebo-controlled, crossover study in healthy women, single oral dose of tadalafil (40 mg) reduced resting AOP statistically significantly compared to placebo. This finding supports previous studies demonstrating beneficial effect of topical sildenafil in patients with IAS hypertonicity associated with anal fissure. The relatively high incidence of adverse events observed during tadalafil treatment, especially complaints about headache, may reflect the relatively high dose (40 mg) administered to treatment-naive, healthy women. A lower starting dose (e.g. 5 mg) with up-titration over time could likely reduce such side effects.

CONCLUDING MESSAGE

Single-dose tadalafil reduces anal resting pressure significantly compared to placebo suggesting that oral doses of tadalafil might be beneficial as a pharmacological treatment alternative for patient with chronic anal fissure.

FIGURE 1

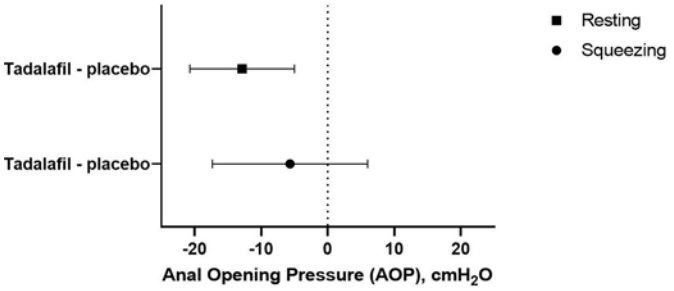

Figure 1. Mean anal opening pressure at tmax corrected for the placebo value (mean AOP, cmH2O [95%CI]).

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AUTOLOGOUS MUSCLE DERIVED CELLS TREATMENT OF FECAL INCONTINENCE: AN ANALYSIS OF EFFICACY IN WOMEN WITH OBSTETRIC INJURY

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HYPOTHESIS / AIMS OF STUDY

Obstetric anal sphincter injuries (OASIS), which involve partial or complete disruption of the anal sphincter muscles, are one of the most common causes of fecal incontinence (FI) in women [1]. Therefore, we examined the efficacy and safety of iltamiocel, a cellular therapy investigational product comprised of autologous muscle derived cells (AMDC), as a treatment for FI in adult women with a history of OASIS.

STUDY DESIGN, MATERIALS AND METHODS

Subjects were enrolled in a prospective, multicenter, nonrandomized Phase 1/2 investigational study (study code: GIFI). Subjects received a single administration of iltamiocel at a dose of 250 million (±20%) cells. The study included subjects with primary symptoms of FI defined as baseline Cleveland Clinic Incontinence Score (CCIS) ≥9 and history of failed conservative treatment. Key exclusion criteria were presence of neuromuscular disorder, prior major sphincter augmentation procedures or anorectal operation leading to anal sphincter damage, inflammatory bowel disease, and non-viable mucosa lining along the anal tract.

Iltamiocel was manufactured from approximately 50-250mg skeletal muscle tissue harvested from the subject's vastus lateralis via outpatient needle tissue procurement procedure. After isolation and expansion, iltamiocel suspension was evenly distributed around the external anal sphincter (EAS) through 8-12 percutaneous injections parallel to the anal canal during a subsequent outpatient procedure. For subjects with a defined sphincter defect, approximately half of the cell suspension was injected in the region of the defect with the remaining volume evenly distributed through the remainder of the EAS.

Efficacy outcomes were change in frequency of FI episodes and days with FI episodes as recorded by a 28-day diary and change in CCIS and Fecal Incontinence Quality of Life (FIQL) questionnaires. Outcomes were assessed by comparing baseline (pre-injection) parameters to those at 3, 6 and 12-months post-treatment. Anorectal manometry was used to explore changes in anal sphincter function from baseline to 12 months. Incidence of iltamiocel- or study procedure-related adverse events (AEs) and serious adverse events (SAEs) was recorded up to 12 months post-treatment.

RESULTS

Thirty-one women with history of OASIS including obstetric tears and/or episiotomy during labor (median age 60 years, range 31-78) received iltamiocel injection. Subjects had a median of 2 vaginal births (range 1-4), 19 (61%) and 20 (65%) presented with obstetric tear or episiotomy, respectively, and 8 (26%) presented with both. Sonographic EAS defect was present in 20 (65%) subjects; the median defect area was 60 degrees (range 30 to 180 degree), 5 (19%) subjects had an EAS defect ≥120 degree and 10 (32%) had previous anal sphincter repair. Of the 31 subjects who received iltamiocel injection, 26 (84%) completed baseline diary and had ≥1 episode at baseline diary. These subjects were included in the efficacy analysis.

The safety profile of iltamiocel treatment in the 31 OASIS subjects enrolled in Study GIFI was favorable with no SAEs related to the product, injection procedure, or tissue procurement procedure. Most AEs were determined to be unrelated to Iltamiocel or study procedures. Only one iltamiocel-related AE of injection site inflammation was reported; the event was grade 1 in severity and resolved without treatment. No secondary interventions due to AEs were necessary following iltamiocel administration.

At 12-months follow-up, 62% of OASIS subjects reported a ≥50% reduction in number of FI episodes, 46% reported a ≥75% reduction and 27% reported 100% reduction which represents a complete restoration of continence over a 28-day period (Table 1). When analysis was restricted to the group of OASI subjects with EAS defect <120 degrees (n=20), 70% and 50% of these achieved ≥50% and ≥75% reduction in FI episodes, respectively, and 35% achieved complete continence at 12 months (Table 1). A significant reduction in both median FI episodes and days with FI episodes compared with baseline was observed in this group of subjects at all time points (Table 2). Improvements in symptom severity and quality of life over the follow-up period, were demonstrated by a statistically significant reduction of CCIS and increase of all FIQL scales at 12 months compared with baseline (Table 2). No significant changes in anorectal manometry measurements were detected at 12 months compared with baseline.

INTERPRETATION OF RESULTS

The significant reduction in both number of FI episodes and days with FI episodes, along with significant improvements in both CCIS and FIQL scales observed after 12 months, demonstrate that a single administration of iltamiocel [250 million (±20%) cells] shows promise in improving FI symptoms and quality of life in women with a history of obstetric injuries. Indeed, the efficacy of the iltamiocel treatment was even higher in the group of subjects with an EAS defect less than 120 degrees. In this group, 70% of subjects achieved at least 50% reduction of FI episode and 35% achieved complete continence (0 episodes in a 28-day diary) at 12 months post iltamiocel injection. Importantly, a ≥75% episodes reduction was previously identified by most subjects as a threshold for FI treatment success [2]. In this study, half of subjects with OASIS and EAS defect <120 degree achieved a ≥75% episodes reduction. In keeping with previous reports [3], these data suggest that patients with FI due to obstetric injury and an EAS defect <120 degrees may be ideal candidates for AMDC therapy.

CONCLUDING MESSAGE

Obstetric anal sphincter injury represents one of the most common cause of FI in women. AMDC therapy, which delivers autologous muscle progenitor cells to the targeted tissue, is hypothesized to increase anal sphincter functionality in patients with FI due to defined structural defects and/or generalized weakening of the EAS. Treatment with iltamiocel may therefore represent a safe, minimally invasive, and potentially transformative option for patients suffering from FI due to obstetric injuries, particularly in those that involve less than one third of the total external anal sphincter area.

FIGURE 1

Subset	≥50% Reduction % (n/N)	≥75% Reduction % (n/N)	100% Reduction % (n/N)
Female with OASIS	62 (16/26)	46 (12/26)	27 (7/26)
Female with OASIS and EAS defect <120 degrees	70 (14/20)	50 (10/20)	35 (7/20)

N = total number of subjects; n = number of subjects achieving indicated level of episodes reduction; OASIS = Obstetric Anal Sphincter Injuries; EAS = External Anal Sphincter.
Note: degree of defect is unknown for 1 subject.

Table 1. Subjects with ≥50%, ≥75% and 100% Reduction in FI Episodes at 12 Months

FIGURE 2

Measurement	Baseline N=20	3 months N=20	6 months N=20	12 months N=20	P-value [a]
Fecal Incontinence Diary [b]					
Number of Episodes	11.5 (1, 47)	8.0 (1, 100)	6.5 (0, 96)	2.5 (0, 127)	0.013
Number of Days with Episodes	11.0 (1, 28)	5.5 (1, 22)	5.5 (0, 28)	2.5 (0, 26)	<0.001
CCIS	13.0 ± 2.9	10.1 ± 2.9	10.1 ± 4.1	9.4 ± 2.9	<0.001
FIQL					
Lifestyle	2.5 ± 0.9	2.9 ± 0.8	2.9 ± 0.9	3.1 ± 0.9	<0.001
Coping/Behavior	1.7 ± 0.6	2.1 ± 0.9	2.2 ± 0.9	2.3 ± 0.9	0.004
Depression/Self Perception	2.5 ± 0.8	3.0 ± 0.8	3.0 ± 0.8	3.0 ± 0.7	0.003
Embarrassment	2.0 ± 0.8	2.6 ± 0.9	2.6 ± 0.9	2.9 ± 0.8	<0.001

Data presented as median, minimum - maximum for FI Diary, and mean ± standard deviation for the other measurements.
N = number of subjects
[a] Wilcoxon Signed-Rank Test comparing median episodes and days with episodes at baseline vs 12 months, paired t-test comparing mean CCIS and FIQL at baseline vs 12 months.
[b] 28-day diary

Table 2. FI Diary, Symptom Severity and Quality of Life Measurements in Subjects with OASIS and EAS defect <120 degree

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THE ROLE OF FRAILTY SCORES IN DECISION MAKING FOR RECTAL PROLAPSE

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HYPOTHESIS / AIMS OF STUDY

Abdominal procedures for rectal prolapse (RP) are associated with lower recurrence rates than perineal operations. However, patients with significant comorbidities may be better suited for a perineal approach. The Risk Assessment Index (RAI) is a quick, easy validated tool to measure frailty that correlates with surgical outcomes [1]. The role of a frailty assessment in decision making for rectal prolapse repair is unknown. The aim of our study was to evaluate how RAI correlates with our existing RP repair decision-making process and postoperative outcomes.

STUDY DESIGN, MATERIALS AND METHODS

Consecutive cases of rectal prolapse were captured in a prospective registry from 2017-2021. Patient and operative characteristics were recorded. All patients received preoperative Risk Analysis Index scores. RAI scores are categorized as robust (<20), normal (21-29), frail (30-39), or very frail (>=40). Patients with significant cardiac comorbidities were offered a perineal operation based on discretion of a single experienced surgeon. RAI was not formally used in the decision-making process. Postoperative Cleveland Clinic Fecal Incontinence Scores, Obstructed Defecation Scores, and Patient Global Impression of Change scores were recorded.

RESULTS

Of the 115 patients in the registry with postoperative data, 86 (74.8%) underwent an abdominal (ab) operation and 29 (25.2%) underwent a perineal (pn) operation (Table 1). Both cohorts were mostly women (ab: 94.1% vs. pn: 93.1%m $p=0.99$) with similar preoperative obstructive defecation scores (ab: 8.0 vs. pn: 6.7, $p=0.14$) and preoperative fecal incontinence scores (ab: 11.8 vs. pn: 13.6, $p=0.19$). The population of patients who underwent perineal operations were older (mean age- ab: 60 vs. pn: 78y, $p<0.001$), with a more significant comorbidity burden (ASA score III or IV- ab:23.5% vs. pn: 65.5%, $p=<0.001$; cardiac comorbidity- ab: 32.6% vs. pn: 69.0%, $p=0.001$). The mean Risk Analysis Index score was higher in the perineal group (ab:20 vs. pn:31, $p<0.001$).

Most patients in the abdominal group underwent minimally invasive ventral mesh rectopexy (75.3%), while most patients in the perineal group underwent Altemeier proctosigmoidectomy (75.9%). The mean postoperative length of stay was longer in the perineal group (ab: 1.6 days versus pn: 2.2 days, $p=0.03$).

Higher recurrence rate in the perineal group (ab: 10.5% vs. pn: 34.5%, $p=0.006$) with a median time to recurrence of 246 days for abdominal patients, and 178 for perineal patients. The abdominal group had a higher complication rate (ab:18.6% vs. pn: 13.8%, $p=0.78$) though most complications were a Clavien-Dindo Grade 2 (ab: 12.0% vs. pn: 6.9%). Patients in both groups experienced a similar significant improvement in CCFIS (mean change: ab:-4.0 vs. pn: -3.0, $p=0.55$) and ODS score (mean change: ab:-2.7 vs. pn: -2.9, $p=0.87$). PGIC scores were similar at a mean of 35.6 days postoperatively (ab: 6.1 vs. pn: 6.0, $p=0.64$).

INTERPRETATION OF RESULTS

The RAI is an easy and quick tool that can be used in clinic and in our cohort, frail patients were more likely to be offered perineal operations. Although these patients had a longer postoperative stay, the complication profile was low, and patients were satisfied with their functional improvement at rates similar to the abdominal cohort. While evaluation of comorbidities can be subjective, the RAI is an objective metric that can help guide the shared decision-making process when determining what operations to offer patients with rectal prolapse. Ongoing research should further refine the role of frailty metrics in guiding decision-making on rectal prolapse surgery.

CONCLUDING MESSAGE

Frail patients are more likely to undergo perineal operations for rectal prolapse repair, but they tolerate these operations well. Frailty scores can be a useful metric in the shared decision-making process.

FIGURE 1

	Abdominal (N=86)	Perineal (N=29)	P-value
Age, years, mean (SD)	60.0	78.5	<0.001
Female, n (%)	80 (94.1%)	27 (93.1%)	1.0
RAI Frailty Score, mean (SD)	19.7 (8.6)	30.8 (6.5)	<0.001
Length of stay, days, mean (SD)	1.6 (1.1)	2.2 (1.7)	0.03
30-day complication, n (%)	16 (18.6%)	4 (13.8%)	0.78
Change in CCFIS, mean (SD)	-4.0 (7.3)	-3.0 (8.5)	0.55
Change in ODS, mean (SD)	-2.7 (4.6)	-2.9 (4.3)	0.87
Postoperative PGIC, mean (SD)	6.1 (1.3)	6.0 (1.3)	0.64
Prolapse Recurrence, n (%)	11 (12.8)	12 (41.4)	0.002

Table 1: Cohort Characteristics

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CRANIOCAUDAL PLICATION OF RECTAL WALL IN ANTERIOR RECTOCELE REPAIR , IS IT EFFECTIVE ? A REVIEW ARTICLE

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HYPOTHESIS / AIMS OF STUDY

Rectocele is a common condition in parous women that may lead to symptoms of obstructed defecation syndrome (ODS) [1]. To move toward surgical intervention, certain indications are required including rectocele >3 cm, significant barium entrapment on defecography, and frequent need for digital assistance of defecation [2]. Surgical treatment of a rectocele can be done by the posterior colporrhaphy or with a site-specific repair. The traditional repair may be done by transvaginal or transperineal approach, transanal approach. Stapled transanal rectal resection (STARR) and ventral mesh rectopexy are also alternatives. Traditionally, the open approach through transperineal or transvaginal has the same method to access the rectocele except for the incision, then the posterior colporrhaphy is done by midline side-to-side (vertical) plication of the rectovaginal septum with or without levatorplasty [3]. Also, some authors reported promising outcomes of horizontal (craniocaudal) plication of the rectovaginal septum through other approaches rather than transanal one .

The aim of this review is to assess the current literature regarding the outcomes of horizontal repair of rectocele through different perineal approaches (transvaginal and transperineal).

STUDY DESIGN, MATERIALS AND METHODS

An organized literature search for studies that assessed the outcome of horizontal repair of rectocele was performed. PubMed/Medline, Embase, Google Scholar, and Cochrane Library were queried in the period January 1991 through December 2021. The main outcome measures, whenever possible, were improvement in ODS symptoms, improvement in sexual functions and continence, changes in manometric parameters, and impact on quality of life (QoL).

RESULTS

After the screening of 67 studies, and with the exclusion of similar transanal techniques (Sarles and Block techniques), 4 articles were found eligible for inclusion in the review.

Through a prospective case series study ,after exposure of the rectovaginal septum through transvaginal incision , Schmidlin-Enderli and Schuessler sutured the rectovaginal fascia in a craniocaudal fashion with sagittally positioned running absorbable sutures with a careful reapproximation of the laterally separated perineal body in the midline with 3-4 sutures, thus covering the perineal part of the rectocele. All the 54 patients suffered from ODS and 70.4 % had protrusion symptoms preoperatively. ODS showed remission or improvement in 72.2 %. Also, the anatomical correction rate was 92.1 % and protrusion symptoms were resolved in 73.6 %. Among sexually-active patients, 5.2 % reported de novo dyspareunia postoperatively. There were no major intra- or postoperative complications. [2].

Similarly, a retrospective study was adopted by Henn and Cronje using the same horizontal plication technique but with the sutures running in a zigzag fashion. Among the 123 female patients, ODS was observed in 35.3% and fecal incontinence in 25.2%. The majority of women (51.8%) had stage 3-4 prolapse. All symptoms significantly improved except for fecal incontinence. There was a significant improvement in rectocele ($p < 0.001$) with the majority of women noted to have a stage 0 or 1 (88.6%) prolapse at follow-up. While a non-significant decline in overall dyspareunia from 18% to 12.2% was observed [3].

Recently, Omar , Elfallal and colleagues prospectively compared horizontal and vertical plication in a randomized control trial . This trial included 40 (20 in each group) female patients with anterior rectocele. There was no significant difference between the two groups regarding the postoperative Wexner score. Complete cure and significant improvement in ODS symptoms were comparable after the two techniques. The reduction in rectocele size after horizontal plication was significantly greater than after the vertical one (1.7 vs. 2.6, $P < 0.0001$). Significant improvement in dyspareunia was recorded after horizontal plication ($P = 0.001$) but not after vertical plication ($P = 0.1$). There was no significant difference between the two groups concerning complications and recurrence [1].

Moreover, Leanza and colleagues adopted the classic plication technique but with the addition of perineorrhaphy (perineal body anchorage) using horizontal sutures (covering the lower part of the rectocele) in comparison to the classic and transanal techniques. All the used techniques were effective to repair posterior compartment defects and improving the QoL. The authors reported lower sexual and better anatomic and pain outcomes with vaginal techniques and better functional outcomes with transanal repair .

INTERPRETATION OF RESULTS

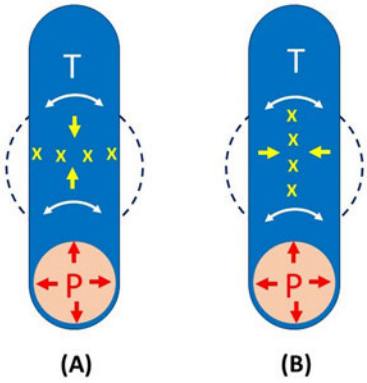
According to the law of Laplace, the anterior bulging of the rectal wall (tubal structure) to form a rectocele (spherical structure) is associated with a decline in both intraluminal pressure and wall tension. The attempt to repair the rectovaginal septum will return the rectum into a tube again. In horizontal repair, the direction of repair in a craniocaudal fashion creates a tension force perpendicular to that in the rectal wall. While, in vertical repair, the direction of repair in a side-to-side fashion creates a tension force that is parallel to and against that in the rectal wall (as shown in Figure 1) rendering them weaker and more liable for disruption.

CONCLUDING MESSAGE

Horizontal (craniocaudal) plication provides a valuable technique with promising outcomes. Unfortunately, only a few studies adopted this technique. So, we recommend performing further studies with larger sample sizes and in comparison to other standard techniques to get more accurate and precise results

FIGURE 1

(T) tension, (P) pressure, (x) line of repair, (white arrows) direction of tension force, (yellow arrows) direction of tension force created by the repair, (red arrows) direction of pressure, (dashed blue line) site of the previous rectocele.



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RECTAL INTUSSUSCEPTION CORRELATES WITH PELVIC FLOOR DESCENT INDEPENDENT OF AGE IN WOMEN

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HYPOTHESIS / AIMS OF STUDY
Rectal intussusception (RI) is often seen in the setting of pelvic relaxation. However, mechanisms are not clear and RI can occur independent of pelvic relaxation. Aging is the biggest risk factor for pelvic relaxation and pelvic organ prolapse. Dynamic MR Defecography (MRD) allows evaluation of functional and structural pelvic floor disorders.

We Hypothesize that there is a correlation between rising grades of rectal intussusception (RI) and grades of uterovaginal and bladder descent associated with increasing pelvic floor relaxation and independent of age.

The primary aim of our study was to assess the correlation between rising grades of RI with measures of pelvic floor descent in MRD. Our secondary aims were the correlation between severity of RI and 1) symptoms of fecal incontinence and obstructive defecation and 2) anorectal pressure profile from High Resolution Anorectal Manometry (HR-ARM).

STUDY DESIGN, MATERIALS AND METHODS
We performed a retrospective analysis of a prospectively maintained registry of patients seen at our tertiary referral academic center. Symptoms were assessed using Cleveland Clinic/Wexner Fecal Incontinence questionnaire (CCFI), and the Obstructed Defecation Syndrome (ODS) questionnaire. All patients underwent MRD and HR-ARM as part of their clinical evaluations. Pelvic floor laxity was measured using the pubococcygeal reference line. The H line was drawn from the inferior margin of the pubic symphysis to the posterior aspect of the anorectal junction and M line was drawn perpendicularly from pubococcygeal line to the posterior end of the H line. Bladder and uterovaginal descent were measured based on descent below the pubococcygeal line. Rectal prolapse was graded using the Oxford classification. Patients were grouped based on Oxford grade 0 vs 1-2 vs 3 vs 4-5. Data was analyzed using Fisher exact test or chi- squared test in univariate analysis. Spearman rank correlation was used with partial and semipartial correlation for covariate adjustment.

RESULTS
A total of 238 women were included with 90(38%) no MRD findings of RI, 43(18%) Oxford grade 1-2, 49(20%) Oxford grade 3 and 56(24%) Oxford grade 4-5. There was a significant correlation between age (not BMI) and grades of RI in women, r: 0.140, P: 0.029. Women with higher grades of RI were more likely to have a history of vaginal delivery (P: 0.043) or pelvic surgery (P: 0.035). Despite comparable scores for obstructive defecation (ODS) , severity of fecal incontinence based on CCFI score, correlated with rising grades of RI, r:0.184, P: 0.007.

HR-ARM showed higher grades of RI correlated with lower anal tone, r: -0.210, P: 0.001 and lower squeeze pressures, r: -0.153, P: 0.018. However these correlations didn't persist after adjustment for age and BMI. There was no association between RI grades and rectal sensory thresholds. Women with higher RI grades were more likely to pass the rectal balloon within 60 seconds (P:0.005).

RI grades correlated with measures of MRD pelvic floor relaxation including resting M (r: 0.191, P:0.003 and H (r: 0.210, P:0.001) lines, defecation M (r: 0.397, P:0.000) and H (r: 0.411, P:0.000) lines and only defecation (not resting or Kegel) anorectal angle (r: 0.252, P:0.000). When adjusted for BMI and age correlation remained significant with defecation M (P:0.000) and H (P:0.000) lines and resting H line (P:0.000). Interestingly there was also significant correlation with Kegel (P:0.008) as well as defecation anorectal angle(P:0.000). Correlation between RI grades and levator hiatus width (P:0.047) didn't remain significant after correction for age and BMI (P:0.466).

Women with higher grades of RI were more likely to have urethral hypermobility (P: 0.000). The grades of rectocele were comparable among patients with various degrees of RI but retaining rectocele was seen less commonly in women with high grades of RI (P: 0.030). Herniation at the level of sigmoidocele (P:0.004), enterocele (P:0.001), and, peritoneocele (P:0.000) were all significantly more common among women with higher grades of RI.

MRD showed a significant correlation between rising grades of RI and rising grades of uterovaginal and bladder descent (P:0.000 for both). These correlations were independent of age and BMI.

INTERPRETATION OF RESULTS
We show that rising RI grades, observed in MRD in women, correlates with increasing age and is associated with worsening symptoms of fecal incontinence. There is no correlation between severity of obstructive defecation symptoms and RI grades. Also rising RI grades correlated with measures of pelvic floor relaxation including uterovaginal and bladder descent and intestinal herniation, independent of age and BMI. When correlated with anorectal function, deterioration of anal sphincter function with rising grades of RI appeared to be affected by aging rather than rising grades of RI.

CONCLUDING MESSAGE
The pathophysiology of RI appears to be associated with pelvic floor relaxation and independent of age.

Funding N?A **Clinical Trial** No **Subjects** Human **Ethics Committee** Stanford IRB **Helsinki** Yes **Informed Consent** No

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POSTERIOR COLPOPERINEORRHAPHY IMPACT ON THE PERINEAL BODY SIZE ON ULTRASOUND AND FUNCTIONAL BOWEL SYMPTOMS

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HYPOTHESIS / AIMS OF STUDY
1. Assess the perineal body area before and after posterior colpoperineorrhaphy for prolapse

2. Assess the bowel function before and after posterior colpoperineorrhaphy for prolapse

STUDY DESIGN, MATERIALS AND METHODS
This was a prospective study of patients undergoing prolapse surgery. A clinical assessment and pelvic floor ultrasound were performed. Patients with previous hysterectomy were excluded from this study. The perineal body was measured before and after surgery with a validated technique (1). Birmingham Bowel and Bladder Symptom Questionnaires were administered before and after surgery (2).

RESULTS
79 patients were considered. 54 had posterior prolapse: 37% (20/54) had only posterior prolapse. 20% (11/54) patients had both anterior and posterior prolapse. 2% (1/54) patient had apical and posterior. 41% (22/54) had all anterior, apical and posterior.

On linear regression analysis, there was a significant association between passive and urge faecal incontinence and a smaller perineal body area ($p < 0.0001$) pre-operatively. The perineal body was significantly larger after posterior repair and perineorrhaphy surgery (2.56cm2 + /-1.14 pre-op vs 3.68cm2 + /- 0.87 post-op; WSR, $p < 0.0001$). There was a significant improvement in BBBSQ scores for defaecation function, interms of straining (WSR, $p = 0.01$), time spent in the toilet (WSR, $p < 0.001$), digitation (WSR, $p = 0.03$), dyschezia (WSR, $p = 0.02$) and feeling of incomplete evacuation (WSR, $p < 0.0001$). There was no change for faecal urgency (WSR, $p = 0.2$), faecal incontinence (WSR, p0.8). There was one patient whose perineal body was normal on ultrasound pre-operative. She did not have symptoms of defaecation dysfunction pre-op. Post-operatively, she reported pain and difficulty with defaecation.

INTERPRETATION OF RESULTS
The perineal body was visualised and measured on 2D midsagittal sections. It was shown to be significantly larger after surgery. POP-Q PB has been shown to be simillar in prolapse and control patients (3). However, the size of the perineal body has been shown to be smaller in prolapse patients (1).Measuring the perineal body on ultrasound may be useful in prolapse patients to guide the pre-operative planning on whether to perform a perineorrhaphy.

The bowel symptoms related to the function of defaecation improved: less time spent in the toilet, less straining, less dyschezia, digitation and better evacuation. There was no improvement in faecal incontinence or faecal urgency.

CONCLUDING MESSAGE
A small perineal body can be restored with posterior repair and perineorrhaphy. Defaecation function improves after surgery in patients with corrected posterior compartment prolapse. Imaging pre-operatively could help provide information to guide the pre-op planning and MDT discussions. A comprehensive pre-operative assessment of symptoms and prolapse anatomy, could help improve prediction of symptom improvement (or deterioration). This would be useful in pre-operative counselling, informed consent, MDT discussion and operative planning.

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BEST IN CATEGORY PRIZE: ANORECTAL / BOWEL DYSFUNCTION

SEVERITY AND IMPACT OF FECAL INCONTINENCE TWO DECADES AFTER NO, ONE AND TWO OBSTETRICAL ANAL SPHINCTER INJURIES

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HYPOTHESIS / AIMS OF STUDY

Estimating the prevalence of specific pelvic floor disorders, their associated severity and consequences for daily life is important information for health care planning. A recent study reported on the prevalence of fecal incontinence (FI) in women with no (12%), one (24%), or two (36%) obstetrical anal sphincter injuries (OASIs) [1]. In the present study we assessed the severity and subjective impact of FI and hypothesized that the severity and subjective impact of FI increased in women with no, one or two OASIs.

STUDY DESIGN, MATERIALS AND METHODS

This is a register-based study initiated in 2015 in women with two deliveries. The Swedish National Board of Health and Welfare was requested to identify the potential study population from the Swedish Medical Birth Register (MBR), resulting in 64,687 non-pregnant 2-para women with singleton vaginal births between 1992 to 1998 and no further births. A sample of 11,000 women was randomly selected by Statistics Sweden and invited to participate in the study by returning a postal or a web questionnaire. The questionnaire was returned by 7145 women; 6760 women had no OASI, 357 had one OASI (253 at the first delivery only, and 104 at the second delivery), and 28 had OASI at both deliveries. To achieve equal-sized groups of women with one and two OASIs, the latter group was oversampled by extending the inclusion period to 1987-2000, resulting in 324 women with two OASIs. Given this size of study cohorts, an alfa level of 0.05, a power value of 80%, and using Fisher's exact test for the analysis, the minimum significant difference in the prevalence of FI was 5% when comparing the control group with either of the two OASI cohorts and 11% when comparing the two OASI cohorts. Third- and fourth-degree OASIs were analyzed as one group. Diagnoses were retrieved from the MBR. OASI was identified by codes 664.2 and 664.3 in the International Classification of Diseases Ninth Revision (ICD-9) (1987-1996), and O70.2 and O70.3 in the Tenth Revision (ICD-10) and by the surgical code MBC33 (1997-2000).

The postal and web-based questionnaire included questions about current symptoms of solid and liquid stool and gas, urinary incontinence, and pelvic organ prolapse. The women were asked to report their current height and weight, menstrual status, hysterectomy, menopause, and hormone treatment. Information from the questionnaire was linked to obstetric details in the MBR.

Continuous variables were presented as mean and standard deviations and categorical data as number and percentage. Pairwise comparisons were analyzed using Fisher's exact test and the Mann-Whitney U-test for categorical and continuous variables. The results were presented as the mean difference for continuous variables and as the difference in percentages for categorical variables, 95% CI, and P value. The trend was analyzed using Mantel-Haenszel Chi-square statistics and Spearman´s rank correlation test. Logistic regression was used for analyzing the risk of bothersome FI or bothersome isolated gas incontinence (IGI). Results were presented as BMI and age-adjusted odds ratio (aOR) and 95% confidence interval (CI). Statistical significance was set at $P < .05$.

RESULTS

Bothersome FI increased 3- and 5-fold, from 3.3% in women without OASI, to 10.4% (aOR, 3.25; 95% CI, 2.23-4.73) in women with one OASI and 16.5 % (aOR, 5.16; 95% CI, 3.69-7.22) in women with two OASIs (Figure 1). The prevalence of IGI was about 40% in each group, but bothersome IGI was higher after one and two OASIs (Trend $P = 0.0024$). 28.2% of women without OASI perceived their FI as bothersome, compared to 43.9% and 46.0% in women with one or two OASIs (Trend $P < .0001$). The frequency of leakage of solid and liquid stool and IGI increased in women with one or two OASIs compared with those without (Trend all $P < .0001$). For example, the frequency of any leakage of liquid stool was 10.8% in women with no OASI, 21.7% in women with one, and 34.9% in women with two OASIs (Trend $P < .0001$). The use of pads was higher in the one and two OASIs groups compared with no OASI, from 2.3% in women without OASI to 7.1% and 8.4% in those with one and two OASIs (Trend $P < .0001$) (Figure 1). The effect on daily life was reported by 8.6% of women without OASI and 19.7% and 29.6% in women with one and two OASI (Trend $P < .0001$) (Figure 1). The mean Jorge-Wexner score increased from 2.44 to 3.26, and 3.88 in women with no, one, and two OASIs (Trend $P < .0001$). In women with a Jorge-Wexner score of six, more than 50% had bothersome anal incontinence (AI), and in those with a score of 9, almost 80% had bothersome AI (Figure 2). Few women had received treatment for bowel leakage, there were however significantly more women with one and two OASIs (3.4% and 4.1%) compared with women without OASI (1.3%) (Trend $P < .0001$) (Figure 1).

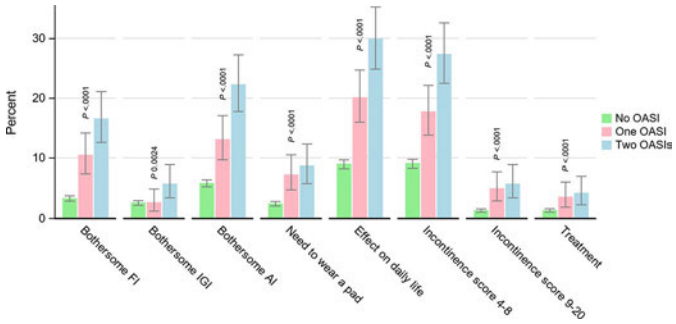
INTERPRETATION OF RESULTS

All components of the severity of anal incontinence – frequency of leakage, its mental impact (bother), coping strategies (use of pads), and the effect on daily life – all increased consistently in women with no, one or two OASIs.

CONCLUDING MESSAGE

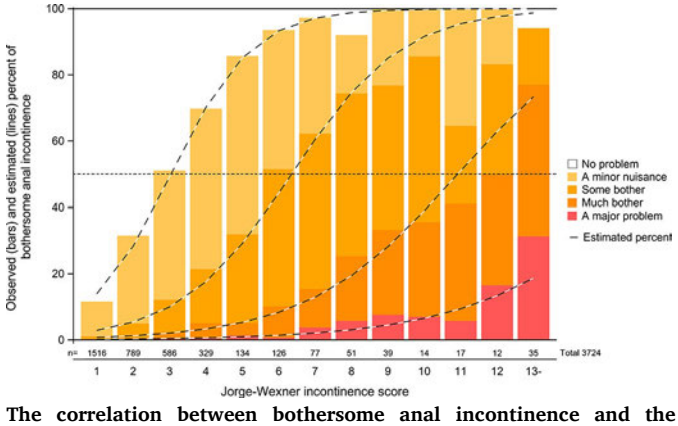
The cumulative long-term risk of anal incontinence associated with sphincter injuries should be acknowledged by obstetricians and midwives and should be communicated to women as part of the antenatal consultation.

FIGURE 1



Measures of subjective impact of anal incontinence.

FIGURE 2



The correlation between bothersome anal incontinence and the Jorge-Wexner incontinence score.

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design, analysis, interpretation, or writing of the report. **Clinical Trial** Yes **Public Registry** No **RCT** No **Subjects** Human **Ethics Committee** Ethical approval was obtained from the Regional Ethical Review Board (reference no 776-13; Nov.18, 2013, Gothenburg). **Helsinki** Yes **Informed Consent** Yes

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ANAL INCONTINENCE FOLLOWING OBSTETRIC ANAL SPHINCTER INJURY: DOES SIZE MATTER? A SYSTEMATIC REVIEW OF GRADE OF INJURY.

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HYPOTHESIS / AIMS OF STUDY

Obstetric anal sphincter injury (OASI) is a serious complication of vaginal delivery and is associated with long-term anal incontinence (AI) [1]. Sultan introduced his classification over 20 years ago, with the aim of further differentiating OASI according to the degree of sphincter injury (3a - < 50% external anal sphincter, 3b - > 50% external anal sphincter, 3c - internal anal sphincter) [2]. There remains uncertainty regarding the risk of OASI subtypes in the literature. The mechanism of AI may also be influenced by a number of factors (e.g. age, parity), and, therefore, counselling women with OASI is often challenging. The purpose of this systematic review was to address the following questions: (a) are women with major OASI (grade 3c and 4) at higher risk of developing AI when compared to women with minor OASI (grade 3a and 3b)? (b) is a fourth-degree tear more likely to cause AI over a third-degree tear?

STUDY DESIGN, MATERIALS AND METHODS

A systematic literature search of EMBASE, PubMed, MEDLINE and CINAHL databases from inception until January 2021. We also searched for grey literature, including conference abstracts of International Continence Society (ICS) and International Urogynaecological Association (IUGA) between January 2000-2021. We considered prospective and retrospective cohort studies, cross-sectional and case-control studies without language restrictions. Records were imported into Endnote and deduplicated. Title, abstracts and relevant full text publications were independently screened by two reviewers for inclusion. The quality of cohort and case-control studies was assessed by the Newcastle-Ottawa Scale (NOS), while the Joanna Briggs Institute (JBI) critical appraisal checklist was used for cross-sectional studies. Risk ratios (RRs) were calculated to measure the effect of different grades of OASI. Findings were summarised with narrative synthesis.

RESULTS

The initial search across the electronic databases identified 1847 records, of which 19 full-text articles were included. In addition, 3 conference abstracts were found eligible. Out of 22 studies, 8 each were prospective and retrospective cohort and 6 were cross-sectional studies. Length of follow-up ranged from 1 month to 23 years, with the majority of the reports (n = 16) analysing data within 12-months post-partum. We included studies from Europe (n = 15), Australia (n = 3), US (n = 2), Canada (n = 1) and Israel (n = 1). Overall, 7218 women were included. Third-degree tears evaluated were 6454 versus 764 fourth-degree tears. As per Sultan classification, we identified women (n = 2979) with 3a (n = 1403), 3b (n = 1178) and 3c (n = 398) tear. Five studies exclusively included primiparae. Data on minor (3a and 3b) and major (3c and 4th) tears were available in 12 studies. Of these, 3 analyses reported only differences in mean scores in patient-reported outcome measures (PROMs) for AI symptoms.

Women from 8 studies were asked to complete the St. Mark's Incontinence Score (SMIS), which represented the most popular PROM. This was followed by the Wexner's score (n = 2) and Fecal Incontinence Severity Index (FISI) (n = 2). Symptoms were assessed through a non-validated questionnaire in 4 studies. With regard to quality assessment, a medium risk of bias was found in 14 cases, while only 3 were deemed to have a low risk of bias. All studies with high risk of bias (n = 5) were retrospective cohort.

There was a wide variation in the reported prevalence of bowel symptoms and impact of OASI severity across the included studies (Table 1 and 2). Prospective studies showed that major (3c and 4th) tears are associated with a two-fold risk of AI, when compared to minor (3a and 3b) tears. This was not confirmed by retrospective and cross-sectional studies. On the other hand, retrospective studies consistently showed a risk of faecal incontinence (FI) which was two- to four-fold higher for major tears versus minor tears. Prospective studies showed a trend towards worsening AI symptoms for 4th degree tears but this failed to reach statistical significance. Cross-sectional studies with long-term (≥ 5 years) follow-up showed that women with 4th degree tear were more likely to develop AI (RR 1.41-2.27). Out of 3, 2 retrospective studies showed similar findings but the follow-up was significantly shorter (≤ 1 year). Contrasting results were noted for FI rates, as only 5 out of 10 studies supported an association between 4th degree tear and FI. There were only 2 out of 7 studies which revealed an increased risk of flatal incontinence with 4th degree tears. Interestingly, rates of flatal incontinence were no different when major (3c and 4th) were compared to minor (3a and 3b) tears.

INTERPRETATION OF RESULTS

There are few good quality data on the consequences of perineal ruptures. Most studies investigate bowel symptoms within few months from delivery and confounding factors (e.g. age, parity) were often not taken into consideration when drawing conclusions. As such, meta-analysis was not possible due to different assessment tools, length of follow-up and population included. Also, there was no consistency in the definition of bothersome AI as different score thresholds were adopted. Despite the Sultan classification being introduced over 20 years ago, the majority of the data do not provide detailed outcomes for subtypes of third-degree tears. Interestingly, there were only two prospective studies reporting AI rates for women with major tears. Women suffering from 3c tear or above appear to be at increased risk of AI and FI. However, evidence supporting worse outcomes for fourth- versus third-degree tears is less compelling. This may reinforce the importance of the internal anal sphincter in the mechanism of AI [3].

CONCLUDING MESSAGE

Women are at increased risk of AI following major OASI (grade 3c and 4). There is no clear evidence to support a higher risk of AI for fourth- versus third-degree tears. Well-designed multicentre studies with adequate power and long-term follow-up are needed to evaluate the risk of AI for each OASI subtype.

FIGURE 1

Study	Assessment	Follow-up	Symptoms prevalence
Prospective studies			
Anglim et al, 2019	SMIS	4-12 m	Different SMIS median between minor and major tears
Borello et al, 2006	FISI	6 m	FI: 3rd (n=48/320, 15%); 4th (n=22/87, 26%)
Cerro et al, 2017	Wexner	6 m	Positive correlation between Wexner's score and degree of tear
Everist et al, 2020	SMIS	2 m	AI: 3a (n=10/58, 17%); 3b (n=11/37, 29%); 3c/4th (n=16/27, 59%)
Gommesen et al, 2020	SMIS	12 m	AI: 3a (n=12/88, 13%); 3b (n=10/66, 15%); 3c (n=7/20, 35%); 4th (n=5/15, 33%)
Patton et al, 2019	SMIS	6 m	Positive correlation between SMIS and degree of tear
Richter et al, 2015	FISI	1-5 m	FI (1 m): 3a (n=10/165, 6%); 3b (n=6/97, 6%); 4th (n=5/45, 11%) AI (5 m): 3a (n=19/96, 25%); 3b (n=6/34, 18%); 4th (n=8/23, 35%) Flatal incontinence (5 m): 3a (n=13/76, 17%); 3b (n=5/34, 15%); 4th (n=8/23, 35%)
Sokolova et al, 2011	Non-validated	3 m	Flatal incontinence: 3a (n=4/47, 9%); 3b (n=3/44, 7%); 3c (n=3/18, 17%); 4th (n=1/8, 14%)
Retrospective studies			
Eisenberg et al, 2015	CCIS	8 m	AI: 3a (n=32/103, 31%); 3b (n=17/33, 51%); 3c (n=11/25, 44%); 4th (n=23/37, 62%) FI: 3a (n=4/103, 4%); 3b (n=5/33, 15%); 3c (n=6/25, 25%); 4th (n=10/37, 28%)
Gold et al, 2021	Non-validated	2-4 m	Flatal incontinence: 3rd (n=9/42, 21%); 4th (n=3/7, 42%) FI: 3rd (n=3/42, 7%); 4th (n=1/7, 14%)
Roos et al, 2010	MHQ	2 m	Flatal incontinence: 3a (n=37/205, 18%); 3b (n=38/198, 19%); 3c/4th (n=22/84, 26%) FI: 3a (n=12/205, 5%); 3b (n=10/198, 5%); 3c/4th (n=11/84, 13%)
Menard et al, 2016	Non-validated	2 m	AI: 3a (n=22/53, 41%); 3b (n=7/15, 46%); 3c (n=5/9, 55%); 4th (n=0/2, 0%)
Jha et al, 2011	ePAQ	3-7 m	Flatal incontinence: 3rd (n=85/301, 28%); 4th (n=9/29, 31%) FI: 3rd (n=47/301, 15%); 4th (n=6/29, 20%)
Joris et al, 2019	Holschneider-modified Kelly	6-7 m	AI: 3a (n=12/43, 27%); 3b (n=14/33, 42%); 3c (n=3/7, 43%); 4th (n=2/5, 40%) FI: 3a (n=3/43, 7%); 3b (n=2/33, 6%); 3c (n=1/7, 14%); 4th (n=2/5, 40%)
Laine et al, 2011	SMIS	10 m	AI: 3rd (n=77/418, 18%); 4th (n=19/37, 51%)
Wan et al, 2020	SMIS	2 m	Flatal incontinence: 3a (n=12/422, 7%); 3b (n=61/420, 14%); 3c (n=13/160, 8%); 4th (n=16/62, 25%) FI: 3a (n=7/422, 1%); 3b (n=13/420, 3%); 3c (n=12/160, 7%); 4th (n=5/62, 8%)
Cross-sectional studies			
Linneberg et al, 2016	SMIS	5 ys	AI: 3a (n=21/27, 77%); 3b (n=10/18, 55%); 4th (n=8/9, 100%)
Nordevall et al, 2004	Pescatori	Median 2 ys	AI: 3rd (n=59/133, 44%); 4th (n=9/17, 53%)
Jango et al, 2018	Danish anal sphincter rupture	10-13 ys	AI: 3rd (n=723/1763, 41%); 4th (n=144/245, 58%) FI: 3rd (n=258/1763, 14%); 4th (n=75/245, 30%)
Sangalli et al, 2000	Non-validated	13 ys	AI: 3rd (n=15/129, 11%); 4th (n=12/48, 25%) Flatal incontinence: 3rd (n=6/129, 4%); 4th (n=4/48, 8%) FI: 3rd (n=9/129, 6%); 4th (n=8/48, 16%)
Turel et al, 2019	SMIS	6 ys	3a/3b (n=40/90, 44%); 3c/4th (n=11/19, 58%)
Halle et al, 2016	Not validated	15-23 ys	Flatal incontinence: 3rd (n=29/58, 50%); 4th (n=4/8, 50%) FI: 3rd (n=11/58, 19%); 4th (n=2/8, 25%)

Table 1. Reported prevalence of bowel symptoms in women with obstetric anal sphincter injury.

FISI: Faecal Incontinence Severity Index; SMIS: St. Mark's Incontinence Score; CCIS: Cleveland Clinic Incontinence (also called Wexner's score).
MHQ: Manchester Health Questionnaire; ePAQ: electronic Personal Health Questionnaire; m: months; ys: years; AI: anal incontinence; FI: faecal incontinence.

FIGURE 2

Study	RR fourth- versus third-degree tear	RR major (3c, 4th) versus minor (3a, 3b) degree tear
Prospective studies		
Anglim et al, 2019	n/a	n/a
Borello et al, 2006	FI: RR 1.73 (95% CI: 1.12 – 2.66)	n/a
Cerro et al , 2017	n/a	n/a
Everist et al, 2020	n/a	AI: RR 2.68 (95% CI: 1.64-4.35)
Gommesen et al, 2020	AI: RR 2.06 (95%CI: 0.94-4.49)	AI: RR 2.42 (95% CI: 1.32-4.40)
Patton et al, 2019	n/a	n/a
Richter et al, 2015	FI: RR 1.83 (95% CI: 0.70-4.73) AI: RR 1.54 (95%CI: 0.79-2.97) Flatal incontinence: RR 2.12 (95% CI: 1.07-4.19)	n/a
Sokolova et al, 2011	Flatal incontinence: RR 1.33 (95% CI: 0.19-9.12)	Flatal incontinence: RR 2 (95%CI 0.63-6.34)
Retrospective studies		
Eisenberg et al, 2015	AI: RR 1.67 (95% CI: 1.21-2.28) FI: RR 3.09(95% CI: 1.47-6.12)	AI: RR 1.5 (95% CI: 1.09-2.05) FI: RR 4.16 (95% CI: 1.95-8.86)
Gold et al, 2021	Flatal incontinence: RR 2 (95%CI: 0.70-5.66) FI: RR 2 (95%CI: 0.24-16.6)	n/a
Roos et al, 2010	n/a	Flatal incontinence: RR 1.4 (95% CI: 0.92-2.11) FI: RR 2.6 (95% CI: 1.31-5.14)
Menard et al, 2016	n/a	AI: RR 1.07 (95%CI: 0.52-2.16)
Jha et al, 2011	Flatal incontinence: RR 1.1 (95% CI: 0.62-1.94) FI: RR 1.33 (95%CI: 0.62-2.83)	n/a
Joris et al, 2019	AI: RR 1.14 (95% CI: 0.37-3.46) FI: RR 5.55 (95% CI: 1.48-20.75)	AI: RR 1.20 (95% CI: 0.57-2.50) FI: RR 4.16 (95% CI: 1.13-15.19)
Laine et al, 2011	AI: RR 2.78 (95% CI: 1.92-4.00)	n/a
Wan et al, 2020	Flatal incontinence: RR 2.5 (95% CI: 1.59-3.92) FI: RR 2.66 (95%CI: 1.07-6.57)	Flatal incontinence: RR 1.18 (95% CI: 0.80-1.73) FI: RR 3.5 (95% CI: 1.87-6.54)
Cross-sectional studies		
Linneberg et al, 2016	AI: RR 1.45 (95% CI: 1.19-1.76)	n/a
Nordevall et al, 2004	AI: RR 1.19 (95% CI: 0.73-1.93)	n/a
Jango et al, 2018	AI: RR 1.41 (95% CI: 1.26-1.56) FI: RR 2.09 (95%CI: 1.68-2.58)	n/a
Sangalli et al, 2000	AI: RR 2.27 (95%CI: 1.17-4.38) Flatal incontinence: RR 2 (95%CI: 0.59-6.7) FI: RR 2.4 (95% CI: 0.98-5.85)	n/a
Turel et al, 2019	n/a	AI RR 1.29 (95% CI: 0.82-2.01)
Halle et al, 2016	Flatal incontinence: RR 1 (95%CI: 0.47-2.08) FI: RR 1.31 (95%CI: 0.35-4.86)	n/a

Table 2. Impact of severe obstetric anal sphincter injuries on bowel symptoms.

RR: Risk ratio; AI: anal incontinence; FI: faecal incontinence; n/a: not applicable.

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AN EVALUATION OF THE INCIDENCE OF OASIS IN THE ERA OF REDUCING EPISIOTOMY RATE

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HYPOTHESIS / AIMS OF STUDY

Obstetric anal sphincter injuries (OASIS) are associated with faecal incontinence, which impair women's quality of life. Episiotomy is the commonest obstetric procedure during a delivery. There are efforts to reduce the episiotomy rate for women to reduce the morbidity of women. However, there is evidence showing that Asian women delivered in areas with a low episiotomy rate had a higher OASIS rates.

This study evaluated the incidence of OASIS in our unit while there was a reducing episiotomy rate throughout the last few years.

STUDY DESIGN, MATERIALS AND METHODS

This was a retrospective study evaluating the incidence of OASIS from year 2015 to 2021. The electronic hospital delivery database was reviewed. The delivery record was entered into the electronic system in the delivery suite immediately after the delivery of women. Generally, normal vaginal delivery (NVD) was conducted by midwives. The use of episiotomy was up to the decision of operator at the time of delivery. Per-vaginal and per-rectal examination would be conducted to explore for OASIS after the delivery. If there were OASIS, obstetrician would confirm and repair it immediately; and the electronic operative record was completed right after the procedure.

RESULTS

There were a total of 30,984 vaginal deliveries of singleton pregnancy. Among them, 28,499 (92%), 2,078 (6.7%) and 407 (1.3%) had NVD, ventous extraction and forceps delivery, respectively. In all, 50.3% and 49.7% were nulliparous and multiparous women. The episiotomy rate for nulliparous and multiparous women having NVD reduced from 90% to 54% and 30% to 19% from 2015 to 2021, respectively.

The OASIS rate for nulliparous NVD women with and without episiotomy ranged from 0.47% to 1.6% and 0.26% to 2.6% per year; while these were 0.15% to 1.6% and 0.1% to 0.4% for multiparous NVD women. There was no statistical significant difference in OASIS rate throughout the 7 years; except a lower OASIS rate in nulliparous women with no episiotomy. However, from 2017 to 2021, there was an increase in OASIS rate in nulliparous NVD women (Chi-square for trend, $P = 0.007$). Among the OASIS, 67(38%), 88(49%), 13(7%) and 9(5%) were 3a, 3b, 3c and 4th degree perineal tears, respectively. There was one button hole tear (1%).

INTERPRETATION OF RESULTS

There was significant reduction of episiotomy rate in both nulliparous and multiparous women having normal vaginal delivery. However, there was no significant difference in rate of OASIS; except a lower OASIS rate in nulliparous women with no episiotomy.

CONCLUDING MESSAGE

Reduction in the rate of episiotomy did not associate with increase in OASIS in nulliparous and multiparous women who had normal vaginal delivery for singleton pregnancy. Other potential confounding factors should also be studied.

FIGURE 1

Table 1: OASIS rate in nulliparous or multiparous women with or without episiotomy during normal vaginal delivery

	2015	2016	2017	2018	2019	2020	2021	P-value
Nulliparous NVD								
With episiotomy	16/2112 0.8%	14/2286 0.6%	7/1487 0.5%	7/1268 0.6%	8/1053 0.8%	8/853 0.9%	10/625 1.6%	0.15
No episiotomy	6/242 2.5%	7/358 2%	4/676 0.6%	9/782 1.2%	2/783 0.3%	3/505 0.6%	3/522 0.6%	0.01
Multiparous NVD								
With episiotomy	5/698 0.7%	1/685 0.1%	8/652 1.2%	2/428 0.5%	7/433 1.6%	3/314 0.9%	3/298 1.0%	0.15
No episiotomy	3/1623 0.2%	5/1865 0.3%	1/1800 0.1%	4/1830 0.2%	2/1730 0.1%	6/1360 0.4%	4/1234 0.3%	0.32

Table 1: OASIS rate in nulliparous or multiparous women with or without episiotomy during normal vaginal delivery

Funding None **Clinical Trial** No **Subjects** Human **Ethics not Req'd** This is an retrospective evaluation of incidence **Helsinki** not Req'd This is an retrospective evaluation of incidence **Informed Consent** No

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405 | www.ics.org/2022/abstract/405

CORRELATION OF ANORECTAL SYMPTOMS AND ENDOANAL ULTRASOUND FINDINGS AFTER OBSTETRICAL ANAL SPHINCTER INJURIES (OASIS)

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HYPOTHESIS / AIMS OF STUDY

Obstetrical Anal Sphincter Injuries (OASIS) are severe perineal lacerations that predispose to development of anorectal symptoms with significant maternal morbidity that compromise women's quality of life. Endoanal ultrasound (EAUS) is the gold standard for morphological assessment of the anal sphincter complex. It is used to assess the anal sphincter integrity and detect any persistent anal sphincter defects post repair.

The purpose of this study was to determine correlation between EAUS findings and anorectal symptoms in women after primary OASIS repair; to determine incidence of residual anal sphincter defects on EAUS after primary OASIS repair; and to determine the rate of clinical overdiagnosis of OASIS.

STUDY DESIGN, MATERIALS AND METHODS

A retrospective cohort study was conducted for all women with singleton vaginal deliveries who had a primary repair of OASIS and attended the Postpartum Perineal Clinic at a large tertiary care centre between July 1st 2017 and December 31st 2020. Exclusion criteria consisted of women who had EAUS outside the institution, did not undergo EAUS, rectovaginal fistula, or had incomplete data. This study was approved by the Research Ethics Board. Records were reviewed for baseline characteristics, risk factors for OASIS, severity of anorectal symptoms based on St. Mark's Incontinence Score (SMIS), and findings on EAUS. Data was analyzed using descriptive statistics. Pearson correlation coefficient was used to assess correlation between anorectal symptoms and EAUS findings.

RESULTS

A total of 330 participants with clinical diagnosis of OASIS met the inclusion criteria. From these participants, 156 (47.3%) had sonographic evidence of OASIS on EAUS. The rate of overdiagnosis was 52.7%. A 3rd degree tear was identified in 126 (38.2%) participants. Of these, 60 (18.2%) participants had 3a perineal tear, while 39 (11.8%) participants had 3b perineal tear, and 27 (8.2%) participants had 3c perineal tear. Fourth degree tear was identified in 30 (9.1%) participants. In participants with sonographic evidence of OASIS on EAUS, there was a statistically significant weak positive correlation ($r = .3723$) between the size of the residual defect of external anal sphincter (EAS) and SMIS ($p < .0001$). There was also a statistically significant weak positive correlation ($r = .3122$) between the size of residual defect of the internal anal sphincter (IAS) and SMIS ($p = .0180$). Residual defect in the anorectal sphincter complex >1 hour was present in 82 (65.1%) participants with 3rd degree tear and 26 (86.7%) participants with 4th degree tear.

INTERPRETATION OF RESULTS

This study demonstrates that the size of residual defect of EAS and IAS have a weak positive correlation with anorectal symptoms, emphasizing the importance of EAUS for counselling about subsequent mode of delivery.

CONCLUDING MESSAGE

The results of this study emphasize the importance of accurate diagnosis and adequate primary OASIS repair.

FIGURE 1

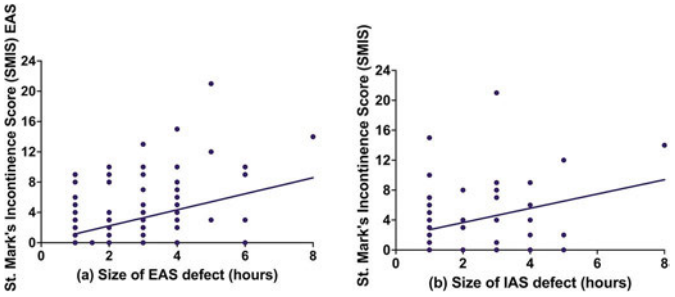

Figure 1: Correlation (shown with regression line) between severity of anorectal symptoms expressed as SMIS and extent of residual defects in EAS (a) and IAS (b) with evidence of defect on EAUS expressed in hours. There was a weak positive correlation pre

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THE CORRELATION BETWEEN DIET, BOWEL FUNCTION AND ISOLATED POSTERIOR VAGINAL DEFECT: A CROSS-SECTIONAL STUDY

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HYPOTHESIS / AIMS OF STUDY

Isolated posterior vaginal defect is one of the entities among pelvic organ prolapse and is considered to have a different pathophysiologic background than other forms of pelvic organ prolapse. Although anterior wall prolapse is most commonly studied in the literature, it has been determined that posterior wall prolapse has a significantly higher prevalence in specific region of the world.(1) The reasons behind this remain unclear in the current literature, however, the associations between obstructive defecation and posterior wall prolapse seem to be increasingly studied throughout the world, as global diets are changing with incredible speed. The current literature regarding chronic obstructive defecation and pelvic organ prolapse has not yet determined the cause and effect relationship between the two, or whether they are independent but concurrent problems. Our aim was to evaluate the relationship between bowel dysfunction and diet to isolated posterior compartment prolapse (IPCP).

STUDY DESIGN, MATERIALS AND METHODS

This cross-sectional study compared the dietary outcomes of Irish and Israeli women who underwent pelvic organ prolapse repair surgery between August 2020 and October 2021. Patients were asked to complete a validated Mediterranean diet questionnaire and a Patient Assessment of Constipation-Symptoms (PAC-SYM) questionnaire over the phone.(2)

RESULTS

During the study period a total of 236 participants were enrolled and thirty two patient were dropped out without answering the Questionnaires. Among the two hundred and four patients, 108 (52.9%) patients adhered to the Mediterranean diet, and 96 (47.0%) did not. It was found that in the non-Mediterranean diet patients, increased symptoms of constipation ($p = 0.047$) and higher BMI ($p = 0.0008$) were significant more prevalent. The non-Mediterranean diet group had a significant higher prevalence of patients with class III obesity (BMI > 39.9) ($p = 0.047$) when compared to the Mediterranean diet group. Surgical repair of the posterior compartment, both combined (26(24%) Vs. 37(38.5%), $p = 0.033$) and isolated (6(5.5%) Vs. 15(21.7%), $p = 0.021$), were more prevalent amongst the non-Mediterranean diet group. Prolapse of all compartments except the apical compartment was found to be more prevalent in the non-Mediterranean diet group.

INTERPRETATION OF RESULTS

Mediterranean diet displays a lower prevalence of posterior vaginal defect, both isolated and combined. This was demonstrated by the inverse relationship found between adherence to Mediterranean diet, decreased symptoms of constipation, and lower BMI values amongst this group. We found a direct link between the demographic diet, constipation and and the degree and prevalence of posterior compartment defect.

CONCLUDING MESSAGE

Adherence to the Mediterranean diet and subsequent bowel dysfunction is a significant contributory factor to the prolapse of the posterior vaginal compartment.

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Funding The authors declare that they have no conflict of interest or source of funding **Clinical Trial** No **Subjects** Human **Ethics Committee** Clinical Research **Ethics Committee** of the Cork Teaching Hospitals **Helsinki** Yes **Informed Consent** Yes

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SESSION 25 - TRANSGENDER HEALTH & SEXUAL DYSFUNCTION

Abstracts 407-418
15:30 - 17:00, Hall K
Chair: Prof Ervin Kocjancic (United States)

407 | www.ics.org/2022/abstract/407

IS OAB A PRE-OPERATIVE FACTOR FOR SEXUAL DYSFUNCTION IN PATIENTS UNDERGOING POP SURGERY? PRELIMINARY RESULTS FROM A CROSS-SECTIONAL STUDY.

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HYPOTHESIS / AIMS OF STUDY
Women with complicated pelvic floor disorders combined or not with urinary incontinence (UI) appear to have decreased rates of sexual satisfaction. Lower urinary tract symptoms are an independent risk factor for decreased female sexual function [1]. The information regarding pelvic organ prolapse (POP) or overactive bladder symptoms (OAB) on women's sexual function is often absent or inadequate. The sexual history in the clinical assessment is usually skipped both by the physicians and patients. The Female Sexual Function Index (FSFI) is considered the "gold-standard" tool widely used to assess and quantify sexual function in clinical practice and research. Sexual dysfunction usually motivates symptomatic women to ask for medical advice even within the context of POP management.

The present study was designed to determine the effect of overactive bladder and pelvic organ prolapse on sexual activity and women's quality of sexual life. As control groups were used healthy women and women who had benign gynecologic surgery other than for POP or UI.

STUDY DESIGN, MATERIALS AND METHODS
This is a cross-sectional study performed in an Urogynecology unit of a Tertiary Academic Hospital. Consecutive women prolapse without OAB (POP group) and with OAB (POP-OAB group) symptoms who had undergone native tissue POP surgery were asked to participate in the study. Post-operatively, all women in the POP and the POP-OAB group filled in the Incontinence Questionnaire-Urinary Incontinence Short Form (ICIQ-UI-SF), Pelvic Organ Prolapse/Urinary Incontinence Sexual Questionnaire (PISQ-12), Sexual Quality of Life Questionnaire – Female (SQOL-F) and FSFI. In addition, all participants underwent clinical examination with POP-Q classification, standardized cough test, and full urodynamics investigation. For control, we enrolled a group of healthy asymptomatic women who did not have any intervention (Healthy group) and women who had undergone gynaecological surgery in the same department but not prolapse surgery or oncologic surgery (Gyn group). Any woman from the control groups with incontinence symptoms was excluded (ICIQ-UI SF $\neq$ 0). Informed oral consent was obtained as appropriately by all the participants, and the Hospital's Ethics Committee approved the study protocol . All data were stored and analysed in Microsoft EXCEL. Paired t-test $\chi 2$, and ANOVA were used to compare the results among the groups; $p < 0.05$ was considered statistically significant.

RESULTS
A total of 82 subjects were included. The POP group and POP-OAB group comprised 19 and 21 participants, respectively. The Healthy and Benign Gynae surgery groups were 22 and 20 subjects. Demographic data such as age and body mass index (BMI), parity, birth weight, instrumental birth, and smoking were collected from the study subjects (see Table 1). Table 2 shows the scores of the given questionnaires. The mean summary scores obtained from the ICIQ-SF, the FSFI, the SQOL-F, and the PISQ-12 questionnaires in each group of patients are described in Table 2. ANOVA was performed to show any difference among the groups. In all questionnaires, the ANOVA showed statistically significant differences between the groups. In the FSFI, the Healthy group and Gyn groups had significantly higher scores than the POP group ($p = 0.015$ and 0.049 respectively). In the SQOL-F, the Healthy group had a significantly higher score compared to the POP group ($p = 0.002$). Women with POP-OAB had significantly higher ICIQ-UI scores ($p < 0.001$), whereas no differences were found in these two groups regarding the PISQ-12 questionnaire.

INTERPRETATION OF RESULTS
Female sexual dysfunction is a common condition that immensely affects the quality of life. Sexual life has a fundamental role during the woman's reproductive life, and pelvic floor disorders may deteriorate women's sexual activity and sexual quality of women. Unfortunately, there are scanty data about the post-operative sexual life of women who had POP surgery.

In the present study, several assumptions can be elicited from the comparisons of the four groups. First, even though the POP group women are older, both FSFI and SQOL-F scores are severely affected, an outcome indicating the effect of pelvic floor surgery on the sexual life of these patients. Further comparisons between the three non-healthy groups reveal that (a) the POP-OAB group scores similarly to the Gyn group in FSFI and the SQOL-F questionnaires, and (b) the POP-OAB group scores higher, although not statistically significant, in the PISQ-12. The last comparison appears to be severely affected by partner-related issues and marginally by behavioral-emotive issues. Finally, the consecutive enrollment of the subject in this study may create a bias regarding the presence and the performance of the partner in the POP group.

CONCLUDING MESSAGE
Even after surgical correction, pelvic organ prolapse appears to significantly affect the sexual activity and the quality of sexual life in women. However, the presence of OAB symptoms in this cohort of patients was not an aggravating factor for the deterioration in sexual life.

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URINARY AND SEXUAL DYSFUNCTION AFTER LOW ANTERIOR RESECTION FOR RECTAL CANCER: ONE-YEAR FOLLOW-UP

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HYPOTHESIS / AIMS OF STUDY

Colorectal cancer is the second most common cancer in women and the third most common cancer in men. Nearly 40% of these tumours are located in the rectum. Standard of surgical care is a nerve and sphincter sparing total mesorectal excision (TME). This technique consists of excising the rectum, together with the total mesorectal envelope. By performing a TME, the rectal reservoir as such is lost. This can result not only in a wide range of bowel symptoms, but also urinary and/or sexual symptoms. [1, 2] The aim of the present study was to assess the impact of TME on urinary and sexual dysfunction in rectal cancer survivors, from preoperatively to 1, 4, 6 and 12 months after surgery (or after stoma closure) as well as to assess the impact of age and neoadjuvant radiotherapy.

STUDY DESIGN, MATERIALS AND METHODS

Patients who had a TME for rectal cancer between January 2017 and January 2021 (in three different hospitals) were eligible, but were excluded if they: (1) had another type of surgery for colorectal cancer: a Hartmann procedure, abdominoperineal excision, transanal endoscopic microsurgical resection, or sigmoid resection, (2) were incontinent for faeces before surgery, (3) had neurological diseases, (4) already had previous pelvic surgery, previous pelvic radiation or LAR for non-cancer reasons.

After consent, patients were asked to fill out a numeric rating scale (NRS) regarding bother from urinary complaints and the International Consultation on Incontinence Questionnaire Male/Female Lower Urinary Tract Symptoms Module (ICIQ-M/FLUTS) regarding urinary symptoms. The numeric rating scale was scored between 0 and 10. The ICIQ-MLUTS consists of 13 questions (scored from 0 to 4) leading to a voiding- and incontinence- subscale score and scores for individual items regarding frequency and nocturia. The ICIQ-FLUTS consists of 12 questions (scored from 0 to 4), leading to a filling, voiding- and incontinence subscale score. The ICIQ bother scales are not incorporated into the overall score, but all of the bother scores were added to provide a general overview. Concerning sexual symptoms, male patients were asked to fill out the International Index of Erectile Function (IIEF) and female patients the Female Sexual Functioning Index (FSFI). The IIEF (15 questions) amounts to subscale scores for erectile function, orgasmic function, sexual desire, intercourse satisfaction and overall satisfaction and the FSFI (19 questions) represent subscale scores for desire, arousal, lubrication, orgasm, satisfaction and pain as well as a total score.

All measurement methods were completed concerning the preoperative period and at 1, 4, 6 and 12 months after surgery. Linear mixed effects models were used to assess changes over time (from 0-12 months). To explore overall trajectories, we included random effects (intercept and slope) and fixed effects (time, age and radiotherapy) into the model. The alpha level was set at 0.05. Analyses were performed by the Biostatistics and Statistical Bioinformatics Centre.

RESULTS

In total, 104 patients participated in this study. The median age for male patients was 61 years (range 32-85) and 55 years (range: 29-84) for female patients. Urinary and sexual dysfunction according to the NRS, ICIQ-MLUTS/FLUTS and the IIEF/FSFI is presented in Table 1.

Linear mixed effects models showed that for male as well as female patients, no significant evolution was found over time for urinary symptoms. I.e., symptoms assessed with neither the NRS nor the ICIQ-MLUTS/FLUTS showed significant differences over time from the preoperative period until one year post-TME/after stoma closure. Regarding sexual symptoms in males, all subscales (erectile function, orgasm, desire, sexual satisfaction, overall satisfaction) of the IIEF showed significant decreases over time ($p < 0{,}001$ for all subscales). In female rectal cancer patients, FSFI-subscales for desire ($p = 0{,}017$), arousal ($p = 0{,}039$) and pain ($p = 0{,}029$) decreased significantly over time. None of the sexual symptoms with a significant evolution over time reached preoperative values after treatment for rectal cancer.

Furthermore, linear mixed effects models showed that neoadjuvant radiotherapy had a negative influence on NRS-scores as well as voiding and incontinence symptoms in male patients and older age was shown to have a negative influence on nocturia and all IIEF-scores, except for overall satisfaction. In female patients after rectal cancer treatment, radiotherapy did not influence urinary nor sexual symptoms. Older age did significantly influence NRS-scores and filling symptoms as well as all FSFI-scores, except for satisfaction. An overview of these results is presented in Table 2.

INTERPRETATION OF RESULTS

Rectal cancer treatment does not seem to significantly influence urinary symptoms over time in male or female patients. Sexual functioning however is affected after TME: male sexual functioning decreases in every aspect, while female patients report problems with desire, arousal and pain. These values for sexual symptoms do not reach preoperative values one year after surgery/stoma closure. Radiotherapy influences the amount of bother from urinary symptoms, voiding and incontinence in male patients. Age influences the trajectory of all sexual symptoms and nocturia in male patients. In female patients, age influences the amount of bother from urinary symptoms and filling symptoms, as well as all sexual symptoms. Overall satisfaction however, is not influenced by age.

CONCLUDING MESSAGE

Functional outcomes such as urinary and sexual symptoms should be questioned during patient follow-up after rectal cancer treatment, certainly in older patients. Furthermore, following the results of this study, sexual symptoms are most definitely present in men as well as women after RC. Therefore, sexual symptoms should not be underestimated, should be questioned adequately in every patient and treated as needed.

FIGURE 1

Table 1: Descriptive values for urinary and sexual outcomes.

		MALE (mean (SD))				
variable (min-max)		**preop**	**1M postop**	**4M postop**	**6M postop**	**12M postop**
Urinary	ICIQ-MLUTS	NRS (0-10)	0,60 (1,28)	1,64 (2,62)	0,74 (1,61)	0,66 (1,28)	0,64 (1,17)
		Frequency (0-4)	0,24 (0,46)	0,41 (0,82)	0,33 (0,61)	0,35 (0,75)	0,36 (0,70)
		Nocturia (0-4)	1,46 (1,07)	1,44 (0,98)	1,54 (1,16)	1,52 (1,18)	1,44 (1,26)
		Voiding (0-20)	4,00 (3,79)	4,99 (4,29)	3,90 (3,65)	3,88 (3,76)	3,95 (3,60)
		Incontinence (0-24)	1,75 (2,31)	1,93 (2,07)	1,71 (1,94)	1,85 (1,99)	2,06 (2,09)
		Bother (0-130)	7,39 (10,80)	11,80 (15,30)	8,09 (11,00)	6,55 (9,03)	7,16 (11,50)
Sexual	IIEF	Erectile func. (1-30)	21,00 (10,50)	9,61 (8,96)	12,00 (10,30)	13,10 (11,00)	11,80 (10,30)
		Orgasm (1-10)	7,34 (3,42)	4,80 (3,55)	5,05 (3,80)	5,57 (3,80)	5,41 (3,84)
		Desire (2-10)	6,35 (2,12)	4,80 (2,26)	5,21 (2,22)	5,11 (2,26)	5,49 (2,29)
		Sexual satisf. (0-15)	8,70 (5,40)	2,90 (4,53)	4,26 (5,11)	4,71 (5,03)	4,51 (5,09)
		Overall satisf. (2-10)	7,58 (2,07)	5,37 (2,76)	5,67 (2,75)	5,50 (2,71)	5,52 (2,80)
		FEMALE (mean (SD))				
variable (min-max)		**preop**	**1M postop**	**4M postop**	**6M postop**	**12M postop**
Urinary	ICIQ-FLUTS	NRS (0-10)	1,06 (1,92)	1,45 (2,59)	1,03 (2,03)	1,22 (2,61)	1,16 (2,19)
		Filling (0-16)	2,13 (1,96)	2,12 (1,73)	2,21 (2,23)	1,89 (1,89)	2,00 (2,53)
		Voiding (0-12)	1,03 (1,51)	1,73 (2,55)	1,24 (1,81)	0,82 (1,33)	0,96 (1,99)
		Incontinence (0-20)	2,25 (2,77)	1,67 (2,58)	2,34 (3,86)	1,70 (2,98)	2,56 (4,08)
		Bother (0-120)	8,16 (10,5)	9,18 (12,7)	9,83 (16,40)	5,96 (13,2)	9,08 (17,10)
Sexual	FSFI	Desire (1,2-6)	2,78 (1,43)	1,78 (0,95)	2,01 (1,05)	2,16 (1,16)	2,48 (1,36)
		Arousal (0-6)	2,78 (2,39)	1,04 (1,61)	1,63 (1,98)	1,70 (2,10)	1,79 (2,07)
		Lubrication (0-6)	2,96 (2,61)	0,96 (1,79)	1,92 (2,41)	1,94 (2,54)	1,81 (2,42)
		Orgasm (0-6)	2,78 (2,43)	1,02 (1,94)	1,82 (2,29)	1,85 (2,52)	2,17 (2,55)
		Satisfaction (0,8-6)	4,07 (1,62)	2,67 (1,69)	3,43 (1,47)	3,58 (1,84)	3,77 (1,63)
		Pain (0-6)	2,89 (2,74)	1,09 (2,09)	1,49 (2,09)	1,66 (2,37)	1,70 (2,44)
		Total (2-36)	19,10 (12,5)	9,34 (9,82)	12,70 (10,90)	14,30 (11,90)	14,60 (11,90)

Table 1: Descriptive values for urinary and sexual outcomes.

FIGURE 2

Table 2: Results from linear mixed models for age and neoadjuvant radiotherapy.

MALE					FEMALE				
variable			Age	RT	variable			Age	RT
Urinary	NRS	Subjective bother	0,490	0,015*	Urinary	NRS	Subjective bother	0,002*	0,338
	ICIQ-MLUTS	Frequency	0,878	0,860		ICIQ-FLUTS	Filling	0,006*	0,397
		Nocturia	0,030*	0,158			Voiding	0,066	0,238
		Voiding	0,532	0,023*			Incontinence	0,235	0,692
		Incontinence	0,157	0,003*			Bother	0,194	0,215
		Bother	0,557	0,092					
Sexual	IIEF	Erectile function	<0,001*	0,472	Sexual	FSFI	Desire	0,004*	0,197
		Orgasm	<0,001*	0,391			Arousal	0,002*	0,263
		Desire	<0,001*	0,972			Lubrication	0,003*	0,304
		Sexual satisfaction	<0,001*	0,955			Orgasm	0,006*	0,193
		Overall satisfaction	0,280	0,442			Satisfaction	0,075	0,455
							Pain	0,003*	0,349
							Total	0,007*	0,382

*p-value < 0,05

Table 2: Results from linear mixed models for age and neoadjuvant radiotherapy.

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CHANGE IN URINARY INCONTINENCE OVER TWO YEARS AMONG SEXUAL MINORITY PROSTATE CANCER SURVIVORS ENROLLED IN AN ONLINE REHABILITATION PROGRAM FOR URINARY AND SEXUAL DYSFUNCTION

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HYPOTHESIS / AIMS OF STUDY

Emerging evidence suggests that sexual minorities with prostate cancer may experience significant health disparities in urinary function after cancer treatment [1]. To date, there have been no investigations on the severity or course of change in urinary incontinence among sexual minorities after prostate cancer treatment, nor have there been any investigations into their response to conservative treatments for urinary incontinence. These disparities may be related to heteronormative care that is not tailored to the needs of sexual minorities. Restore 2 is the first NIH funded randomized controlled trial investigating the effectiveness of a rehabilitation program designed to improve urinary and sexual dysfunction in sexual minority prostate cancer survivors [1]. This analysis examines the impact of Restore 2 on urinary incontinence by 1) describing change in the severity of urinary incontinence over two years; 2) determining if participating in the treatment arm improved severity of urinary incontinence over two years; and 3) identifying subgroups with greater urinary incontinence severity and response to treatment over two years.

STUDY DESIGN, MATERIALS AND METHODS

This is a two year longitudinal analysis of 401 participants enrolled in the Restore 2 trial. Participants were randomly assigned to the intervention group (N = 204) or to the usual care control group (N = 197). The intervention was an online, tailored, multi-component rehabilitation program addressing urinary and sexual dysfunction. Participants self-selected the components they wanted to address. Treatment options for urinary incontinence included pelvic floor muscles exercises, urge suppression techniques, bladder training, avoiding bladder irritants, adequate hydration, and constipation prevention. The pelvic floor exercise prescription was to do 10 quick contractions followed by 10 long contractions three times a day. Treatment options for sexual dysfunction included sildenafil, masturbation exercises, vacuum pump exercises, and anal dilators. Participants were sexual minorities who self-identified as gay, bisexual or as a man who has sex with men. They were recruited mainly from online dating sites, prostate cancer survivor support groups, and social networking sites. Participants had to have been diagnosed with prostate cancer with curative treatment completed, ongoing, or scheduled within two months of beginning the study, be fluent in English, and live in the United States. Data was collected online using Qualtrics software©. Urinary incontinence type and severity was measured with the International Consultation on Incontinence Questionnaire – short form (ICIQ) at baseline, 3, 6, 12, 18, and 24 months follow-up. Adherence to pelvic floor muscle exercises were self-reported as never, less than monthly, 1-3 times a month, 1-4 times a week, and 5-7 times a week at 3, 6, 12, 18, and 24 months. The following self-reported baseline demographic, health, and prostate cancer status characteristics were used to determine their association with urinary incontinence severity over time: age, race, obesity, number of alcoholic drinks consumed in a typical day, health related quality of life measured with the Functional Assessment of Cancer Therapy: General subscale (FACT-G), number of comorbidities, use of anti-incontinence medications, use of sildenafil, HIV status, time since prostate cancer diagnosis, prostate cancer stage, type of prostate cancer treatment, Expanded Prostate Cancer Index Composite (EPIC) bowel and sexual subscales, and climacturia. Descriptive statistics described sample characteristics. Linear mixed effects regression models with unstructured covariance matrixes described change in ICIQ scores over time. Demographic, health, and prostate cancer status characteristics significantly associated ($p < .10$) with ICIQ growth parameters in univariate models were included in a multivariate model to identify independent predictors of incontinence severity and change.

RESULTS

Participants had a mean age of 63.5 years, were on average 5.3 years past diagnosis, and were treated with surgery (59%), radiation (23%), surgery and radiation (11%) or other treatments (7%). The mean ICIQ score at baseline was 6.6(4.9) and only 16 (4%) participants reported no urinary incontinence during the study. Unconditional models showed ICIQ scores varied at baseline ($\beta = 6.44$, $p < .0001$), but did not change over two years ($\beta = -.009$, $p = .295$). Treatment group assignment did not predict severity ($\beta = -.38$, $p = .372$) or change in ICIQ scores ($\beta = -.009$, $p = .293$). Age, race, and prostate cancer stage were not associated with severity or change in ICIQ scores. In univariate models, the following characteristics were associated with ICIQ severity, but not change in ICIQ scores over time: obesity ($\beta = 1.63$, $p = .003$), health related quality of life ($\beta = -.08$, $p < .0001$), comorbidities ($\beta = .44$, $p = .004$), use of anti-incontinence medications ($\beta = 1.94$, $p = .007$), time since prostate cancer diagnosis ($\beta = .09$, $p = .045$), EPIC bowel symptoms ($\beta = -.08$, $p < .0001$), EPIC sexual symptoms ($\beta = -.05$, $p < .0001$), climacturia ($\beta = 3.33$, $p < .0001$), and adherence to pelvic floor muscles exercises ($p < .0001$). The type of prostate cancer treatment predicted the severity of ICIQ scores in the following rank order: radiation and surgery ($\beta = 1.65$, $p = .013$), surgery only ($p < .0001$), radiation only ($\beta = -2.04$, $p < .0001$), other treatments ($\beta = -3.14$, $p < .0001$). The type of urinary incontinence predicted severity of ICIQ scores in the following rank order: mixed urinary incontinence ($\beta = 8.3$, $p < .0001$), stress urinary incontinence ($\beta = 6.61$, $p < .0001$), insensible or continuous urinary incontinence ($\beta = 5.06$, $p < .0001$), urgency urinary incontinence ($\beta = 4.28$, $p < .0001$), and post-void urinary incontinence ($\beta = 4.1$, $p < .0001$). Table 1 presents the multivariate model which showed ICIQ scores were more severe in the control group and were independently associated with obesity, health related quality of life, adherence to pelvic floor muscles exercises, the type of urinary incontinence, and climacturia. Figure 1 illustrates differences between the treatment and control groups in the ICIQ scores predicted by the multivariate model.

INTERPRETATION OF RESULTS

Participating in an online, tailored, multi-component rehabilitation program for sexual minority prostate cancer survivors did not change incontinence severity over two years and no subgroups of participants emerged as having benefited more. While we did not find a treatment effect we gained knowledge to inform future research. First, we had excellent retention of participants indicating they found the tailored content and online approach acceptable. We are also the first to describe the severity and course of change in urinary incontinence over two years in sexual minorities treated for prostate cancer. We found great variability in incontinence severity, but no change in severity over time. On average participants had their cancer treatment five years ago, and most likely represent long term cancer survivors with persistent urinary incontinence. Our inclusion criteria may have been too broad and the treatment options too many to improve urinary incontinence. While participants were provided with information on several conservative treatment options for incontinence, the emphasis was on pelvic floor muscle exercises which participants self-selected as a treatment option. Even though participants with more severe incontinence did more pelvic floor muscle exercises, they did not benefit. However, self-selection of incontinence treatments may not be ideal. Participants reported different types of incontinence, some of which are less amenable to pelvic floor muscle exercises. A comprehensive assessment and management plan produced by a continence specialist may help identify the best conservative treatments in future studies.

CONCLUDING MESSAGE

Incontinence severity did not change over two years for sexual minorities enrolled in an online, tailored, multi-component rehabilitation program for urinary and sexual dysfunction after prostate cancer treatment. This lack of treatment effect may be attributed to the wide heterogeneity in the type and severity of incontinence experienced by participants. Future trials should enroll participants most likely to benefit from conservative treatment and provide more guidance on the types of treatments that will be most effective for their type of incontinence.

FIGURE 1

Table 1

Predictors of Urinary Incontinence Severity and Change over 2 Years in Gay, Bisexual, and Men who have Sex with Men Enrolled in Restore 2 an Online, Tailored, Multicomponent Rehabilitation Program for Prostate Cancer Survivors with Urinary and Sexual Dysfunction

Predictor	Coefficient (Standard Error)	p
Intercept	7.02 (1.59)	<.0001
Linear time	-.01 (.01)	.550
Treatment group assignment	-.90 (.33)	.007
Obesity	1.28 (.55)	.020
Alcholic beverage consumption ≤ 2 drinks vs > 2 drinks	-.42 (.39)	.234
Health related quality of life measured with FACT–G*	-.04 (.01)	.004
Number of comorbidities (range 0-6)	-.03 (.15)	.832
Use of anti-incontinence medications	.88 (.60)	.143
Years since prostate cancer diagnosis	.04 (.04)	.284
Adherence to pelvic floor muscles exercises (compared to never)		
< once a month	.26 (.20)	.190
1-3 times a month	.54 (.24)	.021
1-4 times a week	.99 (.22)	<.0001
5-7 times a week	1.64 (.26)	<.0001
Type of prostate cancer treatment (compared to surgery only)		
Radiation only	-.27 (.51)	0.607
Surgery and radiation	.09 (.57)	0.871
Other	-1.15 (.72)	0.113
Type of urinary incontinence (compared to no incontinence)		
Stress	4.56 (.55)	<.0001
Urgency	3.54 (.58)	<.0001
Mixed stress/urgency	5.42 (.68)	<.0001
Post-void	3.23 (.66)	<.0001
Insensible/continuous	3.93 (.93)	<.0001
EPIC** bowel score	-.02 (.02)	.238
EPIC** sexual function score	-.02 (.01)	.063
Climacturia	1.31 (.42)	.002

Note. Omnibus Chi-square test = 368.88, p <.00001. Longitudinal dependent variable is incontinence severity measured with the International Consultation on Incontinence Questionnaire – short form (ICIQ) at baseline, 3, 6, 12, 18, and 24 months follow-up
*FACT-G = Functional Assessment of Cancer Therapy: General subscale
**EPIC = Expanded Prostate Cancer Index Composite

Table 1

FIGURE 2

Figure 1.

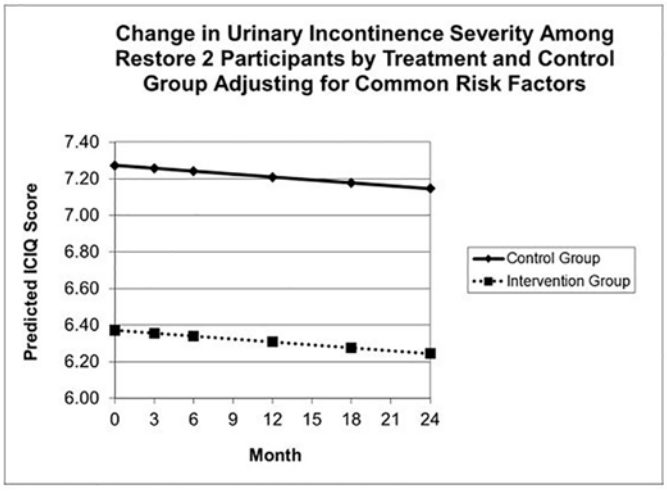

Figure 1

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Funding National Cancer Institute 1R01 CA218657-01 **Clinical Trial** Yes **Registration Number** ClinicalTrials.gov NCT03343093 **RCT** Yes **Subjects** Human **Ethics Committee** University of Minnesota Institutional Review Board **Helsinki** Yes **Informed Consent** Yes

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FRACTIONAL CO2 LASER TREATMENT FOR GENITOURINARY SYNDROME OF MENOPAUSE IN POSTMENOPAUSAL WOMEN

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HYPOTHESIS / AIMS OF STUDY

Genitourinary syndrome of menopause (GSM) commonly affects postmenopausal women with nearly 50% of postmenopausal women reporting at least one symptom related to vaginal atrophy. These wide-ranging symptoms include pain during sexual intercourse, lack of lubrication, vaginal dryness, vaginal itching, dysuria, and recurrent urinary tract infections. Traditionally, treatment for GSM included nonhormonal vaginal lubricants and moisturizers or locally applied estrogen cream. In recent years, vaginal laser therapy has been introduced as a potential new treatment option for women with GSM and sexual dysfunction. Prior studies have presented promising data with regards to improvements in symptoms of GSM. The aim of the current study was to assess the short-term and long-term effects of the fractional CO2 laser system in treating postmenopausal women with clinical symptoms of genitourinary syndrome of menopause.

STUDY DESIGN, MATERIALS AND METHODS

This prospective study included sexually active postmenopausal women who presented to the clinic with symptoms of GSM including vaginal dryness, itching, burning, dysuria, or dyspareunia between September 2019 and February 2021. Three treatment visits were scheduled with intervals of four weeks between each visit. The treatment of the vaginal canal was performed using the fractional CO2 laser system (SmartXide2V2LR, MonaLisa Touch; DEKA, Florence, Italy). Patients were asked to complete questionnaires before the start of treatment, one month following the third treatment, at six months follow-up, and at 1-year follow-up either during in-person clinic visits or by telephone follow-up. Informed written consent was obtained from all study subjects. GSM symptom severity was self-evaluated by study participants on a 10cm visual analogue scale (VAS). The women completed a 19-item Mandarin version of the Female Sexual Function Index (FSFI), a validated standard questionnaire frequently utilized for assessing female sexual function and quality of life. This questionnaire was designed to assess sexual function in women with a specific focus on sexual desire, arousal, lubrication, orgasm, satisfaction, and pain. All statistical analyses were performed using SAS software version 9.4 (SAS Institute, Inc., Cary NC, USA). The changes from baseline in the assessment of GSM symptoms and FSFI scores were evaluated using repeated measures analysis of variance models. Statistical significance was set at $p < 0.05$.

RESULTS

Twenty-eight postmenopausal women who were sexually active and treated with fractional CO2 laser completed the protocol of three laser treatments and a one-year follow-up period. The mean age of the women was 55.37 ± 4.36 years ($\pm$SD), and the mean number of years since menopause was 6.56 ± 5.05 years. VAS scoring of GSM symptoms is presented in Table 1. GSM symptoms such as vaginal itching, vaginal burning, dyspareunia, dysuria, and vaginal dryness were significantly improved at one month following the completion of three laser treatments when compared with baseline. This statistically significant improvement was maintained at both six months and one-year follow-up visits. The short-term and long-term effects of fractional CO2 laser treatment on GSM symptoms were also assessed via the FSFI questionnaire. These results are presented in Table 2. The mean baseline score of FSFI ($\pm$SD) was 10.44 ± 1.53. Following three laser treatments, the one-month follow-up showed a statistically significant increase in total FSFI score to 19.12 ± 2.82, and at the six- and twelve-month follow-up visits, the total FSFI remained significantly higher than at baseline with total scores of 20.16 ± 4.14 and 20.07 ± 4.12, respectively. At one-month follow-up, the FSFI domains of desire (3.44 ± 0.32), arousal (3.28 ± 0.62), orgasm (3.44 ± 0.59), satisfaction (3.70 ± 0.66), and pain (3.47 ± 0.61) showed significant improvements when compared with baseline. Only the lubrication domain did not show a statistically significant improvement when compared with baseline at the one-month follow-up. However, at the six-month follow-up, all six FSFI domains showed significant improvement when compared with follow-up and this improvement continued to be observed at the one-year follow-up.

INTERPRETATION OF RESULTS

Vaginal laser therapy has been reported to be a safe, effective, and noninvasive procedure that can restore vaginal health and improve sexual function. Currently, there are radiofrequency devices that produce tissue contraction as heat develops, CO2 lasers which fractionally ablate the tissue and cause contraction with subsequent tissue remodeling, and Er:YAG lasers which produce wound contraction secondary to tissue heating. Studies have found that laser therapy is able to stimulate angiogenesis, increase fibroblast activity and induce collagen formation without any associated ablative or thermal damage to the vagina. Specifically, fractional CO2 laser therapies have been shown to improve blood flow in vaginal tissues which assists in restoring elasticity and moisture of the vaginal canal. Furthermore, previous studies that have investigated the histological changes in vaginal epithelium found that post-fractional CO2 laser treatments, there was an increased amount of collagen deposits and elastic fibers, a thicker epithelium, and increased submucosal vascularity. The present study evaluated the long-term efficacy of fractional CO2 laser treatment in postmenopausal women with symptoms of GSM. The results presented in this study showed statistically significant improvement in the assessment of GSM symptoms and sexual function by VAS and the FSFI questionnaire. Significant improvements in GSM symptoms of dyspareunia, dysuria, vaginal itching, vaginal burning, and vaginal dryness were seen at one-month follow-up after three laser treatments and these improvements were sustained up to one-year follow-up. Of the FSFI domains, only lubrication did not show a statistically significant improvement at the one-month follow-up. However, at the six-month follow-up, FSFI lubrication domain scores showed a statistically significant improvement when compared with baseline and this improvement was sustained at the one-year follow-up. All other FSFI domains including arousal, orgasm, pain, satisfaction, and desire showed a statistically significant improvement over baseline at the one-month follow-up and these effects continued to be observed at the one-year follow-up. Previous studies showed improvement in the FSFI at shorter follow-up periods of up to six months. Of note, in the current study, a significant improvement in GSM symptoms was able to be maintained up to one year after completion of laser treatments.

CONCLUDING MESSAGE

In conclusion, fractional CO2 vaginal laser treatment is a promising, non-pharmacological, minimally invasive treatment option for postmenopausal women experiencing genitourinary syndrome of menopause. Significant improvements in sexual function, dyspareunia, dysuria, vaginal burning, vaginal itching, and vaginal dryness were noted at one-month follow-up after the three laser treatments and were able to be sustained for up to one-year post-treatment.

FIGURE 1

Table 1. GSM Symptoms

	Baseline	1-Month Follow-Up	6-Month Follow-Up	12-Month Follow-Up
Vaginal itching	2.56±1.12	1.44±0.85*	1.30±0.61*	1.33±0.68*
Vaginal burning	2.63±1.69	1.81±1.33*	1.56±1.34*	1.59±1.37*
Vaginal dryness	7.56±1.31	5.00±1.27*	4.63±1.39*	4.59±1.37*
Dyspareunia	8.52±1.16	4.93±1.30*	4.37±1.52*	4.41±1.58*
Dysuria	2.19±1.11	1.33±0.96*	1.19±0.74*	1.56±1.34*

Mean ± standard deviation.
* Significantly different from baseline, $p < 0.05$.

Table 1. GSM Symptoms

FIGURE 2

Table 2. FSFI Total and Domain Scores

	Baseline	1-Month Follow-Up	6-Month Follow-Up	12-Month Follow-Up
Total Score	10.44±1.53	19.12±2.82*	20.16±4.14*	20.07±4.12*
Desire	2.44±0.16	3.44±0.32*	3.49±0.24*	3.49±0.24*
Arousal	2.42±0.47	3.28±0.62*	3.36±0.62*	3.36±0.62*
Lubrication	1.27±0.24	1.79±0.61	2.24±1.53*	2.27±1.55*
Orgasm	1.38±0.43	3.44±0.59*	3.56±0.76*	3.56±0.76*
Satisfaction	1.67±0.44	3.70±0.66*	3.87±0.78*	3.82±0.80*
Pain	1.26±0.21	3.47±0.61*	3.64±0.78*	3.59±0.71*

Mean ± standard deviation.
* Significantly different from baseline, $p < 0.05$.

Table 2. FSFI Total and Domain Scores

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FEASIBILITY, ACCEPTABILITY AND EFFECTS OF HIGH INTENSITY LASER THERAPY FOR WOMEN WITH VULVODYNIA: A RANDOMIZED PROSPECTIVE PILOT STUDY

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HYPOTHESIS / AIMS OF STUDY
Provoked vestibulodynia (PVD) is the most common subtype of vulvodynia. It is characterized by a sharp pain at the vestibule of the vagina in response to the application of pressure (attempted vaginal penetration, tampon insertion, sexual activity or speculum examination). Women with PVD suffer from psychological distress and dysfunctions affecting all aspects of their sexuality, as well as significant marital difficulties. Despite the availability of some treatments for women with PVD, patients are confronted with limited treatment options with insufficient or conflicting evidence supporting first-line treatments [1]. Non-invasive and non-ablative therapeutic approaches are therefore needed. High Intensity Laser Therapy (HILT) was shown effective for treating various chronic pain conditions [2]. However, there is a lack of evidence supporting the feasibility, acceptability and effects of HILT for PVD, which needs to be addressed. We are, therefore, the first to propose a prospective study exploring the use of HILT in women with PVD.

The primary objective was to assess the feasibility and acceptability of HILT in women with PVD. The secondary objectives were to explore the effects of active and sham HILT on pain intensity, satisfaction and perceived improvement.

STUDY DESIGN, MATERIALS AND METHODS
A parallel, 2-group, randomized prospective feasibility study was conducted. The design and methodology comply with the recommendations of the CONSORT extension for pilot and feasibility trials [3]. The participants were women aged 18-45 years old who had been suffering from PVD for at least three months. More specifically, women needed to report pain at the entry of the vagina during vaginal intercourse with a pain intensity greater than 5 on a numerical rating scale (NRS). The eligibility of the participants was confirmed by a standardized pelvic examination performed by a gynecologist from our team. Women were randomized into the active ($n=20$) or sham HILT ($n=20$) groups. Both groups received bi-weekly sessions for 6 weeks (total of 12 sessions). Fifteen minutes prior to the irradiation, an anesthetic ointment (benzocaine 2.5% + lidocaine 5% + procaine 2.5%) was applied to the vulvar area and a stream of cold air was blown onto the area during the treatment to mask the warming effects. Women in the active HILT group were treated with the Laser Fotona; Nd : Yag 1064 nm while women in the sham HILT received the same treatment regimen using a deactivated probe.

Patients, outcome assessors and data analysts were blinded to group assignation. An experienced pelvic floor physiotherapist who was not involved in the laser intervention, conducted the baseline and 2-week post-treatment assessments. The attendance rate at laser sessions ($\geq 80\%$ of participants attending ≥ 10 sessions), the dropout rate ($^{\sim}15\%$) and the absence of serious adverse events served as feasibility and acceptability outcomes and benchmarks. To explore the effects, patients' perceived improvement (patient's global impression of change), satisfaction (numerical rating scale 0-10), and mean pain intensity during intercourse (numerical rating scale 0-10) were also assessed. A sample of 40 participants was determined to provide sufficient power for evaluating the feasibility and acceptability outcomes (adherence p 75%; δ 15 %; dropout 20%). Chi-square tests were used to compare the two groups for the proportion of participants. Paired and independent t-tests were conducted to examine the effects of treatment.

RESULTS
Out of the 266 participants that showed interest in the study, 45 participants were eligible to participate. Of these, 40 participants were enrolled in the study since their PVD diagnosis was confirmed with the standardized gynecological exam. All the women included ($n=40$) underwent a baseline assessment and randomization (sham $n=20$ and active HILT $n=20$). All participants completed the 12 sessions, except for two women who had 11 sessions due to Covid-related reasons. The dropout rate was only 2.5% (one participant withdrew from the active HILT due to time constraints). No serious adverse events were reported by the patients nor the therapists in either group. Nonetheless, a temporary minor irritating or itching sensation was reported in both groups (sham $n=2$ and active $n=6$; $p=0.12$).

As for treatment effects, a significant reduction in pain from baseline to post-treatment was observed in both groups. Indeed, a significant reduction in pain from baseline to post-treatment was found in women in the active HILT group (baseline 7.3 ± 1.3; post-treatment 4.1 ± 2.2, $p<0.001$) and in women in the sham group but to a lesser magnitude (baseline 7.4 ± 1.6; post-treatment 5.4 ± 3.2; $p=0.002$). Women in the active HILT group were more satisfied with the treatment (mean of 6.6/10 (SD 2.8)) than women in the sham group (4.6/10 (SD 3.1)) ($p<0.05$). Regarding the patients' global impression of change, more women in the active HILT group reported significant improvement (79%) than in the sham group (47%) ($p=0.03$). Interestingly, 10% of women in the sham group reported a worsening of their condition.

INTERPRETATION OF RESULTS
Pre-established benchmarks for the attendance and dropout rates were surpassed, supporting the feasibility and acceptability of this intervention for women with PVD. In contrast to other lasers, such as CO2 and Er:YAG with larger wavelengths, our study, using an Nd:Yag laser, considered a "cold" laser, revealed no serious adverse events. Only temporary mild irritation and minor itching (lasting less than one hour) were reported in both groups. Participants associated their minor symptoms with the use of the topical anesthetic and the intensity of the cooling system. These parameters require special attention for future trials. Women in the active HILT group showed a significant reduction in pain intensity from baseline to post-treatment, greater satisfaction, and a greater perceived change compared to the control group. It is important to highlight that the control group (sham HILT) also had a significant reduction in pain intensity from baseline to post-treatment. This provides further evidence on the relevance of a control group in chronic pain trials due to the placebo effect that may occur. The findings of this study therefore inform the design and methodology to perform a full-scale, adequately powered, randomized controlled trial to confirm the efficacy of HILT treatment for women suffering from PVD.

CONCLUDING MESSAGE
In conclusion, this study supports the feasibility and acceptability of HILT as an intervention to treat women with PVD. With significant improvements observed in terms of pain, satisfaction, and perceived improvement, this study provides a new level of evidence on HILT, which is a promising non-invasive and non-ablative treatment for women with PVD. The findings of this study identified recommendations for conducting a large randomized controlled trial to confirm the efficacy of HILT.

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SEXUAL HEALTH IN WOMEN WITH PELVIC FLOOR DYSFUNCTIONS

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HYPOTHESIS / AIMS OF STUDY
Pelvic floor dysfunctions may impair female sexuality (1, 2, 3). However, sexual health was not routinely assessed in those women. The aim of our study was to analyse sexual activity and function of women who seek care for pelvic floor dysfunctions, through a condition-specific validated tool.

STUDY DESIGN, MATERIALS AND METHODS
Cross-sectional study about sexual health of women attended in an urogynaecology unit of a tertiary university hospital started in 2022. The first consultation of women visited to assess and treat pelvic floor dysfunctions (urinary incontinence [IU], anal incontinence [IA], pelvic organ prolapsed [POP]) were selected consecutively. Exclusion criteria included women with language barriers, unable to understand questionnaires or who reject to fill-in the sexual questionnaire. The study was approved by the Ethics Committee and written informed consent was obtained from all the participants.

Women attended in our urogynaecology unit, follow a standardized health care procedure: a first telematic visit performed by the urogynaecologist and, afterwards, a "pack LUTS" presential appointment which involve 2 visits (urogynaecologist and urogynaecology specialized nurse) and 2 test (urodynamics and pelvic floor ultrasound) scheduled the same day.

Women reported demographical data and 4 Spanish validated questionnaires. To evaluated urinary, anal and prolapse symptoms we used: the International Consultation on Incontinence Questionnaire Short Form (ICIQ-UI-SF) which evaluates frequency, severity and impact on quality of life, range 0-21 (no UI = 0; mild UI = 1-5, moderate UI = 6-12, severe UI = 13-18, more severe UI = 19-21). Moreover, it includes 8 questions regarding the type of UI (just descriptive data, no scoring). The Bladder Control Self-Assessment Questionnaire (B-SAQ) has 8 items to assess symptoms of urgency, frequency, nocturia and UI and the associated bother, based on a 4-points Likert-scale: 0 (not at all), 1 (a little), 2 (moderately), 3 (a great deal), range 0-12 (REF). The Pelvic Floor Distress Inventory-20 (PFDI-20) involves 3 subscales: Pelvic Organ Prolapse Distress Inventory 6 (POPDI-6), Colorectal Anal Distress Inventory 8 (CRADI-8) and Urinary Distress Inventory 6 (UDI 6) is 100, range 0-100 (each subscale) or 0-300 (overall). Based on reported symptoms, we performed a pelvic floor dysfunction clinical diagnosis: 1) IU: ICIQ > 0 + BSAQ Q4 symptoms > 0 + PFDI-20 Q16 o Q17 > 0; 2) POP: PFDI-20 Q3 > 0; 3) IA: PFDI-20 Q9 o Q10 o Q11 > 0. To evaluate sexual activity and function we used: the Pelvic Organ Prolapse/ Urinary Incontinence Sexual Questionnaire IUGA Revised (PISQ-IR), a condition-specific questionnaire for assessing sexuality in both sexually active (SA) and non-sexually active (NSA) patients according to Q1. It includes 14 items (6 subscales) addressed to SA patients and 5 items (4 subscales) for NSA. The scores were calculated with the mean calculation method. Higher scores in SA patients indicate better sexual function, while in NSA patients, these indicate a greater impact on sexual function. Global sexual function was analyzed according to the single summary score of PISQ-IR only available for SA women. We considered dyspareunia for both SA and NSA women: when the SA patient reported sometimes, usually or always to Q11 or coital activity avoidance due to pain, and when NSA women reported pain as a cause of inactivity (Q2e). We considered satisfactory sexual life the answer "1" or "2" to the Q4a (NSA) or Q19a (SA).

At the presential appointment a systematic pelvic examination was performed to all the participants. In the present study we exclusively analyzed: the stage of POP based on POPQ and the pelvic floor muscle function based on the modified Oxford-scale.

Data analysis:

All analyses were performed using the IBM SPSS Statistics 23.0 software (IBM Corp. Released 2015. IBM SPSS Statistics for Windows, Version 23.0. Armonk, NY: IBM Corp.) Data were summarized as frequency and percentage for categorical variables and mean and standard deviation (SD) for quantitative ones. Chi-squared test and Student's t test were used for comparisons. The statistical significance level was established at p-value < 0.05.

RESULTS
Among 111 women attended during the firsts months of 2022, 2 who rejected to fill-in the sexual questionnaire were excluded. 92.5% of participants reported UI symptoms, one-third AI (34.6%) and the 28% of women has a symptomatic POP. The more frequently isolated pelvic floor dysfunction was UI (43.9%). Nearly one-third of the participants informed double incontinence symptoms (27.1%). 43.1% of women presented 2 pelvic floor dysfunctions, whereas 5.6% had 3 of them (UI + AI + POP). Table 1 shows the baseline characteristics of the sample.

NSA rate was 47.7%. The main reason for their sexual inactivity was lack of interest (72.5%), followed by not having a partner (56.9%). The pelvic floor dysfunction, other health issues and the pain were the inactivity reason in a lower proportion (11.7%, 9.8% y 7.8%, respectively). 12 (23.5%) NSA women reported avoidance of sexual activity due to fear related to UI /AI or POP. Most of NSA participants stated to be satisfied with their sexual life (82.3%) without bother about their sexual inactivity.

Related to SA women (n = 57), 29.7% informed about UI/ AI during sexual activity (17.5% rarely, 7.0% sometimes, 3.5% usually y 1.7% always), however, 53.9% of the SA participants limited sexual activity due to fear related to UI /AI or POP (24.6% a little, 17.0% some, 12.3 % a lot). Dyspareunia was present in 54.0% SA women (35.0% sometimes, 8.0% usually, 10.0% always). Barely more than a half of SA women stated to be satisfied with their sexual life (57.9%).

INTERPRETATION OF RESULTS
Only a half of the assessed women were SA. Among them, one out of two diminished their usual sexual frequency due to their pelvic floor dysfunction. Sexual function was affected by dyspareunia and urinary/anal incontinence symptoms in a relevant proportion of SA women with pelvic floor dysfunctions. Consequently, nearly half of these women were unsatisfied with their sexual life.

On the other hand, the pelvic floor dysfunction was the third reason for sexual inactivity, reported only by one out of nine NSA women. Moreover, four out of five NSA with pelvic floor dysfunctions were satisfied with their sexual life. The lower impact of the pelvic floor dysfunction in that subgroup, may be related to NSA women were older, with higher rates of menopause and without a partner than SA participants.

CONCLUDING MESSAGE
Most of the women with pelvic floor dysfunctions are interested in their sexuality assessment. Pelvic floor dysfunctions may affect sexual activity among NSA and SA women, as well as worsen sexual function on SA women. So, satisfaction with the sexual life could be impaired.

It is key to apply standardized and validated tools to systematically assess sexuality to identify the subgroup of patients with unsatisfied sexual life due to pelvic floor dysfunctions and, then, to plan the follow-up and tailored treatment according patient's expectations.

FIGURE 1

Table 1: Baseline characteristics

	All (n=109)	SA (n=57)	NSA (n=52)	p-value
Demographic data				
Age at inclusion, mean, (SD) in years	61.0 (14.2)	54.2 (12.3)	68.4 (12.4)	**<0.001**
Body Mass Index, mean, (SD) in kg/m²	27.4 (5.8)	26.8 (5.3)	28.0 (6.2)	0.290
Number of vaginal deliveries, (mean, (SD)	1.8 (1.4)	1.7 (1.2)	2.0 (1.6)	0.256
Menopausal patients, n (%)	75 (68.8)	30 (52.6)	45 (86.5)	**<0.001**
Vaginal oestrogen therapy, n (%)	38 (34.9)	15 (26.3)	23 (44.2)	**0.034**
Has a partner, n (%)	71 (65.1)	51 (89.5)	20 (35.1)	**<0.001**
Questionnaire outcomes				
ICIQ-SF (0-21), mean (SD)	12.3 (5.9)	11.3 (5.6)	13.5 (5.9)	0.052
No UI (0), n (%)	10 (9.2)	6 (10.5)	4 (7.7)	
Mild (1-5), n (%)	5 (4.6)	2 (3.5)	3 (5.8)	
Moderate (6-12), n (%)	35 (32.1)	23 (40.3)	12 (23.1)	0.121
Severe (13-18), n (%)	40 (36.7)	20 (3517)	20 (38.5)	
More severe (19-21), n (%)	17 (15.6)	5 (8.8)	12 (23.1)	
Not available, n (%)	2 (1.8)	1 (1.7)	1 (1.9)	
CACV symptoms (0-12), mean (SD)	5.9 (3.3)	5.4 (3.2)	6.5 (3.4)	0.093
CACV bother (0-12), mean (SD)	6.1 (3.5)	5.7 (3.5)	6.5 (3.5)	0.278
CACV symptoms (UI >0), n (%)	95 (87.1)	49 (86.0)	46 (88.5)	0.698
PFDI-20 (0-300), mean (SD)	61.1 (47.3)	62.5 (46.2)	59.5 (48.8)	0.742
POPDI-6 (0-100), mean (SD)	17.4 (17.4)	17.1 (16.7)	17.8 (18.4)	0.845
CRADI-8 (0-100), mean (SD)	12.0 (17.2)	11.7 (17.0)	12.3 (17.6)	0.868
UDI-6 (0-100), mean (SD)	38.4 (22.9)	39.5 (22.4)	37.1 (23.6)	0.590
Physical examination				
Oxford scale, n (%)				
0	22 (20.2)	6 (10.5)	16 (30.7)	
1	25 (22.9)	13 (22.8)	12 (23.1)	
2	22 (20.2)	14 (24.6)	8 (15.4)	0.078
3	20 (18.3)	10 (17.5)	10 (19.2)	
4	9 (8.3)	7 (12.3)	2 (3.8)	
5	1 (0.9)	1 (1.8)	0 (0)	
Not available	10 (9.2)	6 (10.5)	4 (7.7)	
POPQ stage, n (%)				
0	63 (57.8)	36 (63.2)	27 (51.9)	
I	4 (3.7)	2 (3.5)	2 (3.8)	
II	26 (23.8)	12 (21.1)	14 (26.9)	0.683
III	13 (11.9)	6 (10.5)	7 (13.5)	
IV	1 (0.9)	0 (0)	1 (1.9)	
Not available	2 (1.8)	1 (1.8)	1 (1.9)	

Table 1: Baseline characteristics

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GENDER-AFFIRMING VAGINOPLASTY: A PATIENT PERSPECTIVE ON INFORMATIONAL NEEDS

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HYPOTHESIS / AIMS OF STUDY
Gender-affirming vaginoplasty lacks universally-adopted guidelines for perioperative management. The Standards of Care developed by the World Professional Association for Transgender Health recommend surgeons provide an extensive consultation with the patient; explaining the surgery itself as well as informing the patient on pre- and post-operative expectations. With the copious amount of information to know about this process, patients may also turn to friends, support groups, the internet, etc. to find the details for themselves. We believe it would be useful to develop an inclusive guidebook outlining the entire vaginoplasty journey.

With this study, we sought to determine what information patients seek throughout their process of gender-affirming vaginoplasty. We hope to use the results from this study to inform the development of patient resources.

STUDY DESIGN, MATERIALS AND METHODS
This study consisted of an anonymous survey emailed to 30 patients who underwent gender-affirming vaginoplasty between September 2018 and September 2020 with our team. The survey was composed of Likert-scale items that explored the importance of various topics. Patients were also asked from whom and how did they receive information regarding perioperative considerations and where they would have preferred to get it from. Descriptive statistics were used to analyse these responses. Free-text boxes allowed patients to comment on any additional topics that may be missing, provide advice for future patients, and offer suggestions for alternative methods of education/information delivery. A thematic analysis was performed on the qualitative portion of the survey.

RESULTS
Seventeen individuals completed the questionnaire (56.6% response rate). All topics received an average rating of moderately important or higher (≧ 3 out of 5 on the Likert scale). The topics which got the lowest scores were Fertility Preservation and Preventative Cancer Screening. Of the 30 pre-operative topics queried, participants preferred to receive information in written form for 29 of them (97%), and from the surgeon (rather than other health care providers, friends, or the internet) for 27 topics (90%). A document outlining the expected five-day hospital course and one with post-discharge instructions were rated as very or extremely helpful by 85% and 77% of participants, respectively. Thematic analysis revealed five main themes; recovery process, satisfaction, trust in healthcare providers, information delivery, and neovaginal dilation and depth.

INTERPRETATION OF RESULTS
Individuals undergoing gender-affirming vaginoplasty have extensive informational needs. Participants recognized the importance of all topics inquired about, however neovaginal dilation and pelvic floor physiotherapy were particularly hot topics as seen in the thematic analysis. Previous research has shown that patient forget much of the information relayed during a medical encounter. To this point, participants in this study reported that the written resources received were extremely helpful. Participants also generally preferred to receive information directly from the surgical team, which may reflect a known variability in surgeon preferences as well as trust in the surgical team. The importance of cultural competence and being able to build a trustworthy relationship with their healthcare providers were prominent findings of this study, underscoring the challenges that transgender patients face in interacting with the health care system.

CONCLUDING MESSAGE
Individuals undergoing gender-affirming vaginoplasty have extensive informational needs and these are likely best addressed by their surgical team with a combination of written resources and verbal discussion with the patient. We hope these findings will contribute to creating patient-centered resources for transgender women undergoing vaginoplasty.

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THE SEXUAL FUNCTION OF TRANSGENDER PEOPLE

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HYPOTHESIS / AIMS OF STUDY

There is a gap in the knowledge of the sexual function of transgender people. This study aimed to evaluate the sexual function in this population.

STUDY DESIGN, MATERIALS AND METHODS

A sample of transgender (trans) people from the Gender Incongruence Clinic was invited to participate in this cross-sectional study. All those that accepted to participate had gender incongruence (GI). The female sexual function index (FSFI) and male sexual function index (MSFI) were used to assess Sexual Function (SF) in both female (n = 38), and male (n = 48) participants. The FSFI questionnaire has 19 questions grouped in six domains (desire, arousal, lubrification, orgasm, pain, and satisfaction). The score ≤ 26.55 is a risk for sexual dysfunction[1]. The MSFI is an adaptation of FSFI by Kalmbach et. al (2015)[2], that has 16 questions grouped in five domains (desire, arousal, erection, orgasm, and satisfaction). The composite score varies between 2 to 36. In addition, participants responded to a semi-structured questionnaire to assess their feelings towards their trans condition, and about their satisfaction within their sexual life. The Hospital Anxiety and Depression Scale (HAD) questionnaire was used to assess the individual's mood. The HAD has 14 items divided in two subscales: seven to assess anxiety, and seven to assess depression. The cutoff score for anxiety and depression is ≥ 8 and ≥ 9, respectively[3]. Clinical data was assessed from medical records.

RESULTS

Forty-eight trans men and 38 trans women participated in this study. For men, the mean age was 27.55 ± 7.46 years, the mean age of sexarche was 14.67 ± 5.38 and the mean time of use of hormone therapy was 2.79 ± 0.33 years, the majority of participants were heterossexual 38 (90.48%), and 9 (77.50%) individuals had gender affirming surgery, 7 (14.89%) complained of low sexual desire, 2 (4.26%) had sexual arousal disorder, and 6 (12.77%) showed difficulty in achieving orgasm. The majority 30 (66.83%) of participants were satisfied or very satisfied with their sexual relation, and 21 (44,68%) with their body appearance. Sixteen (34,04%) of individual's expressed feelings of discrimination in society 7 (17.95%), in their family 2 (5.13%), and 8 (20.51%) in more than one place.

For trans women (N = 38) the mean age was 31.90 ± 9.70, the mean age of sexarche to be 14.68 ± 3.11, and the mean time of use of hormone therapy was 4.09 ± 0.44 years. The majority of trans women considered themselves as heterosexual 27 (87.10%), and 11 (45.85%) had undergone gender affirming surgery. When SF was examined in our cohort of transgender women, we found 9 (24.32%) complained of sexual desire disorder, 6 (16.22%) of sexual arousal, 3 (8.11%) of difficulties in achieving orgasm, and 2 (5.41%) had problems in more than one phase of sexual response. Ten (45.45%) on trans women use their penis in sexual intercourse. Regarding sexual satisfaction, the majority 18 (48.65%) of participants reported satisfaction with sexual life, and 16 (42.11%) with their body appearance. The majority of individual's 20 (54.05%) reported feeling discrimination in society 13 (38.24%), in their family 2 (5.88%), and 9 (26.47%) in more than one place.

The Table 1 shows the Demographic and clinical characteristics of the studied population.

The Table 2 shows the total score, and the score for the domains of FSFI, and MSFI of transgender men and women. We found no significant differences between the mean scores of the HAD for either transgender cohort.

INTERPRETATION OF RESULTS

In comparison to women, trans men had better total FSFI scores (P = 0.01), and for the domains of arousal (P = 0.01), lubrication (P = 0.01), orgasm (P = 0.01) and satisfaction (P = 0.01). Moreover, they had better MSFI total score (P = 0.02), and for the domains of arousal (P = 0.01), orgasm (P = 0.01) and satisfaction (P = 0.01).

CONCLUDING MESSAGE

The total scores of both, the FSFI and MSFI, indicated a risk of sexual dysfunction for transgender men and transgender women. Transgender men reported better satisfaction with their sexual life in relation to transgender women.

In the semi-structured evaluation, more than half of men and almost half of women were satisfied or very satisfied with their sexual life.

FIGURE 1

Table 1 – Demographic and clinical characteristics of population

Variable	Transgender men (N = 48)	Transgender women (N = 38)	P
HT	Cipionato de Testosterona	Estradiol	
Age	27.55 ± 7.46	31.90 ± 9.70	0.05
BMI	27.05 ± 5.63	24.46 ± 3.75	0.18
Menarche	12.90 ± 2.22		
Number of children	0.12 ± 0.39	0.03 ± 0.18	0.32
Stable relationship	14 (35.90%)	6 (22.22%)	
Sexarche	14.67 ± 5.38	14.68 ± 3.11	
Number of sexual partners	4.52 ± 3.42	12.93 ± 8.88	0.01
Sexual frequency	1.38 ± 1.47	2.08 ± 1.88	0.16
HT use (years)	2.79 ± 0.33	4.09 ± 0.44	0.63
Comorbidities	12 (34.29%)	17 (65.38%)	
Adverse event of HT	13 (35.14%)	8 (33.33%)	
Satisfaction with HT	34 (89.47%)	18 (81.82%)	
Sexual orientation			
Heterosexual	38 (90.48%)	27 (87.10%)	
Bisexual	1 (2.38%)	2 (6.45%)	
Homosexual	3 (7.14%)	2 (6.45%)	

HT: hormone therapy, BMI: body mass index

Table 1 – Demographic and clinical characteristics of population

FIGURE 2

Table 2: Total score, and by domains of Female Sexual Function Index, and Male Sexual Function Index

Domain	Transgender men (N=48)	Transgender women (N=38)	P-value
FSFI			
Total score	24.01 ± 8.05	16.63 ± 9.57	0.01
Desire	5.00 ± 6.57	3.63 ± 1.54	0.13
Arousal	4.54 ± 1.52	2.77 ± 2.04	0.01
Lubrification	4.71 ± 1.74	2.66 ± 2.16	0.01
Orgasm	4.51 ± 1.82	3.15 ± 2.33	0.01
Satisfaction	4.66 ± 1.88	2.99 ± 2.24	0.01
Pain	1.39 ± 2.33	1.34 ± 1.67	0.33
MSFI			
Total score	21.80 ± 7.68	14.98 ± 8.93	0.02
Desire	4.30 ± 1.42	3.74 ± 1.57	0.08
Arousal	4.50 ± 1.67	2.82 ± 2.13	0.01
Erection	3.69 ± 2.41	2.76 ± 2.22	0.06
Orgasm	4.61 ± 1.79	2.89 ± 2.29	0.01
Satisfaction	4.57 ± 2.01	3.34 ± 4.07	0.01

Table 2: Total score, and by domains of Female Sexual Function Index, and Male Sexual Function Index

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Funding Funding of the research was by the Higher Education Personnel Improvement Coordination (CAPES), a foudation linked to Ministry of Education of Brazil **Clinical Trial** No **Subjects** Human **Ethics Committee Ethics Committee** of Clinical Hospital of Ribeirão Preto (number CAAE: 29969419.8.0000.5440) **Helsinki** Yes **Informed Consent** Yes

Continence 2S2 (2022) 100388
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SCIENTOMETRIC EVALUATION OF PUBLISHED ARTICLES ON FEMALE SEXUAL DYSFUNCTION

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HYPOTHESIS / AIMS OF STUDY

Female sexual dysfunction (FSD) is a prevalent and debilitating condition and has been a focus of many recent studies. The aim of this study was to perform a scientometric evaluation of published articles on FSD.

STUDY DESIGN, MATERIALS AND METHODS

We searched the Web of Science and Scopus for the scores published from January 1991 to March 2022. Two independent reviewers evaluated the included scores for eligibility and they removed the irrelevant scores and duplicates. We extracted complete scores as well as their references and bibliographic information. We performed the analysis using Biblioshiny (a Shiny app for Bibliometrix)[1].

RESULTS

The search resulted in 2075 documents published in 84 resources (journals, books, etc.). The average citation per document was 25.01. Of the included scores, 1401 were original articles, 356 were review articles and 314 were meeting abstracts. The average number of authors per document was 3.21.

In the co-occurrence network, "sexual", "female", "dysfunction" and "women" were the most common one-word title keywords. "sexual function", "female sexual" and "sexual dysfunction" were the most common two-word keywords.

A manuscript addressing the definition and classification of FSD by Basson et al [2] was the highest cited document in this field with 860 total citations. The USA with 18132 citations and Italy with 5049 citations were the most cited countries. Goldstein I. with 64 manuscripts and Maggi M. as well as Rosen RC. were the most productive authors. Rosen R., Laumann EO., and Basson R. had the strongest co-citation networks (fig.1).

The journal of sexual medicine was the leading journal to publish manuscripts on FSDwith 1102 documents. International journal of impotence research with 143 documents and Journal of Urology with 119 documents were the second and third on the list.

The University of Florence, Case Western Reserve University, and the University of Amsterdam were the main cores of the collaboration networks(-fig.2). the USA, Canada, and the United Kingdom had the strongest collaboration networks.

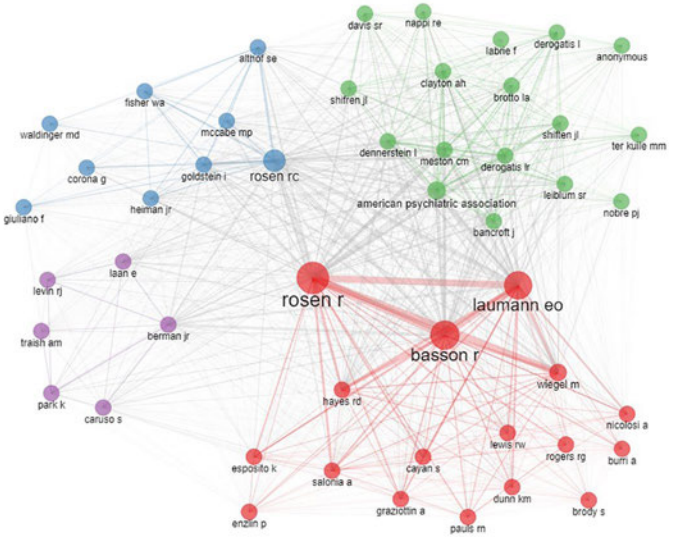
INTERPRETATION OF RESULTS

The scientometric evaluation aims to demonstrate the structure and the dynamics of scientific research. The conceptual structures, for instance, the co-occurrence networks demonstrate the current trends in scientific research. A limited number of journals published the majority of the FSD studies. This indicates that only a few articles tend to publish studies that address FSD. As seen in the figure.2, some institutions have stronger collaboration networks and each color represents a cluster of collaboration. This graph represents how the institutions interact with each other in performing studies on FSD. An application of the scientometric evaluation is finding the thematic evolution during time. This can aid in understanding the gaps in research and ultimately finding the best way to have a major impact on science.

CONCLUDING MESSAGE

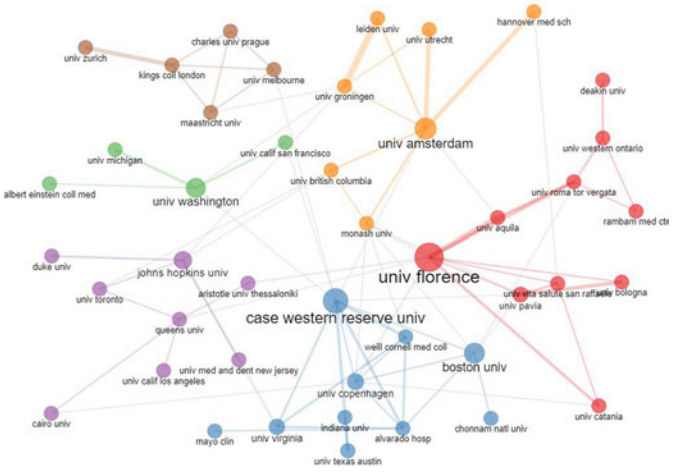
This study showed the most active researchers, institutions, and countries. Scientometric evaluations have the potential to show the most active research trends and the major gaps we are facing in the field of FSD.

FIGURE 1



Co-citation network of authors in the published scores on female sexual dysfunction

FIGURE 2



Collaboration network of institutions regarding female sexual dysfunction research

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Funding no **Clinical Trial** No **Subjects** None

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BEST IN CATEGORY PRIZE: MALE SEXUAL DYSFUNCTION

INTRACAVERNOSAL INJECTION OF BOTULINUM TOXIN IN THE TREATMENT OF ERECTILE DYSFUNCTION: A SYSTEMATIC REVIEW AND META-ANALYSIS

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HYPOTHESIS / AIMS OF STUDY

Erectile dysfunction affects a large proportion of mainly the aging male population. In the era of minimally invasive medicine, a novel treatment strategy emerges necessary to avoid morbid and irreversible surgeries. The aim of this review is to evaluate the role of botulinum toxin in treating erectile dysfunction.

STUDY DESIGN, MATERIALS AND METHODS

This study was based on the Preferred Reporting Items for Systematic Review and Meta-analysis (PRISMA) statement. The study protocol on the part of human studies was registered on PROSPERO (CRD42021283751). A systematic review of literature of PubMed, Embase and Medline databases was conducted, in order to identify studies investigating the role of botulinum toxin to treat erectile dysfunction, published in English, from January 1990 through July 31, 2021. Evidence included human and animal data.

The study design was established according to the Population, Intervention, Comparator, Outcome, Studies (PICOS) process. Population: Patients with erectile dysfunction. Intervention: Intracavernosal injection of botulinum toxin. Comparator: Standard-of-care or other techniques. Outcomes: improvement of sexual function, improvement in erectile function. Studies: Case series, retrospective/prospective cohorts, comparative studies and randomized controlled trials (RCT) were included. Reviews, case reports, non-English language articles, congress abstracts, letters to editor, and editorial comments were excluded.

A meta-analysis was performed on three outcomes included commonly in at least two studies. Among the different parameters assessed were, Erection Hardness Score (EHS), Peak Systolic Velocity in cavernosal artery (PSV) and the Sexual Health Inventory for Men (SHIM) score.

RESULTS

Seven studies in total were included in our review including two pre-clinical studies. Table 1 summarizes the studies included. Figure 1 represent the respective meta-analysis done regarding EHS, PSV and SHIM. The Cochrane bias risk assessment was performed for the 3 studies from which data were extracted. A clear benefit was noted for intracavernosal injection (ICI) of botulinum toxin (BoNT-A) on PSV (Figure 1) with a HR of 10.82 [4.99, 16.65] and a heterogeneity of I2 = 61%. EHS results favored BoNT-A as well over placebo with a HR of 0.7 [0.47, 0.93] and a heterogeneity of I2 = 94%. As for SHIM score, with a heterogeneity of I2 = 85%, no statistically significant difference was found (HR 0.58 [-0.03, 1.20]) (Figure 1).

INTERPRETATION OF RESULTS

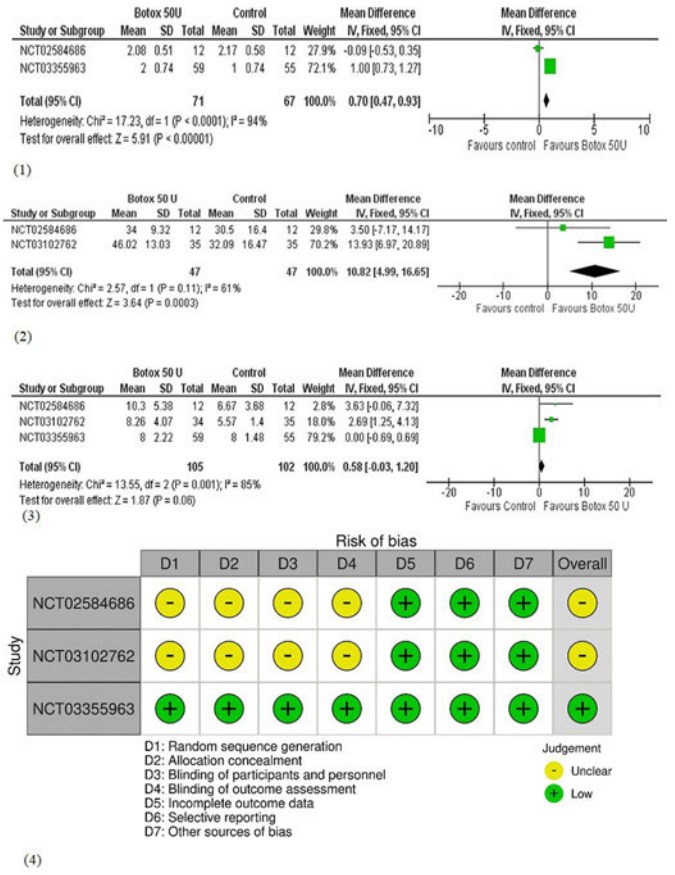
The rationale for using ICI of BoNT-A arises from its mechanism of action. One of the physiological hypotheses of its mode of action is that BoNT-A disables the exocytotic activity of presynaptic neurons by inhibiting neurotransmitter containing vesicles to fuse at the level of the synapse hence decreasing the influx of norepinephrine (NE) inhibiting the contraction of the cavernosal muscle cells. In addition to its effect on inhibiting NE release, BoNT-A increases the generation of nitric oxide (NO) by blocking the release of Acetylcholine (Ach) from cholinergic neurons which inhibits NO synthase [1]. The interplay of these effects results in a clinically inhibited cavernosal smooth muscle tone hence a more satisfactory blood flow is attained. This is the first systematic review to include 2 pre-clinical and 5 clinical studies results with a meta-analysis performed on 3 primary outcomes showing an efficacy of ICI of BoNT-A compared to other strategies on 2 of the 3 identified criteria, in particular EHS and PSV. There is, however, a narrative review in the literature from 2020 that supports the use of BoNT-A in male sexual pathologies extending to primary ejaculation, Peyronie's disease, and penile retraction [2].

The studies included in our review did not adapt a single treatment strategy, each studied different parameters and questionnaires during the study to objectify improvement in erectile dysfunction, there were different doses, serotypes and regimen of botulinum toxin as depicted in Table 1. However, the meta-analysis was done on the three similar trials adopting resembling regimens, and there was a significant benefit in PSV and EHS.

CONCLUDING MESSAGE

ICI of BoNT-A showed promising results in the first animal trials, these results were reproducible in the first human trials as well. BoNT-A may find its place in the therapeutic arsenal for the treatment of ED. Nonetheless, further studies and human trials are required to confirm the efficacy and durability of this novel treatment and bring forward more evidence.

FIGURE 1



(1) Forest plot assessing Erection Hardness score (EHS) (2) Forest plot assessing mean Peak Systolic Velocity (PSV) in the cavernosal arteries (3) Forest plot assessing the Sexual Health Inventory for Men (SHIM) (4) Graphical representation of the Cochran

FIGURE 2

First author	Year of publication	Type of study	Participants (n)	Study design	Botulinum toxin dosage	Side effects	Efficacy
Young et al.	2017	Animal study	10 male rats	BoNT-A group vs. Control group	10 U	No side effects	*Significantly higher intracavernosal pressure (=> better erectile function) *Larger sinusoidal volumes but not statistically significant
Ghanem et al.	2017	Animal study	30 male rats	1 U of BoNT-A vs. 2 U of BoNT-A vs. control	Group receiving 1U Group receiving 2 U	No side effects	Significantly larger sinusoidal volume
Giuliano et al.	2019	Retrospective case series	47 male patients	One retrospective arm, abobotulinumtoxinA molecule used as add-on therapy	250 U, then 500 U when the 250 U are ineffective	Local transitory pain on injection (2 patients)	* Total response rate 54% * IIEF significant improvement by 4.7 for 250 U of aboBoNT-A and by 5.6 for 500 U of aboBoNT-A
Taleb et al.	2019	Prospective comparative study	45 male patients	100 U of BoNT-A vs. 50 U of BoNT-A vs. control stand-alone therapy	Group receiving 100 U Group receiving 50 U	Local transitory pain on injection	* Significant subjective improvement of IIEF, EHS, SEP, GAS * Significant objective improvement on penile Doppler ultrasound * Improvement observed after 2 weeks and 3 months, but not durable to 6 months in some patients
El-Shaer et al. (NCT03355963)	2021	Randomized double-blinded placebo controlled trial	176 male patients	100 U of BoNT-A vs. 50 U of BoNT-A vs. control stand-alone therapy	Group receiving 100 U Group receiving 50 U	One hematoma One pain on injection site Four prolongeg sustained erection successfully managed One priapism managed successfully No systemic toxicity	* Significant subjective improvement of IIEF, EHS, SEP, GAS * Significant objective improvement on penile Doppler ultrasound * 40% response to treatment and successful sexual intercourse * Efficacy more durable at 6 months with 100 U of BoNT-A than 50 U
Ghanem et al.(NCT02584686)	Unpublished	Phase I randomized controlled trial	24 male patients	BoNT-A group vs. control group stand-alone therapy	50 U	No side effects	* Significant PSV improvement * Significant subjective improvement of EHS, SHIM, GAS * No difference for the SEP-score
Ghanem et al. (NCT03102762)	Unpublished	Phase II randomized double-blinded placebo controlled trial	70 male patients	BoNT-A group vs. control group stand-alone therapy	100 U	No side effects	* PSV improvement trend * SHIM improvement trend * No effect on penile size or IVLT

BoNT-A: botulinum toxin A; IIEF: international index of erectile function; aboBoNT-A: abobotulinum toxin A; EHS: erection hardness scale; SEP: sexual encounter profile; GAS: global assesment score; PSV: peak systolic velocity; SHIM: sexaul health inventory for men; IVLT: intravaginal latency time

Table summarizing all the studies included

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2. Reddy AG, Dick BP, Natale C, Akula KP, Yousif A, Hellstrom WJG. Application of Botulinum Neurotoxin in Male Sexual Dysfunction: Where Are We Now? Sexual Medicine Reviews. 2021;9

Funding None **Clinical Trial** No **Subjects** Human **Ethics not Req'd** Since it is a systematic review and meta-analysis **Helsinki** Yes **Informed Consent** No

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RELATIONSHIP BETWEEN SEVERITY OF ERECTILE DYSFUNCTION AND SYSTEMIC IMMUNE INFLAMMATION INDEX AND NEUTROPHIL LYMPHOCYTE RATIO

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HYPOTHESIS / AIMS OF STUDY
Endothelial dysfunction has an important place in the pathogenesis of erectile dysfunction (ED). The aim of this study was to evaluate the relationship between ED severity and systemic immune inflammation index (SII) and neutrophil lymphocyte ratio (NLR).

STUDY DESIGN, MATERIALS AND METHODS
The data of male patients over the age of 18 who applied to the urology clinic with the complaint of ED between January 2018 and September 2021 were analyzed. Patients with known diabetes mellitus, hypertension, coronary artery disease, and previous pelvic surgery were excluded from the study. The erectile functions of the patients were evaluated with the international erectile function index-erectile function (IIEF-EF). The patients were divided into two groups according to the severity of ED as mild (IIEF-EF >17) and moderate-severe (IIEF-EF ≤ 17). Demographic data of the patients were recorded. SII value was calculated by neutrophil*platelet/lymphocyte formula and NLR was recorded.

RESULTS
A total of 185 patients were included in the study (mild ED: 74, moderate- severe: 111). The mean age of the patients was 48.18 ± 11.58(20-79), and the mean IIEF-EF was 13.34 ± 6.55 (0-25). The mean SII was 594.89 ± 348.90, and the mean NLR was 2.27 ± 1.19. The mean total testosterone level of the patients was 3.25 ± 1.48ng/dl.

When the patients were divided into two groups according to the severity of ED, a significant difference was observed between IIEF-EF scores and SII values of the patients ($p<0.001$ for IIEF-EF, $p=0.008$ for SII). No significant difference was found with NLR values ($p=0.950$)(Table-1). There was a moderate negative correlation between IIEF-EF score and SII value ($p=0.042$, $r=-0.569$). No significant correlation was observed between NLR and IIEF-EF ($p=0.625$, $r=-0.124$). SII cut-off value was determined as 436.73 and AUC was 0.674 (CI 95%: 0.448-0.717). At this value, the sensitivity was 70.1% and the specificity was 64.8%.

INTERPRETATION OF RESULTS
SII has taken its place as an important inflammatory marker in determining the severity of Erectile dysfunction. The severity of the Erectile dysfunction degree can be determined with a cut-off score of 463 for SII. SII index was negatively correlated according to the severity of Erectile dysfunction, and erectile functions decreased with the increase in systemic inflammation.

CONCLUDING MESSAGE
It was determined that the SII index was negatively correlated according to the severity of ED, and erectile functions decreased with the increase in systemic inflammation. During the evaluation of patients, the severity of ED can be revealed more clearly with the use of SII. Further randomized studies are needed to better understand the relationship between SII and ED.

Funding None **Clinical Trial** Yes **Public Registry** No **RCT** No **Subjects** Human **Ethics Committee** Prof. Dr Cemil Tascioglu City Hospital **Helsinki** Yes **Informed Consent** Yes

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THE EFFECT OF VITAMIN D REPLACEMENT IN PATIENTS WITH LOWER URINARY TRACT SYMPTOMS/ERECTILE DYSFUNCTION RESISTANT TO TADALAFIL 5MG TREATMENT

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HYPOTHESIS / AIMS OF STUDY
The aim of this study was to evaluate the effect of vitamin D replacement in patients with lower urinary tract symptoms (LUTS)/erectile dysfunction (ED) who did not respond to tadalafil 5 mg treatment.

STUDY DESIGN, MATERIALS AND METHODS
Patients who applied to the Andrology Clinic with LUTS/ED between September 2017 and August 2020 and used 5 mg Tadalafil daily for treatment and did not benefit from treatment for one month were included in the study. Vitamin D levels of the patients were analyzed and Vitamin D3 100,000 IU/week oral therapy was administered for a month to the patients with low levels of Vitamin D(< 20ng/ml).The values of the patients before and after Vitamin D replacement were compared.

RESULTS
A total of 84 patients were included in the study.The mean age was 49.175 ± 11.63(28-70) years and the mean BMI was 25.93 ± 6.82(18.26-37.87). Testosterone levels of the examined patients were 3.45 ± 0.99 ng/ml. After one month of Vitamin D replacement + Tadalafil 5 mg/d treatment, the IIEF-EF (pre-treatment: 10.73 ± 6.12, post-treatment: 24.18 ± 4.87; $p = 0.001$) and IPSS (pre-treatment: 9.12 ± 7.16, post-treatment: 3.11 ± 1.08; $p = 0.003$) scores of the patients improved significantly. Testosterone levels of the patients increased to 3.77 ± 1.23 ng/ml ($p < 0.001$) and 25(OH)D levels increased to 30.50 ± 7.56 ng/ml ($p < 0.001$).

There was a moderately significant linear correlation between IIEF-EF scores and Vitamin D levels after the treatment ($p < 0.001$; $r = 0.661$) There was a moderate linear correlation between IIEF-EF scores and testosterone levels ($p < 0.001$; $r = 0.674$). There was a moderately significant negative correlation between IIEF-EF scores and IPSS scores after the treatment ($p = 0.003$, $r = 0.458$). A weak positive correlation was found between testosterone levels and Vitamin D levels ($p = 0.013$; $r = 0.321$). There was no significant correlation between IPSS scores and testosterone levels ($p = 0.356$; $r = 0.221$)

INTERPRETATION OF RESULTS
The study results showed that Tadalafil 5 mg treatment together with Vitamin D replacement had improvement on erectile functions and LUTS in patients with Vitamin D deficiency who took Tadalafil for ED and did not respond. Moreover, it was shown that the improvement in Vitamin D levels was moderately correlated with erectile functions. The results of the present study suggest that the efficacy of Tadalafil increases with Vitamin D replacement administered by examining 25(OH) Vitamin D level in patients who do not respond to Tadalafil 5mg treatment and do no have sufficient improvement in their IIEF-EF scores. It is considered that this is caused by both the efficacy of Vitamin D replacement in the endothelial system and in increasing testosterone levels. There are similar studies in the literature; however, this is the first study, to the best of our knowledge, to evaluate the efficacy of the combined treatment after treatment ineffectiveness.

CONCLUDING MESSAGE
Low levels of Vitamin D in LUTS/ED patients have an effect on tadalafil non unresponsiveness. With vitamin D supplementation, patients' LUTS and ED symptoms improved. Evaluation of Vitamin D levels is important to improve treatment response, especially in patients who do not respond to PDE-5 inhibitors. Further studies are needed the role of Vitamin D in the pathophysiology of ED.

Funding None **Clinical Trial** Yes **Public Registry** No **RCT** No **Subjects** Human **Ethics Committee** Prof. Dr Cemil Tascioglu City Hospital **Helsinki** Yes **Informed Consent** Yes

SESSION 26 - FISTULA, DIVERTICULUM AND WILD CARD

Abstracts 419-428
15:30 - 17:00, Hall G
Chairs: Dr Elise Jaques Billings De (United States), Dr Milena M Weinstein (United States)

419 | www.ics.org/2022/abstract/419

MINIMALLY INVASIVE REPAIR OF VESICO-VAGINAL FISTULAE: A COMPARISON OF TECHNIQUES

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INTRODUCTION
Minimally invasive approaches to vesico-vaginal fistula repair include both vaginal and laparoscopic techniques. When the fistula is located in an accessible portion of the vagina and the risk of recurrence is low, a vaginal repair may be appropriate. When the fistula is located in an inaccessible portion of the vagina, or if excision of the tract and/or interposition of a layer between the bladder and vagina is desired, a laparoscopic approach may be appropriate. This video compares the two techniques.

DESIGN
The first section of the video shows the repair of a small vesico-vaginal fistula in an accessible portion of the vagina via a vaginal technique. A pediatric feeding tube is inserted into the fistula for traction. Stay sutures are placed lateral to the fistula, and the vaginal epithelium is undermined. The fistula tract is then closed with a purse-string suture and inverted. The epithelium is then closed. The tract is not excised and no tissue or material is interposed between the suture lines.

The second section of the video shows the laparoscopic repair of a larger fistula located high in the vagina of a patient without uterine descent. The bladder is dissected away from the cervix and upper vagina and opened. The fistula tract is identified and excised. The bladder wall is separated from the vagina and closed in two layers. The vaginal defect is repaired in a single layer and an absorbable adhesion barrier is placed between the two suture lines.

RESULTS
Catheters were removed after 7 days and both patients had complete resolution of symptoms. Neither fistula has recurred.

CONCLUSION
Both vaginal and laparoscopic repairs are feasible for vesico-vaginal fistula, and the choice of technique may be driven by patient factors and surgeon experience.

Funding None **Clinical Trial** No **Subjects** None

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420 | www.ics.org/2022/abstract/420

BEST IN CATEGORY PRIZE: TRANSGENDER HEALTH

SINGLE PORT ROBOTIC-ASSISTED VESICOVAGINAL FISTULA REPAIR WITH BUCCAL MUCOSA GRAFT IN A TRANSGENDER FEMALE

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1. University of Illinois at Chicago, 2. University of Chicago

INTRODUCTION

Since the FDA approved the use of Da Vinci Single Port (SP) robotic platform, its applicability has revolutionized the field of Urology, especially in lower urinary tract & pelvic reconstruction as it facilitates complex procedures in difficult-to-access anatomical locations with its flexible camera and floating dock feature. Herein, we demonstrate a SP robotic-assisted vesicovaginal fistula repair using buccal mucosa graft (BMG) in a transgender woman.

DESIGN

This is a 38-year-old transgender female with no apparent medical history, presenting a status post-vaginoplasty penile inversion. Due to a shortened vaginal canal, she underwent a robotic SP revision with a peritoneal flap (Davydov technique). The Prostatic urethra was injured during this procedure, and a multi-layer primary repair was used intraoperatively. The postoperative course was complicated by a urethro-neovaginal fistula that was not healed by urinary diversion. Cystoscopy with retrograde urethrography confirmed a 2 cm fistula between the prostatic urethra and the neovaginal cavity. Stenosis of the vaginal canal was found on examination under anesthesia. CT angiography documented adequate vascular supply in the affected area. Joint decision to proceed with another SP robotic reconstruction procedure, this time transvesical and tissue insertion using BMG.

RESULTS

Patient was placed in lithotomy and 45° Trendelenburg positions. Flexible cystoscope was introduced, and bladder was distended with CO2. A vertical 4-cm infrapubic skin incision was made. Following cystotomy, SP access port was placed into the bladder. A 5-mm assistant port was placed juxtavesically under digital guidance. Robot was docked. Dissection line was marked circumferentially at the level of bladder neck. Atrophic prostate tissue was enucleated. Dissection plane was developed circumferentially, fistulous tract was identified at the posteromedial aspect of the prostatic urethra. Following complete excision of the fistula, peripheral part of the prostate was approximated in midline as an interpositional layer between the neovagina and the urethra. BMG was sutured distal to the bladder neck. A 16 Fr. Foley catheter was placed into the bladder. Robot was undocked and cystotomy was closed. Patient was discharged home on postoperative day 1. Retrograde cystourethrogram demonstrated absence of extravasation on postoperative day 29 and catheter was removed.

CONCLUSION

Treatment of urinary fistulas after gender-affirming feminized genital reconstruction often requires additional procedures. The SP robotic platform is an important asset in urological equipment and can be used in both primary and revision settings for reconstructive purposes. The transvesical approach, with its flexible camera and floating dock features, In addition to BMG insertion, can be successfully used for lower urinary tract fistulas after vaginoplasty.

Funding N/A **Clinical Trial** No **Subjects** None

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ROBOTIC URETHRO-VAGINAL FISTULA REPAIR AND CONCOMITANT FASCIAL SING INSERTION

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1. university of rennes

INTRODUCTION

Urethrovaginal fistula (UVF) can result in severe stress urinary incontinence (SUI) due to intrinsic sphincter deficiency (ISD) in some instances. The therapeutic approach can be staged but some authors have reported vaginal UVF repair with concomitant pubovaginal sling insertion. Fistula located at the proximal urethra/bladder neck can be challenging to repair through a vaginal approach. In the present video, we report and describe a new robotic surgical technique aiming to treat concomitantly urethrovaginal fistula and severe SUI due to ISD

DESIGN

We present the case of a 49-year-old female patient with a history of vesicovaginal fistula after hysterectomy for fibroids. After open transvesical vesicovaginal fistula repair she presented a bladder neck stricture along with bilateral ureteral stricture. She underwent an open bilateral ureteral reimplantation. Self-dilation of her bladder neck stricture was initiated and resulted in a UVF. She underwent a vaginal bladder neck reconstruction and UVF repair with Martius flap interposition. Unfortunately, a UVF recurrence was observed at 1 month postoperatively, located at the bladder neck, with severe SUI, a positive cough stress test and a fixed urethra. Several options were discussed with the patient including an ileal conduit. After discussion, a robotic UVF repair + rectus fascia sling insertion was planned.

RESULTS

Five ports are placed. The Da Vinci Xi robot is docked on the left side of the patient (side docking). A malleable retractor is inserted in the vagina for vault manipulation. The intervesicovaginal dissection is carried out and difficult due to severe adhesions between the bladder and vaginal walls. The urethrovaginal fistula is intubated with a ureteral catheter and the fistulous orifice is found. The dissection is pursued to separate the bladder neck from the vagina distally, beyond the fistulous orifice to allow tension-free vaginal and bladder neck closure. To facilitate proper visualization of the fistulous orifice the posterior bladder wall is incised on 5 cm medially The vaginal and bladder neck fistulous orifices are excised and specimens ar sent for pathological examination. The vaginal orifice is closed by two V lock running sutures transversally and the bladder is closed longitudinally with two V lock running sutures as well. A passage around the bladder neck for the fascial slign is created by dissecting the vaginal fornices on both sides of the bladder neck, with an assistant's finger placed in the vagina to put tension on the vaginal wall and facilitate its dissection.

To harvest rectus fascia sling, a 7 cm suprapubic incision is made and carried down to the rectus fascia. A 10x1.5 cm rectus fascial sling is harvested. The fascia is then closed using two running sutures. The fascial sling is inserted through the 12 mm assistant port and placed around the bladder neck.

The sling is sutured above the fascia by the assistant An omental flap is then harvested and sutured between the vagina and the bladder neck, below the fascial sling with a V lock. Two tissue layers are then interposed between the bladder and vaginal sutures

The operative time was 290 minutes with estimated blood loss of 100 ml. There was no postoperative complications. The patient was discharged on postoperative day 2. The urethral catheter was removed at day 14 and the patient resumed spontaneous voiding with post-void residual of 20 ml. At 6 months, she is socially continent, wearing 1 pad per day and there has been no UVF recurrence

CONCLUSION

Robotic urethro-vaginal fistula repair and concomitant fascial sing insertion appears feasible. The technique can be of help in female patients with UVF and SUI due to ISD in case were a vaginal repair is challenging to allow a one-stage surgical treatment.

Funding None **Clinical Trial** No **Subjects** Human **Ethics Committee** CNIL **Helsinki** Yes **Informed Consent** Yes

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ROBOTIC REPAIR OF VESICOVAGINAL FISTULA

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INTRODUCTION

Vesicovaginal fistula (VVF) is a pathological communication between the posterior bladder wall and anterior vagina. A variety of techniques have been described in the literature but there has only recently been a consensus on best robotic surgical practice. [1] Robotic surgical technique has not been well described with visual demonstrations. We present an original video of a robotic-assisted repair of a VVF with trans-vesical approach and omental interposition.

DESIGN

We outline the key steps in VVF repair, including a cystoscopy to establish the number, size and location of VVF. Bilateral double-J ureteric stents were inserted to protect the ureteric orifices. The VVF was marked by placing a guidewire through the defect via the vagina. A robotic-assisted VVF repair with trans-vesical approach was performed using the da Vinci Xi surgical system. The vesicovaginal space was dissected, the fistula track exposed and fistulectomy performed. Multi-layer, tension-free closure of the vagina and bladder with omental interposition was performed, followed by a leak test to ensure water tight closure. An indwelling catheter (IDC) was inserted at the conclusion of the case.

RESULTS

There were no intra or post-operative complications. The patient was discharged on post-operative day 3 and the IDC was removed on post-operative day 10. At three month follow-up, she did not have ongoing incontinence or recurrence of the fistula.

CONCLUSION

Robotic repair of VVF is both safe and effective. Robotic surgery facilitates dissection of the vesicovaginal space, mobilization of an omental flap and multi-layer tension-free closure of the bladder and vagina.

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Funding None to declare **Clinical Trial** No **Subjects** Human **Ethics Committee** Northern Sydney Local Health District Human Research **Ethics Committee Helsinki** Yes **Informed Consent** Yes

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ENDOSCOPIC VESICOVAGINAL FISTULA REPAIR FROM NATURAL ORIFICE: TRANSURETHRAL APPROACH

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INTRODUCTION
Minimally invasive surgical approaches have become highly popular in line with technological advancements. In vesicovaginal fistula (VVF) repair, numerous minimally invasive surgical techniques, namely laparoscopic, robotic, and transvaginal techniques, are used. However, these techniques require invasion though minimally. In this report, we present a patient with iatrogenic VVF in whom we applied a novel “zero-invasion” technique, Natural Orifice Transurethral Endoscopic Vesicovaginal Fistula (NOTE-VVF) Treatment, to repair the fistula tract by advancing the laparoscopic trocar through a natural orifice, i.e. urethra.

DESIGN
Case

A 45-year-old female patient was admitted to our clinic with the complaint of continuous urinary incontinence that started immediately after total abdominal hysterectomy that was performed due to uterine myoma in another center about three weeks earlier. Patient history indicated that she had no complaint of urinary incontinence prior to hysterectomy.

Urogynecological examination indicated urine leakage from the vagina, not from the urethra. Serum creatinine level, complete urinalysis, urinary culture, and urinary ultrasonography were normal. Due to a suspicion of VVF, a 14 Fr urethral catheter was inserted in the bladder and the methylene blue test revealed urinary leakage from the vagina. The diagnosis of VVF was confirmed by the visualization of a fistula tract approximately 5 mm in diameter in the bladder trigone region on cystoscopy which was performed on an outpatient basis . Elective surgery was planned for the fistula repair.

Following preoperative preparation, the patient was placed in the lithotomy position at operation room under spinal anesthesia. After cleaning and draping, the location and width of the fistula tract was determined by entering the bladder with the cystoscopy. An optical lens (for imaging) and a 5mm laparoscopic trocar (working trocar) were carefully inserted into the bladder through the female urethra. Subsequently, the VVF line was sutured at 1-2 mm intervals and the bladder side was closed using 4/0 absorbable sutures that were advanced into the bladder through the working trocar. The procedure was completed after inserting a 14 Fr urethral catheter in the bladder.

RESULTS
In this case, VVF repair was performed with the NOTE-VVF repair technique and the patient was discharged 24 hours after surgery (total operative time, 23 min). On day 10 after surgery, the patient had no urinary incontinence and no methylene blue leakage from the vagina following the Valsalva maneuver and thus the urethral catheter was removed. No urinary incontinence was present at later follow-up visits, and the cystoscopy performed at month 3 showed complete closure of the fistula tract. No peri- or post-operative complication occurred in the patient.

CONCLUSION
NOTE-VVF technique introduced in the present study, which can be applied by entering the bladder through the urethra only by using 5 mm laparoscopic trocar and a thin optical lens, can be successfully used in the treatment of small, non-complicated, acute-stage, iatrogenic VVFs.

Funding No **Clinical Trial** No **Subjects** Human **Ethics not Req'd** This abstract was a case report so ethical committee approval was not taken. **Helsinki** Yes **Informed Consent** Yes

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RECURRENT VESICOCERVICAL FISTULA - UNRAVELLING THE MYSTERY !

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INTRODUCTION
Vesicocervical fistula (VCxF) is an extremely rare entity among all the urogenital fistulas. Due to upsurge of caesarean section rate associated with prolonged labor, obstructed labor and rise in instrumental deliveries, cervicovaginal tears and inadvertent vaginal suturing, VCxF is no more limited to text. The differentiation of VCxF from vesicovaginal fistula (VVaF) is crucial as the former requires great skill for repair.

DESIGN
A 31 year, 150cm tall, P2L2 lady had previous 2 lower segment caesarean section (LSCS) 8 years and 4 years ago respectively. Her first caesarean delivery was done for second stage arrest in a private setup. She had spontaneous onset and progress of labor at 38.3 weeks, with total duration of first and second stage of labor >24 hours. Her operative, immediate and late postoperative period was uneventful following which she had her second pregnancy after a span of four years. Her antenatal period was uncomplicated till she went into spontaneous labor at 37.2 weeks gestation, and opted for trial of labor after caesarean section (TOLAC). She delivered a 2.8kg baby by an emergency LSCS for fetal indication in advanced labor. She had urinary leakage from vagina on postoperative day 7. CT urography showed a 3.1 cm VVaF, while cystovaginoscopy showed two fistulas, VCxF and Vesicouterine (VUtF).

Patient underwent a Robotic VUtF and VCxF repair following which she had delayed urinary incontinence 4 weeks post catheter removal. Cystovaginoscopy showed a small 0.5cm supratrigonal fistula 3cm above the right ureteric orifice communicating with and a 0.5cm right juxtacervical fistula. Patient underwent cystoscopic fulguration with Bugbee cautery six months after the previous surgery. Patient again had continuous urinary leakage two months post catheter removal, although the amount was reduced to half.

Patient underwent a repeat cystovaginoscopy revealing same fistula sites in bladder and cervix, confirmed by dye test. Although the complete fistulous tract was not negotiable, the guide wire directed into the vaginal fistulous orifice had a false paracervical tract, the lateral edge of which was in the fistulous tract and was used as a pointer for localisation of cervical end of the tract. Robotic vesicocervical fistula repair with omentum interposition flap was planned. Port placement and docking was done. Peritoneoscopy and adhesiolysis was begun in pelvis. Localisation of exact direction of dissection was guided by the dimple of traction on guide wire partially in the fistulous tract. Mini-cystostomy was done to locate the ureteric orifices and with repeated intermittent traction given by the assistant sitting on vaginal end. Proceeding which, a plane was made between the posterior bladder wall and anterior vagina. The dissection plane was deepened further down posterior to bladder till the guide wire was visible and extended 1cm beyond it. A fistulous tract and its surrounding unhealthy bladder mucosa, extending from the lateral cervical edge to the bladder side wall was excised. After mobilising the bladder well away from the excision site, cervicovaginal layer and bladder was sutured with omental flap interposition. This was followed by placement of drain, and removal of trocars and skin closure.

RESULTS
Patient's drain was removed on postoperative day two and discharged with catheter for three weeks. Patient is under regular follow up and is doing fine.

CONCLUSION
Vesicocervical fistula repair is one of the most difficult urogenital fistulas for diagnosis and repair. Role of Bugbee cautery in small VCxF did not prove helpful as opposed to its proven role in uncomplicated small VVaF. Robotic route of VCxF repair provides excellent results compared to transvaginal VCxF repair oughing to better dexterity, visualization and ease in identification and repair.

Funding None **Clinical Trial** No **Subjects** Human **Ethics not Req'd** It was not a clinical trial .. informed consent has been taken **Helsinki** Yes **Informed Consent** Yes

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LAPAROSCOPIC APPROACH OF RECURRENT CIRCUMFERENTIAL URETHRAL DIVERTICULUM

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INTRODUCTION

Female urethral diverticulum is a rare condition and occurs in 1-6% of women. Recurrence after surgery, although, is common, occurring at a rate of 8-20%.

It usually affects women between the third and seventh decade of life, but it can appear at any age. Usually, it presents as a bulge underneath the urethra, lined by urethral mucosa. Factors associated with major complications are horseshoe-shaped and circumferential diverticula, size over 3-4 cm, and proximal location.

The classic triad of symptoms is: dysuria, dribbling, and dyspareunia, but it presents in only 5% of women. The most common symptoms are recurrent urinary tract infection, dysuria, and a vaginal mass.

A high suspicion associated with an image exam is necessary for the diagnosis. Voiding cystourethrography and Magnetic Resonance Imaging (MRI) are considered the most used diagnostic methods, with increasing evidence that MRI is the most sensitive radiological examination for the diagnosis of the urethral diverticulum and has great value for surgical planning7.

The urethral diverticulectomy can be done by vaginal or abdominal approach. The choice depends mainly on the surgeon's expertise and diverticulum location, and the vaginal one is usually prefered.

The aim of this video is to present a stepwise laparoscopic approach of recurrent urethral diverticulum.

DESIGN

A 42 year-old female reported recurrent urinary tract infection and chronic pelvic pain. She was submitted to a vaginal diverticulectomy six months before, presenting new episodes of recurrent urinary tract infections and chronic pelvic pain. Magnetic resonance showed a urethral diverticulum involving the urethra circumferentially.

The procedure was done under general anesthesia, in trendlemburg position with open legs in semi-litothomy. We placed five trocars: one at the midline, above the umbilicus, two pararectal, and two medial to the anterior superior iliac spine. We decided on a laparoscopic approach to avoid the risks associated with vaginal technique including transection of the urethra. A 16 French urethral Foley catheter was inserted and the cuff helps to identify bladder boundaries. The diverticula sac was identified and opened to identify the diverticulum boundaries in order to excise it. This approach was chosen due to adherences identified between the diverticulum and surrounding tissues caused by the previous procedure and recurrent infections. Digital vaginal manipulation and an intraoperative cystoscopy helped to identify the neck of the diverticulum, at 4 o'clock position. The diverticula was freed flush with the wall of the urethra. A ureteral catheter was used to help expose the urethral defect which was sutured with 3-0 caprofyl stitches in a watertight fashion without any tension. A Jackson Pratt drain was located to watch for leaks. A 16Fr urethral catheter was maintained for 2 weeks.

RESULTS

The drain was withdrawn and the patient was discharged on the first postoperative day. The urethral catheter was removed after 14 days. At the follow-up six months later, she was satisfied, with no urinary tract infections recurrence or local complications.

CONCLUSION

In circumferential diverticula, the laparoscopic approach allows direct access, avoiding transection of the urethra. In this case, it proved to be an efficient and safe option, which can be carried out with widely available resources.

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Funding None **Clinical Trial** No **Subjects** Human **Ethics Committee** Research **Ethics Committee** (CEP) of the State University of Campinas (UNICAMP) **Helsinki** Yes **Informed Consent** Yes

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ONABOTULINUMTOXIN A TO BLADDER NECK: MINIMALLY INVASIVE TREATMENT FOR BLADDER NECK OBSTRUCTION

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INTRODUCTION

Bladder outlet obstruction is often under diagnosed in women. It is associated with voiding lower urinary tract symptoms consisting of weak stream and incomplete bladder emptying as well as storage symptoms consisting of frequency, nocturia, and urinary incontinence. The categories of bladder outlet obstruction are divided into anatomical and functional causes. Anatomical causes include pelvic organ prolapse and post-urinary incontinence surgeries while functional causes include primary neck obstruction and small fiber neuropathy leading to autonomic dysfunction. In order to accurately diagnose bladder outlet obstruction, a comprehensive history, physical exam, and diagnostic testing need to be undertaken. On urodynamic studies (UDS), increased detrusor pressure, no Valsalva or change in abdominal pressure, minimum urinary flow, and EMG synergy in the presence of sustained bladder contraction represent bladder outlet obstruction. The obstruction may also be seen on cystography at the level of the bladder neck. We sought to evaluate the effectiveness of onabotulinumtoxin A at the level of the bladder neck in patients with bladder neck obstruction, many of whom have small fiber neuropathy.

DESIGN

During the chemodenervation procedure, a female urethral cystoscope, 100 units of onabotulinum toxin A, and a 23 gauge cystoscopic injection needle are needed. The 100 unit onabotulinum toxin is reconstituted with 2cc of preservative free injectable saline, making it more concentrated than standard mixing based on the small target for delivery. Using a 30-degree lens and rigid cystoscopic sheath a cystoscopy is performed for general surveillance prior to the onabotulinum toxin A administration.

After the cystoscopic injection needle is primed and loaded into the cystoscope injection port, 0.5cc of reconstituted onabotulinum toxin is injected four times evenly across the meat of the bladder neck at the 1, 5, 7, and 11 o'clock positions. During the procedure, the needle is cautiously directed distally enough to prevent through and through passage of the needle and wasting of the onabotulinum toxin into the bladder. The syringe is then changed to injectable saline with the tip of the needle still inserted in the bladder neck to prevent loss of the onabotulinum toxin held within the needle. The last injection is followed with an injection of 0.5cc of saline to clear the needle. Lastly, the bladder is drained, and the cystoscope is removed.

RESULTS

In patients with bladder neck obstruction either due to primary cause or due to small fiber neuropathy, we have found that onabotulinum toxin A can be used at the level of the bladder neck to relieve obstructive symptoms for about 6 months. This treatment is best applied to patients who have UDS evidence of bladder neck obstruction, small fiber neuropathy, symptoms of hesitancy and dysuria, and have had inadequate response or poor tolerance to alpha blockers. Bladder outlet obstruction symptoms may worsen for one to three weeks as the chemodenervation treatment takes hold. Formal analysis of data has not been performed for this video technique demonstration. This is currently an off label chemodenervation treatment.

CONCLUSION

Onabotulinum toxin to the bladder neck is a treatment option in those with non-anatomic bladder neck obstruction who have not responded to conservative therapy. Pelvic floor physical therapy and relaxation techniques are usually offered as adjunct therapy for often present concurrent voiding dysfunction. Patients should be counseled on potential symptom flare-ups as the chemodenervation treatment is taking hold and that it may take one to three weeks for the treatment to set in.

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Funding Dr. De has affiliations with Ironwood, Flume, Consumer Medical, and Glycologix. **Clinical Trial** No **Subjects** Human **Ethics not Req'd** formal analysis of data has not been performed for this video technique demonstration. **Helsinki** Yes **Informed Consent** Yes

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EMG GUIDED ONABOTULINUM TOXIN TO PELVIC FLOOR MUSCLES: A STRAIGHT FORWARD TECHNIQUE TO CONFIRM INJECTION ACCURACY

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INTRODUCTION

Chronic pelvic pain affects millions of women. Per the American College of Obstetrics and Gynecology, chronic pelvic pain is any pelvic pain that lasts for more than six months and occurs in the pelvis or lower abdomen. Its etiology can be from organs, muscles, nerves, bones, and vessels within the pelvis. Pelvic floor muscles with increased pelvic floor muscle tone are excellent targets in the approach to treating pelvic pain. The European Association of Urology's guidelines on chronic pelvic pain start with conservative management prior to pain management and more invasive measures. A detailed history of chronic pain is undertaken to identify the possible origin. This includes the patient's obstetric, gynecologic, genitourinary, gastrointestinal, and skeletal history. During the pelvic exam, the pubococcygeus, iliococcygeus, ischiococcygeus, puborectalis, and obturator muscles are assessed for tone, strength, and discomfort. We sought to evaluate the effectiveness of using onabotulinum toxin A for patients with disorders of increased tone due to pelvic floor tension myalgia and pelvic floor myofascial pain syndrome as well as pelvic floor pain due to pelvic floor myalgia. These are patient who have not had success with pelvic floor targeted physical therapy training.

DESIGN

During the procedure, the main instruments used include a Chalgren 75 mm injectable monopolar needle electrode, EMG return electrode, LifeTech MiniStim peripheral nerve stimulator, split Graves speculum, and 100 units of onabotulinum toxin. The 100U of onabotulinum toxin is reconstituted with 2cc of preservative free injectable saline, making it more concentrated than standard mixing based on the small target for delivery.

The patient is counseled that an awake exam will be performed in the operating room. The surgeon performs a pelvic exam assessing which muscles exhibit increased tone and elicit tenderness, thereby mapping which muscles will benefit from injection. Often this exam is informed by input from the pelvic floor physical therapist preoperatively. The patient is then sedated. Then the EMG electrode is placed at the 2 or 10 o'clock position on the perineum just anterior to the anus. It should be noted that more stimulation will be required to transmit on the contralateral side. Using the peripheral nerve stimulator EMG device, with the dial turned to an intensity of about 4 to start, a double burst is administered to confirm appropriate localization of pelvic floor muscles. Contraction of the pelvic floor muscle without activation of the leg will be appreciated when the injection needle is optimally placed. The appropriate puborectalis, pubococcygeus, iliococcygeus, ischiococcygeus, and obturator muscles are targeted based on the physical exam. Each muscle receives two injections about one to two centimeters apart. The 100 units of onabotulinum toxin is equally divided among the targets.

RESULTS

Using onabotulinum toxin A at the pelvic floor muscles can relieve disorders of increased pelvic floor tone and pelvic floor pain for about 6 months. This treatment is best applied to patients who have hit a plateau in pelvic floor physical therapy, have been unable to tolerate physical therapy, or have continued promotors of high tone pelvic floor dysfunction. Formal analysis of data has not been performed for this video technique demonstration. This is currently an off label chemodenervation treatment. However, there is currently some data in the literature on this.

CONCLUSION

Clinical observation shows that in patients with refractory high tone pelvic floor muscle dysfunction, onabotulinum toxin can be used to augment relaxation. Pelvic floor physical therapy can often be resumed after onabotulinum toxin injection and often can augment results. Patients should be counseled that symptoms can worsen for one to three weeks while the chemodenervation is taking hold.

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Funding Dr. De has affiliations with Ironwood, Laborie, Flume, Consumer Medical, and Glycologix. **Clinical Trial** No **Subjects** Human **Ethics not Req'd** formal analysis of data has not been performed. **Helsinki** Yes **Informed Consent** Yes

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WHY MEN URINATE MORE EFFICIENTLY WHILE STANDING THAN IN A SUPINE POSITION: MORPHOLOGICAL ANALYSIS WITH REAL-TIME MAGNETIC RESONANCE IMAGING

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INTRODUCTION
Few studies have examined the effects of body position on urination efficiency morphologically. We aimed to dissect out the anatomical changes of pelvic organs during urination in the upright and supine positions by a real-time magnetic resonance imaging (rtMRI) system.

DESIGN
Thirteen healthy male volunteers aged 26-60 years were included in the study. The sagittal real-time 2D images were taken to evaluate urinary efficiency, along with change in five morphological indices at the time of storage and the beginning of voiding, in both upright ant supine positions.

RESULTS
Urination was more efficient in upright position than in supine position, as expressed by higher average rate of bladder emptying (9.9 ± 4.2 vs. 6.8 ± 2.9ml/sec, $p < 0.05$), and also by fewer participants showing significant residual urine (1/13 vs. 7/13, $p < 0.05$). At the onset of voiding in standing position, the levator ani muscle moves downward and backward followed by descent of the bladder neck and rotation of the prostate around the symphysis. Such changes were expressed by two morphological indices. One was posterior vesicourethral angle at the start of voiding, 152 ± 7 vs. 140 ± 1 in upright and supine position ($p < 0.05$). The other index was the change in angle between levator ani line and pubo-coccygeal line in upright and supine position, 9.4 ± 9.9 vs 1.6 ± 7.9 before voiding ($p < 0.05$), and 30.2 ± 14.0 vs 17.3 ± 12.9 after the start of voiding ($p < 0.05$).

CONCLUSION
This is, to our knowledge, the first report to capture the anatomical changes of pelvic organs during urination in the upright position. In addition, we introduced a novel parameter to quantify the dynamic relaxation of the levator ani as the angle LA/PC, which seemed to be a key movement related to efficient urination.

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SATURDAY 10TH SEPTEMBER

SESSION 27 - BEST UROGYNAECOLOGY AND FEMALE & FUNCTIONAL UROLOGY

Abstracts 429-434
09:35 - 11:05, Hall K
Chair: Dr Alex Digesu (United Kingdom)

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THE ASSOCIATION BETWEEN DIETARY INFLAMMATORY INDEX AND PELVIC FLOOR DISORDERS AMONG ADULT WOMEN

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HYPOTHESIS / AIMS OF STUDY
To investigate the association between dietary inflammatory index with pelvic floor disorders in a nationally representative U.S. sample.

STUDY DESIGN, MATERIALS AND METHODS
A cross-sectional survey was conducted using data from the 2005-2010 National Health and Nutrition Examination Survey. Non-pregnant women ≥ 20 years who completed the questionnaires on 24-hour dietary recall and pelvic floor functions were included for analysis. Weighted multivariable logistic analysis adjusting for possible confounders was used to evaluate the association between the dietary inflammatory index and pelvic floor disorders. The exposure-response relationship was further explored by restricted cubic spline functions.

RESULTS
Among 6406 women, the dietary inflammatory index ranged from -5.20 to 4.83. The weighted prevalence of pelvic floor disorders was 23.87 (22.49-25.31) %, with 16.69 (15.34-18.13) % of urinary incontinence, 9.17 (8.26-10.16) % of fecal incontinence, 2.80 (2.32-3.37) % of pelvic organ prolapse. With a one-unit increment of the dietary inflammatory index, the risk of pelvic floor disorders would increase 8% (OR 1.08, 95% CI: 1.02-1.13). Compared with women in the lowest dietary inflammatory index group, such risk raised 56% in pelvic floor disorders (95% CI: 1.22-1.99), 34% in urinary incontinence (95% CI: 1.02-1.78), and 95% in fecal incontinence (95% CI: 1.22-3.13) among those in the highest group. The exposure-response associations were linear. (P for non-linearity =0.606, 0.884, and 0.188). In the analysis stratified by BMI, only among the obese group (BMI ≥ 30 kg/m2), women in the highest DII group had a 69% higher risk of pelvic floor disorders (OR 1.69, 95% CI: 1.13-2.53), 57% increased risk of urinary incontinence (OR 1.56, 95% CI: 1.19-2.12), and about three times risk of fecal incontinence (OR 2.90, 95% CI: 1.28-6.53) compared with those in the lowest DII group.

INTERPRETATION OF RESULTS
Results from our study indicated that nearly one-fourth (23.87%, 95% CI: 22.49-25.31%) of U.S. nonpregnant women aged 20 or more complained of one or more pelvic floor disorders. Urinary incontinence was the most common among three subsets. Meanwhile, we found that women with a pro-inflammatory diet pattern (higher DII score) have a significantly increased risk of pelvic floor disorders even after controlling potential confounders. Such risk would significantly increase 56% among women with a pro-inflammatory diet pattern compared to women with an anti-inflammatory one. The same was true for urinary and fecal incontinence, except for POP. Furtherly, the exposure-response curves revealed linear relationships between DII and pelvic floor disorders and their subsets, meaning that the odds of pelvic floor disorder and their subsets would linearly increase with an increased DII. The BMI-stratified subgroup analysis revealed that obese women with consumption of a pro-inflammatory diet could increase the risk of pelvic floor disorders.

CONCLUDING MESSAGE
Women with a pro-inflammatory diet have an increased risk of pelvic floor disorders, including urinary and fecal incontinence, which is more obvious in those with obesity.

Funding The authors report no conflict of interest **Clinical Trial** No **Subjects** Human **Ethics not Req'd** The data used in this study were from public databases with the ethics committee approval. **Helsinki** Yes **Informed Consent** Yes

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BEST IN CATEGORY PRIZE: PELVIC ORGAN PROLAPSE

A RANDOMISED CONTROLLED TRIAL OF THE CLINICAL AND COST-EFFECTIVENESS OF VAGINAL PESSARY SELF-MANAGEMENT VS CLINIC-BASED CARE FOR PELVIC ORGAN PROLAPSE

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HYPOTHESIS / AIMS OF STUDY

To determine the effectiveness and cost-effectiveness of self-management of a vaginal pessary on prolapse-specific quality of life for women with pelvic organ prolapse when compared to clinic-based care.

STUDY DESIGN, MATERIALS AND METHODS

This was a parallel two-arm, superiority, multicentre randomised controlled trial, which assessed the effectiveness of self-management compared to clinic-based care on prolapse-specific quality of life at 18 months for women who use a pessary for vaginal prolapse. The setting was NHS outpatient pessary clinics in the UK. The inclusion criteria were age ≥18 years, pessary use of any type/material (except Shelf, Gellhorn or Cube pessaries) and retention of a pessary for at least two weeks. Women were excluded if they had limited manual dexterity, were judged to have a cognitive deficit that prevented informed consent or self-management, were pregnant, or would have required the self-management teaching in a language other than English.

The primary outcome was prolapse-specific quality of life at 18 months, measured using the Pelvic Floor Impact Questionnaire-7 (PFIQ−7) (1), which ranges from 0 to 300 with higher scores indicating worse adverse impact. Secondary outcomes included participant-reported complications (study-specific Pessary Complications Questionnaire), general self-efficacy (the General Self-Efficacy Questionnaire) (2), pessary-specific self-efficacy (study-specific Pessary Confidence Questionnaire), and adverse events.

A sample size of 330 women (165 per group) was required to provide 90% power to detect a difference of 20 points in the PFIQ−7 score at 18 months after randomisation, assuming a standard deviation of 50, two-sided alpha of 0.05, and 20% loss to follow-up. Women were randomised to either self-management or clinic-based care on an even allocation basis. Group allocation was by remote web-based application, with minimisation by age, pessary user type (new or existing) and recruiting centre. No participants, researchers or those delivering the intervention were blinded to group allocation.

Women in the self-management group received a 30-minute self-management teaching appointment, an information leaflet, a two-week follow-up call and a support telephone number for their local centre. Women in the clinic-based care group returned to clinic as advised by the treating health care professional in line with that centre's usual pessary practice. Women completed a baseline questionnaire and outcome data were collected via follow-up questionnaires at 6, 12 and 18 months post-randomisation.

A single final analysis was undertaken, with the primary analysis conducted according to the intention-to-treat principle with all randomised participants included. The PFIQ-7 was summarised using descriptive statistics by group for each time-point and comparisons between randomised groups were made using repeated measures mixed models. The analysis adjusted for baseline PFIQ-7 scores and minimisation covariates (age and pessary user type as fixed effects and centre as a random effect). The analysis of secondary outcomes was similar to PFIQ-7, other than repeated measures were not included in the mixed model for general self-efficacy and only counts were reported for adverse events. Pessary complications were measured for each participant by calculating the number of complications reported as a proportion of all the applicable complications listed in the Pessary Complications Questionnaire.

Sensitivity analyses of the primary outcome were carried out under a range of assumptions and analysis methods to investigate, for example, the effect of missing data and crossover. Subgroup analyses of the primary outcome were also conducted (subgroups were age <65 vs >=65, new vs existing pessary user and hysterectomy at baseline vs no hysterectomy at baseline).

A within-trial economic evaluation was conducted to compare the costs and benefits of self-management with clinic-based care over the 18 months after randomisation, measured in terms of quality adjusted life years (QALYs) which was the primary outcome for the cost-effectiveness analysis. Resource use data were collected using a study-specific Health Resource Use Questionnaire.

RESULTS

Participants were recruited between May 2018 and February 2020 at 21 centres across the UK where pessary care was delivered. The recruitment target was met, with 340 women with prolapse and receiving pessary care being randomised; 169 to self-management and 171 to clinic-based care. The PFIQ-7 scores at each time point are summarised in Table 1 along with the results of the primary analysis. The sensitivity analyses and subgroup analyses of the PFIQ-7 data all showed no significant difference between groups. Analysis adjusting for clinic-based care appointments cancelled due to COVID-19 also did not alter the findings.

At 18 months, there was a lower mean proportion of pessary complications (Table 2) in the self-management group (16.7% vs 22.0%, adjusted mean difference –3.8%, 95% CI –6.9% to –0.8%). There was no statistically significant difference between groups in general self-efficacy at 18 months, however self-managing women were more confident in pessary self-management and statistically significant differences were found for all three activities analysed (managing pessary problems, removing their pessary, and inserting their pessary).

There were no reported unexpected serious adverse reactions. There were 30 serious adverse events (17 self-management, 13 clinic-based care), all of which were unrelated to the intervention received.

There was no significant difference in the mean number of QALYs gained between self-management and clinic-based care, but the mean cost was lower for self-management compared to clinic-based care (£578 vs £728). These costs refer predominantly to clinic support and NHS primary and secondary resource use. The incremental net benefit at a willingness to pay of £20,000 per QALY gained was estimated at £564, with an 80.8% probability of cost-effectiveness when compared to clinic-based care. Decision analytic modelling suggested the intervention is likely to remain cost-effective for a minimum of 5 years after the completion of the trial.

INTERPRETATION OF RESULTS

There is no evidence that pessary self-management improves prolapse-specific quality of life, based on no difference being found between groups in the primary outcome measured by PFIQ-7 at 18 months. This primary finding is corroborated by sensitivity and subgroup analyses. However, there is evidence that self-management is effective in reducing complications and improving self-efficacy specific to pessary management activities. There is evidence that pessary self-management is cost-effective, and the absence of any related adverse events indicates that pessary self-management is safe.

CONCLUDING MESSAGE

Self-management as an option for women who use a vaginal pessary to manage pelvic organ prolapse is an acceptable intervention that will not make women's quality of life better or worse than clinic-based care. Self-management will however reduce the pessary-related complications that women experience and will cost health services less to deliver than standard clinic-based care models.

FIGURE 1

Table 1: Summary of PFIQ-7 responses and analysis of differences between groups

Time-point	Self-management			Clinic-based care			Unadjusted[a] mean difference (95% CI)	Adjusted[b] mean difference (95% CI)
	N	Mean	SD	N	Mean	SD		
Baseline	165	32.5	49.6	166	31.7	48.0		
6 months	149	22.7	36.7	157	29.4	47.7	-6.7 (-16.3 to 2.9)	5.8 (-3.2 to 14.9)
12 months	144	30.3	52.0	148	33.1	53.3	-2.9 (-14.9 to 9.2)	-2.4 (-11.9 to 7.0)
18 months	139	32.3	50.9	152	32.5	47.8	0.10 (-11.2 to 11.4)	-5.9 (-15.4 to 3.6)

[a] The unadjusted analysis included no random effects or covariates; [b] Adjusted for age group, pessary user type (new versus existing) and baseline PFIQ-7 score and included random intercepts for participant and centre.

FIGURE 2

Table 2: Percentage of complications reported

	Self-management			Clinic-based care		
	N	Mean	SD	N	Mean	SD
Baseline	167	15.3	13.5	167	17.4	15.8
6 months	152	17.2	14.2	157	18.3	16.3
12 months	144	16.8	14.1	152	21.0	17.7
18 months	142	16.7	13.2	152	22.0	17.3

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BEST IN CATEGORY PRIZE: FEMALE SEXUAL DYSFUNCTION

PELVIC FLOOR DYSFUNCTION ONE YEAR AFTER FIRST CHILDBIRTH IN RELATION TO PERINEAL TEAR SEVERITY.

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HYPOTHESIS / AIMS OF STUDY

The aims of this study were to evaluate pelvic floor dysfunction symptoms one year after delivery and investigate whether adverse functional outcomes after childbirth were related to the degree of perineal injury at delivery. We hypothesized that the prevalence of symptoms of postpartum pelvic floor dysfunction would be related to the degree of perineal trauma

STUDY DESIGN, MATERIALS AND METHODS

This study was part of a large interdisciplinary project involving birth-related perineal injuries, endoanal ultrasonography and postpartum pelvic floor disorders. The present study is a follow-up study in the cohort of the aforementioned project. Women who agreed to participate in the study were examined immediately after birth to diagnose perineal injury. The clinical examination consisted of inspection and bidigital palpation in the lithotomy position. Laceration grade was documented according to the International Classification of Diseases Tenth Revision (ICD-10) World Health Organization (WHO) guidelines. (1) Only mediolateral episiotomy was performed. Data on maternal, obstetric and neonatal characteristics were obtained from medical records. Self-reported pelvic floor function data were obtained using a web-based questionnaire. The scored items of the questionnaire were validated. Women with no/first-degree injuries, second-degree injuries, third-/fourth-degree injuries (obstetric anal sphincter injury, OASIS) and cesarean section were compared. Statistical analyses were performed by analysis of variance for continuous data (ANOVA). The chi-square test or Fisher's exact test was used as needed for categorical data, and the independent-sample t test was used for normally distributed continuous data. Odds ratios were calculated with binary logistic regression analysis, with 95% confidence intervals (CIs). Odds ratios were adjusted for age, body mass index (BMI) and fetal weight when appropriate. Analysis of power was performed in the initial study of the project; because the current study is a follow-up study involving the same cohort, power analysis was not applicable.

RESULTS

The one-year follow-up questionnaire was distributed to 776 women, and 511 participants completed the questionnaire, accounting for a response rate of 66%, 74 (14.2%) were excluded from the analysis of symptoms due to de novo pregnancy, and 12 (2.3%) datasets were illegible/incomplete. There were no differences among the three injury groups regarding maternal age, body mass index, infant head circumference, gestational age at delivery, induction rate, labor augmentation or epidural use. The duration of the active secondary stage of labor was significantly longer in patients with second-degree injuries than in those with an intact perineum or first-degree injuries. There was a significant difference in infant birthweight between patients with no or minor perineal trauma and OASI, with the highest infant birthweight among women affected by OASI. Occiput posterior presentation was more common in the OASI group than in the other groups.

Degree of trauma and odds ratios for symptoms of prolapse, urinary incontinence, anal incontinence, sexual function and other outcomes are presented in Table 1.

Symptoms of prolapse were found in 8.3% of the primiparas one year after delivery. OASI was a risk factor for developing symptoms of prolapse (OR 6.9). In total, 6.2% of patients had to use a finger in the vagina to assist in emptying their bowels.

Urinary stress incontinence was present in 31.0% of women, and 18.0% suffered from urge incontinence. Second degree trauma was a risk factor for stress incontinence (OR 1.6) and giving birth by cesarean section was protective against stress incontinence (OR 0.2) The risk for urge incontinence was elevated in the group with the largest injuries (OR 4.4) An impact on lifestyle was reported by 12.1% of the women with urinary incontinence, and for women with OASI the risk of reporting that they had urinary incontinence that affected their lifestyle was significantly elevated.

Anal incontinence was experienced by 13.9% of women. OASI was a risk factor for anal incontinence (OR 3.1). Severe incontinence with leakage of solid stool was found only after vaginal delivery. The severity of the symptoms seemed more prominent among women in the OASI group, who also had an increased risk of reporting that anal incontinence affected their lifestyle (OR 9.8).

Most of the women were sexually active, although 9.7% of the women had not resumed sexual relations. Dyspareunia was experienced by a large proportion, making up 38.3% of the women who were sexually active. The rate of dyspareunia ranged from 31.3-41.4% in the groups with first/second-degree injuries and cesarean sections and was up to 62.5% in the group with OASI. The risk of experiencing dyspareunia was elevated in women with OASI (OR 2.8) The feeling of being too tight (14.6%) was more common than that of feeling too wide (8.6%).

Perineal pain was experienced by 11.6% of women, and 21 women had mentioned pain that was severe enough to prevent most activities in the last 3 months. This type of severe pain was present in all groups, with elevated risk in the OASI group (OR 4.0) OASI was a risk factor for reporting that that symptoms that originated from their injury still had an impact on daily activity (OR 15). Patients with OASI reported the highest rate of complications.

INTERPRETATION OF RESULTS

OASIS is an evident risk factor for pelvic floor dysfunction after childbirth, but symptoms of pelvic floor disorder were found to be common, even in women with mild to moderate perineal laceration. Dyspareunia and urinary incontinence were the most common symptoms of pelvic floor dysfunction one year after childbirth. Women who underwent cesarean section generally had a low incidence of dysfunction apart from dyspareunia (31%), for which the prevalence was in line with that in women with an intact perineum. Perineal trauma has been recognized as a risk factor for postpartum sexual heath issues. (2)

An elevated risk for pelvic floor dysfunction associated with a larger injury was observed in our study, and women with OASIS reported a significant impact of their symptoms on daily life. This indicates that strategies should remain focused on preventative measures and improved diagnostics for large perineal lacerations.

Functional impairment is an easy way to identify patients who need further evaluation and treatment. In the aftermath of childbirth-related trauma, early identification of pelvic floor dysfunction enables us to intervene with effective strategies (such as pelvic floor rehabilitation) to prevent subsequent aggravation of pelvic floor dysfunction requiring surgery. Predicting and preventing long-term morbidity due to injury to the pelvic floor will also decrease healthcare cost. (3)

CONCLUDING MESSAGE

Pelvic floor dysfunction is common one year after childbirth, even in women with moderate injury. Women with OASIS had significantly higher risks of symptoms of prolapse, urge urinary incontinence, pain, dyspareunia and impacts on daily life. Sexual dysfunction was experienced by a large proportion of women one year after giving birth, indicating a further requisite to address women´s sexual health after childbirth.

FIGURE 1

Outcome measure	No injury/1st degree n = 175 (41.2%)	2nd degree n = 176 (41.6%)	OASIS n = 19 (4.5%)	Cesarean section† n = 54 (12.7%)
Adjusted OR¤ for symptoms of				
Prolapse				
Sense of something bulging	Reference	1.4 (0.6–3.3)	7.7 (2.1–29)	0.5 (0.1–2.0)
Help empty bowel	Reference	0.7 (0.3–1.7)	1.4 (0.2–8.9)	1.0 (0.3–3.4)
Urinary incontinence				
Stress incontinence	Reference	2.6 (1.3–5.1)	2.6 (0.7–10)	0.2 (0.1–0.9)
Urge incontinence	Reference	1.2 (0.7–2.2)	4.8 (1.6–15)	0.6 (0.2–1.4)
Anal incontinence				
Any anal incontinence	Reference	0.9 (0.5–1.7)	2.8 (0.9–9.3)	0.3 (0.1–1.1)
Crude OR for				
Sexual function				
Pain during intercourse	Reference	1.3 (0.8–2.1)	3.1 (1.1–9.0)	0.7 (0.4–1.3)
Other				
Pain (not intercourse)	Reference	1.4 (0.7–2.7)	3.3 (1.1–10)	0.6 (0.2–1.7)
Injury affects daily life	Reference	1.2 (0.4–3.6)	18 (5.1–59)	na
Urine incontinence that affects lifestyle	Reference	1.8 (0.9–3.5)	4.6 (1.5–14)	0.3 (0.1–1.1)
Anal incontinence that affects lifestyle	Reference	2.9 (0.5–17)	23 (2.5–213)	na
Satisfied with suture of injury	Reference	0.5 (0.3–0.9)	0.3 (0.1–0.8)	na

Table 3. Degree of trauma and odds ratios for symptoms of prolapse, urinary incontinence, anal incontinence, sexual function and other outcomes. †Cesarean section was compared to vaginal delivery. Data are OR (95%CI) ¤ Adjusted for age and fetal weight and BMI na = not analysed.

Table 1. Degree of trauma and odds ratios for symptoms of prolapse, urinary incontinence, anal incontinence, sexual function and other outcomes.

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SEXUAL FUNCTION AND PELVIC PAIN AFTER MID-URETHRAL SLING SURGERY

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HYPOTHESIS / AIMS OF STUDY
Since more than thirty years back the mid-urethral sling (MUS) has been used to cure women who suffer from stress urinary incontinence (SUI). Due to last years discussion and doubt about the long-term efficacy and safety we decided to investigate sexual function and risk of pelvic pain for women who had a MUS inserted more than ten years ago.

Our main objective was to examine and assess dyspareunia and pelvic pain after insertion of a MUS due to SUI.

STUDY DESIGN, MATERIALS AND METHODS
All women who 2006-2010 went through MUS-surgery in Sweden (n = 4894) were identified via the Swedish National Quality Register of Gynecological Surgery. Questionnaires were sent to all eligible women in November 2020 (n = 4348). By June 2021 the study closed. The two main techniques for inserting the MUS, the retropubic (TVT) technique and the transobturator technique (TVT-O or TOT) were represented by 1562 and 859 women respectively. Nine cases of absorbable slings and 125 cases of mini-slings were also included in the analysis.

Questions being asked concerned general gynecological background, bladder function and dyspareunia, the Pelvic Organ Prolapse/ Urinary Incontinence Sexual Questionnaire short form (PISQ-12) and Urinary Distress Inventory (UDI-6).

Dyspareunia and pelvic pain were defined as primary outcomes.

RESULTS
A total of 2555 (59%) women returned the questionnaires. From this group we excluded women who did not give information concerning childbirth (n = 53). Hence, left being 2502 participants. Mean age was 64 years (SD 11) and childbirth was reported by 96% with a median parity of 2. Mean BMI at time for surgery was 26. At the ten-year follow-up 80% reported being in a better or much better condition than before the surgery.

Among the responding women 71% answered the question concerning dyspareunia and 77% answered whether suffering from pelvic pain or not. In the group that reported better or much better condition after surgery the rate of dyspareunia was 13%, and 14% admitted pelvic pain. In the group that reported stable or worsened condition after surgery 30% reported dyspareunia and 31% reported pelvic pain, respectively.

In a multivariate logistic regression analysis of dyspareunia we found significant difference between women reporting an improved condition ten years after surgery compared with women who reported stable or worsened condition (odds ratio (OR) 2.9 %, 95% CI 1.9-4.4).

Additionally, pelvic pain turned out to increase with unsuccessful MUS-surgery (OR 1.7 95% CI 1.2-2.3).

Interestingly, there was no difference in dyspareunia when comparing the different techniques, TVT to TVT-O/ TOT (17% vs 15%, OR 0.9, 95% CI 0.9-1.2). Equally important the same was true for pelvic pain (17% vs 18%, OR 1.1, 95% CI 0.8-1.5).

INTERPRETATION OF RESULTS
Ten to fourteen years after having a MUS inserted due to SUI the risk of dyspareunia seems to be higher than normal (1). But, the risk is associated with the outcome of the earlier performed MUS-surgery and depending on whether women consider their condition improved or not. The same applies regarding pelvic pain.

The main techniques, TVT and TVT-O/ TOT do not differ in terms of dyspareunia and pelvic pain.

CONCLUDING MESSAGE
A successful MUS-surgery due to stress urinary incontinence decrease the risk of developing dyspareunia and pelvic pain, also after many years. The technique used for insertion of the MUS is insignificant regarding dyspareunia and pelvic pain.

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PERCEIVED HEALTH STATUS AFTER SUB-URETHRAL SLING REVISION, ABOUT 290 WOMEN FROM THE VIGIMESH REGISTRY.

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HYPOTHESIS / AIMS OF STUDY

Following mid-urethral sling (MUS) insertion, a proportion of women experienced complications. Sling revision may be required in around 3.8% of women after MUS insertion [1]. The purpose of the VIGI-MESH observatory is to collect complications after surgery for urinary incontinence in 30 centers in France and to assess women's health status. The aim of our analysis was to evaluate health status and recovery of women after mid-urethral sling revision.

STUDY DESIGN, MATERIALS AND METHODS

Our sample came from the VIGI-MESH registry considering women who had grade-III complications (Clavien-Dindo classification [2]) after MUS insertion. Grade-IV complications were not included. In case of multiple complications, we considered the first occurrence. Each woman included received a health questionnaire. To appreciate global health status, we used the Minimum European Health Module (MEHM); the first question is about self-perceived health, the second is about chronic morbidity, and the third is the Global Activity Limitation Indicator. The MEHM is used by EuroStat to assess health in European countries every year : https://ec.europa.eu/eurostat/ (last update 2020).

We modeled health status in our sample considering women characteristics, MUS type (retropubic or transobturator), and types of complication (logistic analysis). We compared health status in our sample to the survey of the French population by Eurostat. A good health status was determined by a "good" or "very good" self-perceived health. Women were considered as disabled if they answered "severely limited" in every-day activities. Improvement after MUS revision was defined as "Better" or "Much better" at the PGI-I scale. Physical pain was assessed by a question from the European Health Interview Survey. We added Pelvic Floor Distress Inventory (PFDI-20) to the health questionnaire and question 3 of the Urinary Distress Inventory (UDI-6) was used to assess stress urinary incontinence.

We encouraged women to express themselves freely. A qualitative textual analysis was performed to deduce if women linked their current health status to continence surgeries (MUS insertion and revision) or to persistent urinary trouble, or conversely, if women linked their current health status to other issues. All analysis were performed by an author who was not the women's surgeon.

RESULTS

Among the 393 women who received our questionnaire, 290 returned it (74%) and constitute our sample. MUS insertions took place between January 1998 and December 2020 and revisions between March 2017 and May 2021. Mean age at time of the MUS insertion was 53 +/- 14 and MUS revision was done 62 +/- 70 months (mean) after insertion. MUS were Trans-Vaginal Tape for 61% or Tans-Obturator Tape for 39%. Indications for MUS revision were pain in 127 cases (44%), pain-free exposition in 75 cases (26%) and pain-free urinary trouble in 101 cases (35%). MUS procedures at revision resulted in total or partial removal for 195 cases of the women (67%), MUS section for 38 cases (13%), MUS loosening for 30 cases (10%), or other procedures for 27 cases (9%).

At follow-up, half of women (51%, 144 cases) reported a good health status. It was lower than expected in the French population: 58% according to Eurostat (age standardized). Women noted improvement in 54% of the cases after MUS revision. (Figure 1). Women classifying themselves as having a good health status did not differ from the other regarding Body Mass Index, MUS type, revision indication, revision procedure, and delay to revision (multivariate analysis). Have a good health status was associate with younger age (Odds Ratio (OR) per 10 years (95%CI) = 0,73 (0,55-0,96) p = 0,0248), less reported comorbidity (OR = 0,31 (0,16-0,60) p = 0,0005) and lower proportion of smokers (OR = 0,18 (0,07-0,52) p = 0,0013).

Nine-teen per-cent of women (54 cases) expressed severe limitations in their every-day activities. Comorbidity and smoker status were different between severely limited women and others. MUS type, revision indication, revision procedure and delay to revision were similar. Women who self-classified as severely limited more often encountered multiple revisions (26 vs. 8%, p < 0.0001), more often reported physical pain (51 vs. 11%, p < 0.0001), pelvic pain (70 vs. 50%, p = 0.0177), and stress urinary incontinence (68 vs. 47%, p = 0.0181).

The textual analysis shows us that among the 54 women severely limited, 30 linked their limitations to the MUS procedure or urinary trouble (10% of our sample, 30/290), and 24 to other health issues (Table 1).

INTERPRETATION OF RESULTS

After MUS revision, 54% of the women considered themselves improved by the revision and 51% considered themselves in good health. MUS type, revision indication, or revision procedure were not related to health. The health status was weaker than expected in the French population. In our sample, 10% linked their severe limitations to the MUS insertion or revision. If we exclude these women severely limited, a good health status was reported by 56%; this almost corresponds to the Eurostat data regarding the French population which is 58%. This last result suggests that most of women who experience complication after MUS insertion may have a comparable life to general population.

CONCLUDING MESSAGE

According to our results, a good recovery is achieved for half of women after MUS revision. Nevertheless, 10% remains disabled. Our results are useful to inform women before MUS insertion and after in cases of MUS revision.

FIGURE 1

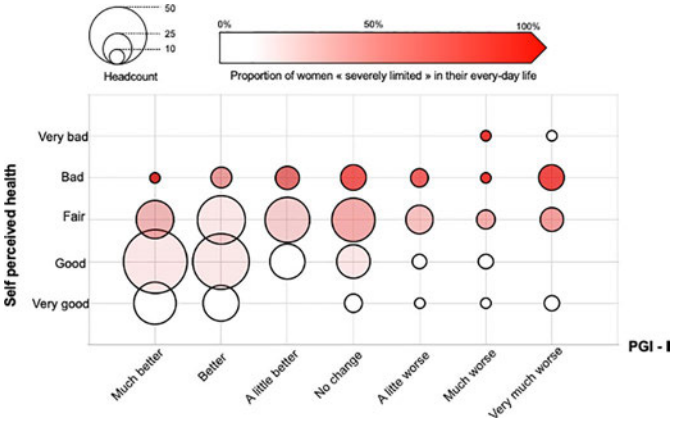

Figure 1: Self perceived health and Patient Global Improvement Impression after mid-urethral sling revision. (n = 290)

FIGURE 2

Topic	Potential link with the mid-urethral sling or urinary trouble
Pain	*"Burns and severe pain"; "The pain has remained"; "very important vaginal pains during my sexual intercourse involve today a new form of disability"; "I can't have sex"; "It is difficult for my husband and I to conceive of a normal sex life"*
Urinary trouble	*"Urinary tract problems"; "I still have to use underwear protection to avoid getting dirty all the time"; "Overactive bladder has not changed, it remains and is disabling"*
Failure	*"It didn't work"; "No changes"; "I expected much more improvement"; "So few results"; "Since the removal, urine leakage is still there, but I have no more pain at all"*
Despair	*"This operation destroyed my life"; "My life has been a long descent into hell."; "I even thought about suicide... my life is hell"; "The mesh ... destroyed my sports life, sex life, etc."; "Quality of life degraded" ; "Broken life" ; "I feel mutilated" ; "My life is in brackets"*
Work	*"Adjustment of workstations to reduce heavy loads"*
	Limitation related to another health issue
Other issue	*"On chemo ..."; "My health is bad because of my severe emphysema"; "Perceived health at 80 because in rehabilitation for total knee prosthesis"*
Success	*"I have my dignity back"; "I have been able to cycle again since the last operation"; "My concerns about bladder leakage were resolved after the tape was removed"*

Table 1: Sample of free expressions about their health among severely limited women.

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Funding ANSM (Agence Nationale de Sécurité du Médicament) **Clinical Trial** No **Subjects** Human **Ethics Committee** CPP (Comité de Protection des Personnes) Ouest III **Helsinki** Yes **Informed Consent** Yes

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434 | www.ics.org/2022/abstract/434

MEDICAL-GRADE MANUKA HONEY INHIBITS MAST CELL DEGRANULATION THROUGH DOWNREGULATION OF PROTEIN KINASE-B/AKT PHOSPHORYLATION: POTENTIAL INTRAVESICAL AGENT IN THE MANAGEMENT OF INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME?

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HYPOTHESIS / AIMS OF STUDY
Interstitial cystitis/bladder pain syndrome (IC/BPS) is a chronic debilitating inflammatory disease that significantly lowers the life quality of its patients. Despite several treatment guidelines, most treatments show variable, short-term improvements, which can vary from one patient to another making IC/BPS difficult to diagnose and treat. Thus, there is an unmet need for more effective therapeutic agents be they naturally derived or synthetic. Whilst the pathophysiology is elusive and multi-factorial, neurogenic inflammation is believed to underlie the chronic bladder inflammation seen in IC/BPS. Histology shows the urothelium in IC/BPS to be thin and denuded with or without ulceration. This allows harmful urinary constituents to leak into the sub-urothelial layer and depolarize bladder sensory nerve endings, resulting in the release of neuroactive substances including substance P (Sub P). Supporting this theory are studies showing that the density of SP-positive nerve endings in IC/BPS is not only significantly higher compared to controls but are located in close proximity to mast cells.

Upon binding to its G protein-coupled receptors (MRGPRX2 and NK-1), Sub P triggers intracellular signalling events resulting in mast cell activation and degranulation. Upon activation, mast cells release of both pre-stored and de-novo synthesized pro-inflammatory mediators, which promote chronic bladder wall inflammation and pain in IC/BPS bladders. The intracellular signalling events underlying mast cell activation and degranulation include phosphorylation of the enzymes phospholipase C-β (PLC-β), phosphoinositide-3 kinase (PI3K), protein kinase B/Akt, extracellular signal-regulated kinase (ERK1/2) and the signal transducer and activator of transcription 3 (STAT3).

Manuka honey is a unique type of honey from New Zealand with a wide range of properties including antimicrobial activity and biofilm inhibition with recent reports highlighting its potential anti-inflammatory and anti-oxidant effects. Interestingly, Medihoney (MH), a medical-grade Manuka honey, has been shown to inhibit the Calcium ionophore-induced degranulation and histamine release in vitro using a human mast cell line (LAD-2).

The aim of the present study was to investigate the potential anti-inflammatory effect of MH against Sub P-induced mast cell degranulation (as a model for neurogenic inflammation), and to explore the potential cellular mechanisms through which MH might exhibit such properties using an in vitro mast cell model.

STUDY DESIGN, MATERIALS AND METHODS
For mast cell activation, human LAD2 mast cells were incubated with Sub P at 37 ˚C and 5% CO2 for 40-min with or without 20-minute pre-incubation with MH at 2, 4 and 6% concentrations. Mast cell degranulation was assessed by quantification of the lysosomal enzyme β-hexosaminidase in the cell culture supernatant. In addition, the effect of MH pre-incubation on the intracellular signalling events underlying mast cell activation was assessed using a specific proteome profiler Phospho MAPK array kit (Cat# ARY003C, R&D Systems, USA) and Phospho(Ser473)/Total Akt Whole Cell Lysate Kit (Cat# K15100D, MSD, USA).

Lactate dehydrogenase (LDH) activity assay (Cat# MAK066, Sigma) was performed to rule out any cytotoxicity on the LAD2 cells.

RESULTS
(1) The effect of MH on Sub P and compound 48/80 (C48/80)-induced LAD2 cell degranulation:

Both the neuropeptide substance P and the MRGPRX2 agonist C48/80 induced 42% and 61% release, respectively. Pre-incubation with MH at 2%, 4% and 6% induced 79%, 97% and 94% inhibition of β-hexosaminidase release induced by both Sub P or C48/80, respectively (Figure 1).

(2) The effect of MH pre-incubation on the Sub P-induced intracellular signalling pathways in LAD2 cells (Phospho MAPRK array kit, ARY003C, R&D Systems):

Over 5-independent assays, 15-minute incubation of the LAD2 cells with Sub P induced significant increase in the levels of phosphorylated protein kinases Akt, at the serine 473 position, lysine deficient protein kinase 1 (WNK1), at the threonine 60 position, and ERK1/2, in addition to STAT3 at the serine 727 position. Akt, WNK1 and STAT3 phosphorylation was significantly and consistently inhibited upon pre-treatment of the LAD2 cells with 4% MH. However, MH did not induce statistically significant inhibition of ERK1/2 phosphorylation (Figure 2).

(3) The effect of MH and substance P on the viability of LAD2 cells (LDH assay, MAK066, Sigma):

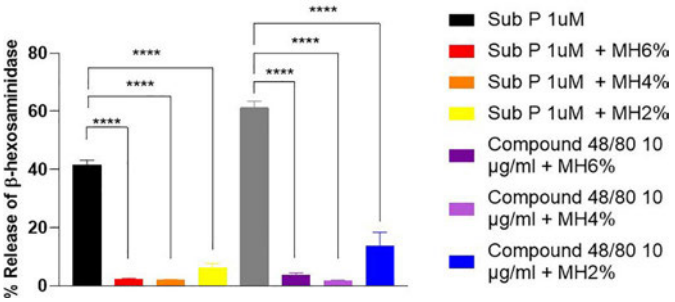
MH at both 2% and 4% concentrations, in addition to substance P 1μM, did not caused any rise of the lactate dehydrogenase activity when compared to the spontaneous levels (controls), suggesting no cytotoxic effect on the LAD2 cells.

It is worth mentioning that this assay was repeated four times using two different batches of LAD2 cells.

INTERPRETATION OF RESULTS
MH strongly and significantly inhibited mast cell degranulation induced by the neuropeptide Sub P or C48/80 in a dose dependent manner. This effect culminated in 97% inhibition of degranulation at 4% MH concentration. Such effect indicates a strong potential for MH as a potent anti-inflammatory agent against neurogenic inflammation. Interestingly, 4% MH inhibited the Sub P-induced phosphorylation of Akt (Serine 473), WNK1 and STAT3 (Serine 727). Besides its crucial role in the positive regulation of mast cell development and survival, PI3K-mediated Akt activation is essential for the pro-inflammatory responses of mast cells upon activation by variable secretagogues, a finding which is consistent with our results. Akt and WNK1 phosphorylation are known to enhance the membrane trafficking of the membrane glucose transporter GLUT1 resulting in increased intracellular glucose uptake and the subsequent metabolic changes, which enhance mast cell activation and pro-inflammatory mediator release. At the same time, STAT3 induces mitochondrial oxidative respiration, thus enhancing mast cell activation. In addition, STAT3 phosphorylation at the position serine 727 position has been reported to be an essential event for mast cell degranulation. This evidence might provide a possible explanation for the mast cell stabilising effects of MH through the inhibition of glucose uptake and subsequent metabolic activity in mast cells. However, this would require further studies investigating GLUT1 membrane trafficking levels, lactic acid and ATP production, and oxygen consumption during LAD-2 activation with or without MH.

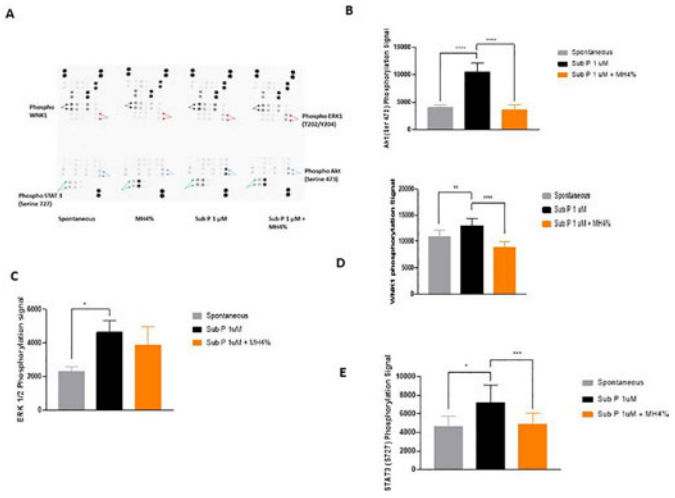
CONCLUDING MESSAGE
Our findings demonstrate for the first time the potential anti-inflammatory properties of MH, through its ability to inhibit mast cell degranulation induced by the neuropeptide Sub P. Moreover, the study provides the first scientific explanation for the stabilisation of mast cells by MH through the inhibition of intracellular Akt, WNK1 and STAT3 phosphorylation. These data support the potential use of MH as an anti-inflammatory agent in neurogenic inflammatory conditions including atopic dermatitis, chronic urticaria, and IC/BPS. Specifically, aqueous solutions of MH might be instilled intra-vesically (via a bladder catheter) to aid the management of patients with IC/BPS.

FIGURE 1



Percentage release of β-hexosaminidase upon incubation with 1µM Sub P and 10 µg/ml C 48/80 with or without pre-incubation with 2, 4 and 6% MH in LAD2 cells. Each bar represents mean ± SEM (** P value <0.0001, n = 9, One way ANOVA).**

FIGURE 2



Phosphorylated levels of 37 protein kinases on nitrocellulose membrane (A) (ARY003C, R&D system). Graphs (B), (C), (D) and (E) show phosphorylation of Akt, ERK1/2, WNK1 and STAT3 (* P value <0.05, ** P value <0.005, *** P value <0.001, n = 8, 2 Way ANOVA)

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SESSION 28 - PROSTATE & URETHRA

Abstracts 435-446
09:35 - 11:05, Hall G
Chair: Prof Kari A O Tikkinen (Finland)

435 | www.ics.org/2022/abstract/435

STRIATED URETHRAL SPHINCTER MOBILITY AND ITS ASSOCIATION WITH POST-PROSTATECTOMY INCONTINENCE

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HYPOTHESIS / AIMS OF STUDY
Post-prostatectomy incontinence (PPI) is common but the underlying mechanisms are not well-understood. There has been recent suggestion that dynamic pelvic floor muscle (PFM) mobility as seen on transperineal ultrasound (TPUS) may predict PPI [1]. We investigated the longitudinal relationship between PPI and PFM mobility pre-operatively and at three and six weeks post-operatively.

STUDY DESIGN, MATERIALS AND METHODS
This is an original prospective study of 40 patients who underwent robotic-assisted radical prostatectomy (RARP) between February and November 2019 by a single surgeon at a high volume robotic centre. Patients completed a 24-hour pad test, assessing pad weight and number, and underwent a transperineal ultrasound (TPUS) to record sagittal images of pelvic structures during maximal voluntary PFM contraction pre-operatively and at post-operative three and six weeks. TPUS images were analysed using InteleViewer software to calculate displacement of striated urethral sphincter, bulbocavernosus and puborectalis muscles. PFM mobility was analysed to determine whether mobility differs between men who are continent and incontinent.

RESULTS
There was significant correlation between pre-operative and post-operative PFM mobility ($p < .05$). With continence defined as use of ≤ 1 pad daily, which was 70% and 95% of patients at three and six weeks, respectively. There is significantly more SUS mobility at post-operative three weeks in continent men (median = 5.13mm) compared to incontinent men (median = 3.90mm), $p = .029$. Whilst the median mobility at post-operative three weeks for BC and PR was greater in continent men than incontinent men, this did not reach statistical significance ($p = .13$, $p = .59$, respectively).

INTERPRETATION OF RESULTS
This study evaluated the longitudinal relationship between pre- and post-operative dynamic PFM mobility and PPI using objective outcome measures of pad number. We showed that there is significantly more SUS mobility in continent men compared to incontinent men at post-operative three weeks. Investigation of dynamic PFM mobility is a novel area of inquiry and to our knowledge, there is no longitudinal data on dynamic PFM mobility pre- and post-prostatectomy. Only one previous cross-sectional study has evaluated the activation of SUS, BC and PR [1]. Stafford et al. analysed which combinations of pelvic anatomy variables, including activation of SUS, BC and PR, functional urethral length and resting position of the anorectal and urethrovesical junctions, best distinguished between men with and without PPI [1]. They observed that greater SUS displacement was associated with continence and was able to compensate for poor BC and PR function and vice versa, to a lesser extent. Our results are in keeping with Stafford et al.'s paper, however, we used a more robust study design with longitudinal data, greater consistency of control variables and more reliable outcome measures.

CONCLUDING MESSAGE
Pelvic floor muscle mobility of SUS may be a reliable independent predictor of PPI. Mechanisms of continence control remain poorly understood and further research is warranted.

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Funding None to declare **Clinical Trial** No **Subjects** Human **Ethics Committee** Western Sydney Local Health District Human Research **Ethics Committee Helsinki** Yes **Informed Consent** Yes

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436 | www.ics.org/2022/abstract/436

THE IMPACT OF PARITY ON URETHRAL MOTION PROFILE: A TRANSLABIAL ULTRASOUND STUDY

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HYPOTHESIS / AIMS OF STUDY
This study describes and compares the urethral motion profile (UMP) of primiparae and multiparae in the immediate postpartum period. The aim is to determine the impact of multiparity on urethral mobility.

STUDY DESIGN, MATERIALS AND METHODS
This descriptive prospective study recruited 65 women (29 primiparae, 36 multiparae) at the maternity ward of a tertiary hospital between March 2021 and December 2021. A sample size of 114 was needed to compare the means of the two sample groups with a power level of 80% (b = 0.20) and a significance level of 95% (a = 0.05). Women were included if they had a vaginal delivery one to seven days prior to recruitment. Patients underwent a two dimensional translabial ultrasound (TLUS) and a standardized interview based on possible confounders such as age, BMI, gestational age, days postpartum at the moment of TLUS performance, birthweight, (history of) grade of perineal rupture and (history of) delivery mode.

46 of the archived ultrasound volumes were eligible for offline analysis. To evaluate UMP, the urethra was manually traced and divided in five segments with six equidistant points on both rest and valsalva volumes (figure). The mobility vector (MV) for each of the six points was calculated using the formula $\sqrt{(Vy-Ry)^2 + (Vx-Rx)^2}$. The intra-rater reliability was calculated using intraclass correlation coefficient (ICC) on a test-retest series of five datasets, suggesting a moderate to good intra-rater reliability (ICC 0.86, 95% CI [0.60-0.98], p < .001).

An independent T-test was performed for all normally distributed data. When the assumption of normality was not fulfilled, a non-parametric Mann-Whitney test was performed. Afterwards, all UMP vectors and the possible confounding factors were correlated to each other and a univariate regression analysis was executed. Data was processed using IBM SPSS version 28.0.

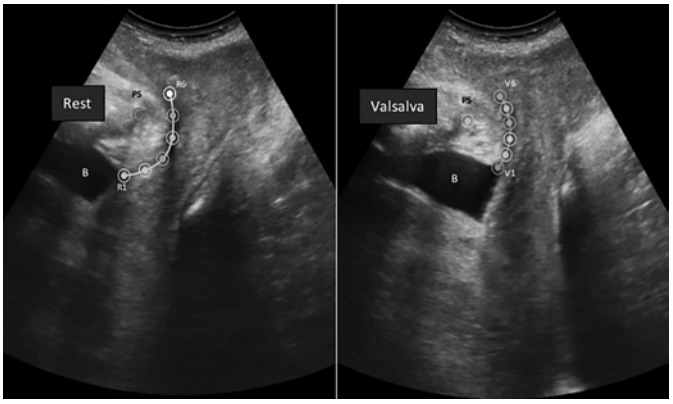
RESULTS
Both groups (primiparae and multiparae) were comparable in terms of age, BMI, gestational age and birthweight. The majority of participants (86.2%, n = 56) was Caucasian. 80.0% (n = 52) had given birth by non-instrumental vaginal delivery, 20.0% (n = 13) by vacuum extraction, none by forceps.

A significant difference between the MV1 to 4 of primiparous and multiparous women was demonstrated, with T-values and p-values of respectively t(44) = 3.88 (p < .001) for MV1, t(44) = 3.82 (p < .001) for MV2, t(44) = 2.65 (p = .012) for MV3 and t(44) = 2.54 (p = .015) for MV4. MV 1 and 2 had the greatest effect sizes with Cohen's d = 0.54 (95% CI [-1.77, -.52]) and d = 0.48 (95% CI [-1.73, -.48]) respectively, followed by MV3 (d = 0.39, 95% CI [-1.36, -.16]) and MV4 (d = 0.28, 95% CI [-1.33, -.14]). The assumption of normality was not fulfilled for MV5 and MV6. A significant difference between primiparae and multiparae was found for MV6 (U = 150.00, exact sig. two-tailed = .012), but not for MV5 (U = 199.50, exact sig. two-tailed = .237). MV1 and MV2 were almost perfectly correlated to each other and strongly correlated with MV3 and MV4. Of all tested confounders, only the overall highest grade of perineal rupture was found to have a significant negative effect on proximal urethral mobility. Univariate generalized linear regression analysis was performed for each of the mobility vectors to investigate the predictive value of parity and the statistically significant correlated factors. Multiparity predicted urethral mobility for MV1 (R2 = .26, F(1,44) = 15.1, p < .001), MV2 (R2 = .24, F(1,44) = 14.1, p < .001), MV3 (R2 = .13, F(1,44) = 6.76, p = .013), MV4 (R2 = .13, F(1,44) = 6.27, p = .016) and MV6 (R2 = .12, F(1,44) = 6.20, p = .017). When overall highest grade of perineal rupture is added to the regression model, the difference in MV1 is predicted for adjusted R2 = .28, F(2,43) = 9.79, p < .001 and in MV2 for adjusted R2 = .29, F(2,43) = 10.15, p < .001.

INTERPRETATION OF RESULTS
The urethral motion profile was found to be significantly greater in multiparae compared to primiparae, with the greatest effect seen in the proximal urethra. Since MV1 and MV2 were strongly correlated to each other and to MV3 and MV4, the added value for clinical practice of measuring all mobility vectors compared to bladder neck mobility can be questioned. Only MV6 was not strongly correlated to the other five mobility vectors. However, the clinical significance of this most distal segment is not yet investigated. Multiparity was found to predict up to 26% of the difference in urethral mobility, being most predictive for MV1 and MV2.

CONCLUDING MESSAGE
This was the first study, as far as the authors know, to assess the UMP of primiparae and multiparae on TLUS in the first week postpartum. The association between multiparity and bladder neck mobility, proven by previous research, can now be extended to the entire urethra (1, 2). However, more research is needed on the superiority of UMP compared to bladder neck mobility, as for clinical significance of MV6. The impact of distinct parity grades on urethral mobility must be further investigated.

FIGURE 1



Translabial ultrasound image at rest (left) and on Valsalva (right). Six equidistant points from the bladder neck (R1, V1) to the external meatus (R6, V6) are indicated. B, bladder; PS, pubis symphysis.

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FEMALE URINARY CONTINENCE AN ENIGMA – LESSONS LEARNED FROM DREADED COMPLICATIONS OF FEMALE URETHRAL SURGERY

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HYPOTHESIS / AIMS OF STUDY
Female urinary continence has a multitude of contributing factors. The pathophysiology behind the continence mechanism in females is far from unraveled. Female urethral surgeries like bladder neck resection (BNR) and urethroplasty carry a risk of incontinence, precluding their active utilization in clinical practice. We present our experience of two significant complications associated with female urethroplasty and their successful management. We have also tried to demonstrate that the risk of incontinence should not hinder the surgeon from offering surgical management for the underlying female urethral pathology.

STUDY DESIGN, MATERIALS AND METHODS
Case one: Total urinary incontinence post female urethroplasty in post-radiation urethral stricture

A 55-year-old lady known case of carcinoma cervix(IIIb) post chemoradiotherapy underwent buccal mucosal graft dorsal onlay urethroplasty for radiation-induced female urethral stricture disease two years back. She presented with a history of urine leak on sneezing and coughing for one year, which progressed to continuous urinary incontinence. On examination, there was a narrow and fibrosed vagina with dry, atrophic periurethral tissue. Urinary incontinence was demonstrated on the stress test. She was treated on conservative measures initially for six months, but her symptoms worsened in the next six months. Her Medical, Epidemiologic, and Social Aspects of Aging (MESA) score was 26 for stress (question 1-9), and her Urogenital Distress Inventory (UDI-6) score was 62.5. Q-tip test was positive suggestive of stress urinary incontinence. On video-urodynamic study (VUDS), she demonstrated multiple stress leak (the first leak came at around 60 ml filling) and abdominal leak point pressure (ALPP) less than 50 cm of H2O with insignificant postvoid residual (PVR). Urethroscopy showed a patulous bladder neck. She was planned for an autologous pubovaginal sling. During surgery, lateral pockets were developed to the level of the bladder neck. An 8X2 cm rectus sheath sling was harvested and placed at the level of the bladder neck with both ends tied in a tension-free manner and taken out through two incisions made two cm lateral to pubic symphysis. She had a smooth postoperative course. The per urethral catheter was removed after one week. She voided normally with no episode of incontinence with voided volume (VV) 170 ml, maximum urinary flow (Qmax) of 31.5 ml/sec with negligible PVR on uroflowmetry. She remained dry after more than one year of follow-up. (Image 1)

Case two: Primary bladder neck obstruction misdiagnosed as female urethral stricture disease post vaginal graft urethroplasty managed successfully with bladder neck resection

34 years old female patient presented with straining to void, incomplete emptying and poor flow. She was managed with regular urethral dilatation and clean intermittent catheterization (CIC) outside with mild improvement. The local examination was unremarkable. Uroflowmetry showed plateau shaped curve with voided volume of 180 ml, Qmax 7.8 ml/sec with PVR of 200 ml. VUDS study was suggestive of bladder outlet obstruction(-BOO). Bladder neck funneling was poor, with constriction was seen at the level of the proximal urethra. A streak of contrast was seen coming till the proximal urethra. On urethroscopy, dense fibrous whitish ring was encountered at the level of proximal to the mid urethra. A diagnosis of female urethral stricture disease was made because of urethroscopy findings, and the patient was subjected to dorsal onlay vaginal graft urethroplasty. However, her Qmax was 9 ml/sec in the immediate post-operative period, which was decreased gradually. She continued to have voiding lower urinary tract symptoms (LUTS) after the removal of the catheter with high PVR. She was subsequently managed with CIC for one more year. A repeat VUDS study showed bladder outlet obstruction with no funneling of the bladder neck. Finally, a diagnosis of primary bladder neck obstruction (PBNO) was made, and she underwent bladder neck resection (BNR). During surgery, circumferential resection was done between 5 and 7 O'clock position from the bladder neck to the end of the proximal urethra, and a good channel was created. Postoperatively Trial without catheter (TWOC) was successful after one week of surgery with Qmax of 22 ml/sec, voided volume of 360 ml, and negligible PVR on uroflowmetry. She is now voiding with good flow after six months of follow-up. (Image 2)

RESULTS
Both the patients of female urethroplasty with complications, one with urinary incontinence and the other with misdiagnosis were managed with additional procedures like puvovaginal sling (first patient) and bladder neck resection (second patient) with a successful outcome. Both patients are voiding well with good flow (Qmax 31.5 ml/sec and 22 ml/sec, respectively) without incontinence.

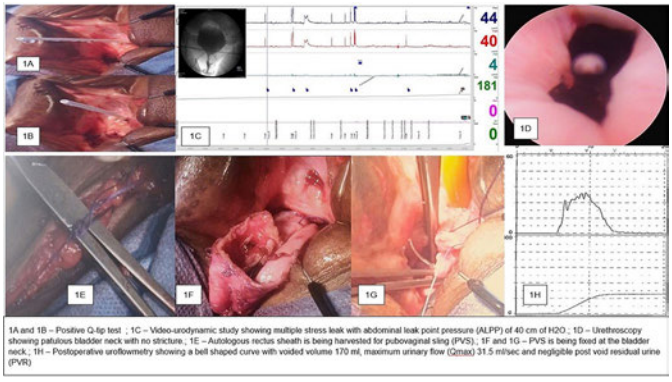
INTERPRETATION OF RESULTS
Besides the Hammock and Integral theories, new evidence like active reflex urethral closing mechanism has emerged recently to understand the pathophysiology of female urinary continence (1). The factors behind continence have both extrinsic and intrinsic components like contraction of the periurethral striated pelvic muscles, the tone of the smooth muscles at the bladder neck, the length of the female urethra, the centripetal force by both rhabdosphincter and lissosphincter, the hormone-sensitive cushioning vascular channel in the submucosa and the transference of intra-abdominal pressure, especially in moments of stress (2). Besides these, age, body mass index, parity, ethnicity, and comorbidities like diabetes, smoking, previous surgery, malignancy, and radiation are the other contributing factors.

In the first case, the outcome of urethroplasty was successful as the patient was voiding well for one year with good flow without the need for additional dilatation. However, her incontinence became bothersome to the extent of total incontinence. The possible reasons are the proximal location of the stricture with long urethrotomy during urethroplasty along with post-radiation changes in carcinoma cervix, which led to the poor periurethral supporting tissue and poor vascularity due to fibrosis along with a narrow atrophic vagina. Initially, conservative management was tried but failed. Poor quality of tissue bed and restricted mobility of the urethra led us to take autologous fascia as pubovaginal sling as the rescue measure in this case (3). The patient ultimately had a satisfactory outcome with the good urinary flow without any leak. So, in a case of post-radiation urethral stricture where the chance of stress incontinence is more due to multiple factors, we should not shy away from giving surgical management in the form of urethroplasty as an anti-incontinence procedure can be performed subsequently for a satisfactory end result.

Inadvertent dilatation for BOO in women can lead to anatomical and functional changes that can create a diagnostic dilemma. In the second case, although initial VUDS was suggestive of the possibility of PBNO, but the history of regular dilation and urethroscopy led us in the wrong direction of urethral stricture disease. The unrestored urinary flow in the post-operative period of urethroplasty questioned the diagnosis. There was a possibility that part of the sphincter might have been damaged while performing the dorsal onlay vaginal graft urethroplasty. Yet, BNR came to the rescue without any further complications like incontinence. Contrary to the first case, young age, healthy periurethral supporting tissue, and adequate waiting time for sphincter healing might have provided the continence mechanism.

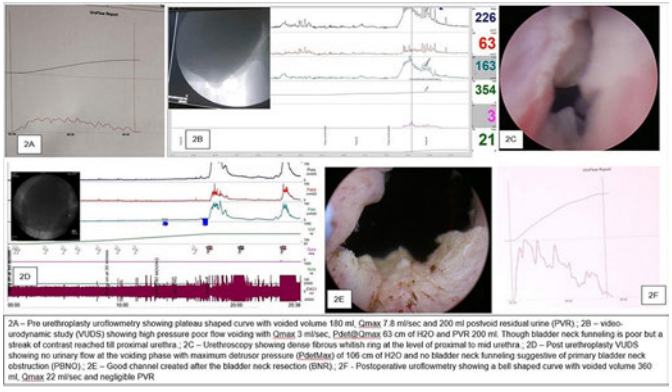
CONCLUDING MESSAGE
Female urinary continence is still undeciphered in many ways. The fear of incontinence should not preclude the reconstructing surgeon from correcting voiding dysfunction in patients, and an anti-incontinence measure can be taken afterward to achieve a successful outcome ultimately.

FIGURE 1



Uroflowmetry, video-urodynamic and operative images of the 55 years old female of carcinoma cervix post radiation post buccal mucosa graft urethroplasty for radiation stricture presented with stress urinary incontinence and underwent pubovaginal sling

FIGURE 2



Uroflowmetry, video-urodynamic and operative images of the 34 years old female of primary bladder neck obstruction (PBNO) misdiagnosed as female urethral stricture disease post vaginal graft urethroplasty managed successfully with bladder neck resection

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LATE COMPLICATIONS OF ADULT HYPOSPADIAS SINGLE STAGE REPAIR IN A TERTIARY CARE CENTRE: A PROSPECTIVE OBSERVATIONAL STUDY

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HYPOTHESIS / AIMS OF STUDY
In our part of the world, many patients present with hypospadias in adult age, where results are often poor and associated with increased complications. Undoubtedly, patients with primary hypospadias should undergo repair between 6 and 12months of age, as recommended by the American Academy of Pediatrics. Nevertheless, in developing countries like India with such a high rate of illiteracy and ignorance, many patients seek attention in adulthood. Complications of hypospadias surgery are more in the later age than in children. Adult hypospadias repair is associated with a longer healing time, higher risk of infections due to hair growth in the penile area, more pain, and bleeding due to nighttime erections. Understanding the risk factors associated with the complications of hypospadias surgery among adults may help in achieving better outcomes. This study was conducted to assess the late complications of single-stage hypospadias surgery in adults.

STUDY DESIGN, MATERIALS AND METHODS
A prospective observational study was conducted at the Department of Urology & Renal Transplant of a tertiary care hospital from February 2018 to August 2019 after approval from the Institutional Ethical Committee [No. 262 (35/2018)]. All hypospadias patients >12years of age were included in this study, and a written informed consent was obtained. Hypospadias cripples (>2 failed hypospadias surgeries), patients with previous unsuccessful repair in the last 12 months, and those undergoing staged repair were excluded from this study. All patients were operated on by a single experienced surgeon, who had an experience of more than 100 hypospadias surgeries. The type of surgery to be performed was decided based on various factors like urethral plate width and degree of chordee, location of hypospadias, glans width, etc.

Relevant predictive factors such as history of previous hypospadias surgery and local examination findings were obtained. Necessary investigations including uroflowmetry were done with optional studies such as RGU/ MCU and cystoscopy when required. Appropriate surgery was performed for each patient, and intraoperative factors such as degree of chordee and spongiofibrosis were noted. Late (after 1 month) complications were studied. Patients were assessed clinically at 1, 3, and 6 months postoperatively and with uroflowmetry. Successful surgery was defined as any patient having all three parameters at 6 months of follow-up: (a) cosmetic—meatal opening in the glans, (b) clinical—clinically satisfied patient voiding well, and (c) investigative—flow on uroflowmetry >12 mL s. Data analyzed using SPSS version 21.0 (IBM SPSS Corp.; Armonk, NY, USA).

RESULTS
50 patients with hypospadias (primary and secondary) were reported during the study period. Of these, 31 patients were enrolled in this study, while 19 patients were excluded (nine crippled hypospadias, seven underwent staged repair, and three refused surgery). Of the 31 patients enrolled, 12 (38.7%) patients had a history of previous hypospadias surgery, while 19 (61.29%) patients were naive. Distributions of pre-operative and Intra-operative parameters are given in Tables 1 and 2.

At the 6month follow-up, urethrocutaneous fistula, glans dehiscence, and urethral stricture were present in eight (25.8%), five (16.12%), and four (14.89%) patients, respectively. Patients were divided into two groups: Group A—patients with complications (n = 17) and Group B—patients without complications (n = 14). Group A had less mean glans width (16.17 mm vs. 19.21 mm) and less mean urethral plate width (5.94 mm vs. 7.35 mm) compared to patients of Group B (statistically significant). There were more patients with poorly developed spongiosum (57.89% vs. 42.11%), history of previous surgery (83.33% vs. 16.67%), and flat urethral plate (76.47% vs. 23.53%) in Group A (statistically significant). The mean stretched penile length (7.88 cm vs. 8 cm), chordee, type of hypospadias, presence of penile torsion, presence of scrotal transposition, type of surgery, and barrier used were comparable between the two groups.

INTERPRETATION OF RESULTS
On univariate logistic regression analysis, parameters comprising glans width (P < .0001), urethral plate shape (P = .011), urethral plate width (P = .005), and history of surgery (P = .018) were found to be significantly associated with post-surgery complications.

With an increase in glans width and urethral plate width by one unit, risk of post-surgery complications decreased by 98.9% and 77.5%, respectively. On the other hand, patients with a history of surgery and flat urethral plate had significantly higher chances of post-surgery complications with odds ratio of 8.571 and 8.125, respectively.

Furthermore, on multivariate logistic regression analysis, glans width (P < .0001) was the only parameter found to be significantly associated with post-surgery complications. On increasing the glans width by one unit, risk of post-surgery complications decreased by 80.3% with an adjusted odds ratio of 0.197.

CONCLUDING MESSAGE
Several factors are associated with significant complications in adult hypospadias single stage repair. Small glans width, flat urethral plate, small urethral plate width, history of previous failed repair, and poorly developed spongiosum were found to be significant on univariate analysis, whereas glans width was the only significant factor on multivariate analysis.

Our study was limited by a small sample size and short-term follow-up of patients. This study being an observational study is prone for observer bias.

FIGURE 1

Pre-operative parameter	Frequency
Mean age	20.8+7.87
Uroflowmetry pattern	
Normal	31(100)
Type	
Sub coronal	1(3.22)
Distal Penile	15(48.38)
Mid penile	9(29.03)
Proximal penile	6(19.35)
Median meatus and urethral calibre (Fr)	12-14 Fr
Glans	
Cleft	31(100)
Flat	0
Mean Glans width (mm)	17.54 + 1.76
Previous Repair	
Yes	12(38.7)
No	19(61.3)
Urethral Plate	
Grooved	14(45.16)
Flat	17(54.83)
Mean Urethral plate width (mm)	6.58+1.18
Mean Stretched penile length (cm)	7.8+0.75

Table 1. Distribution of preoperative parameters

FIGURE 2

Intra-operative Parameter	Frequency
Chordee	
Yes	25(80.6)
No	6(19.4)
<30	2184)
30-60	4(16)
Spongiosum	
Poor	19(61.3)
Moderate	12(38.7)
Surgery	
TIP Urethroplasty	24(77.41)
Tubularized transverse preputial island flap urethroplasty	6(19.35)
Mathieu Flap	1(3.22)
Barrier layer	
Spongiosum + Tunica Vaginalis	14(45.17)
Dartos + Tunica Vaginalis	11(35.48)
Tunica Vaginalis	6(19.35)
Orthoplasty (n=25)	
Degloving	11(44)
Dorsal Plication	12(48)
Ventral Corporotomy	2(8)
Neo Meatus	
Glans	31(100)

Table 2. Distribution of Intra-operative parameters

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THE CLINICAL FRAILTY SCORE AS A PREDICTOR OF TRIAL OF VOID OUTCOMES IN MEN UNDERGOING TRANSURETHRAL RESECTION OF PROSTATE SURGERY

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HYPOTHESIS / AIMS OF STUDY
With the growing geriatric population, the prevalence of frailty has exponentially increased with a subsequent surge in the number of frail patients undergoing surgeries. One such common operation is the transurethral resection of prostate (TURP) for the treatment of benign prostatic hyperplasia. Whilst there is a link demonstrating frailty and general adverse post-operative outcomes, there is limited research specifically on frailty and trial of void (TOV) outcomes post TURP.

This study aims to investigate possible associations between frailty, TOV outcomes, and post-operative complications following a TURP.

STUDY DESIGN, MATERIALS AND METHODS
A retrospective review was conducted on adult patients treated with TURP from two hospitals within Australia, from 01 January 2018 to 31 December 2020. Patient demographic data, pre-operative Clinical Frailty Scores, trial of void outcomes, and complications were recorded and analysed. Clinical frailty scores (CFS) were recorded in accordance to the Dalhousie University Clinical Frailty Scale, ranging from 1 (very fit) to 9 (terminally ill). Complications were categorised according to the Clavien-Dindo (CD) grading system.

Data was analysed using IBM SPSS V27. Descriptive analyses were performed. Normally distributed data was analysed using independent t-tests and ANOVA whilst categorical variables were analysed using Chi-square and Fisher's exact tests. P-values < 0.05 were considered statistically significant.

RESULTS
226 patients (mean age 78.1 years, range 46-92 years) were identified for this study. Of these patients, 59 were identified as having a CFS of 1-2 (very fit – well, Group A), 140 patients had a CFS of 3-4 (managing well – vulnerable, Group B), and 27 patients had a CFS of 5-7 (mildly, moderately or severely frail, Group C). No patients were identified as having a frailty score of 8-9 (extremely frail – terminally ill). Within the initial TOV, there was a statistically significant difference in failure rates amongst the 3 groups with Group C having the highest failure rate of 33.3% (9/27), followed by Group B with 14.3% (20/140) and then Group A with 13.6 % (8/59) ($p = 0.04$). On analysis of patients who underwent a second TOV after failing the initial TOV, no significant difference in TOV success was found amongst the patient groups ($p = 0.08$).

Overall 49 patients experienced a post-operative complication. The majority of these complications were CD Grade I and II with 22 and 20 patients respectively. There was one mortality in a patient who had a CFS of 7. No significant association was found between frailty groups and rate of complication or severity ($p = 0.06$).

INTERPRETATION OF RESULTS
In conclusion, greater pre-operative frailty is associated with higher rates of initial TOV failure in post-TURP patients.

CONCLUDING MESSAGE
Early objective identification of elderly patients with increased frailty is useful to help pre-operative counselling and decision making, manage patient post-operative expectations and optimise patient care.

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BEST IN CATEGORY PRIZE: PROSTATE CLINICAL / SURGICAL

SHORT-TERM EFFICACY AND SAFETY OF BIPOLAR TRANSURETHRAL ELECTRO VAPORIZATION AND HOLMIUM LASER ENUCLEATION OF THE PROSTATE FOR MODERATE AND LARGE BENIGN PROSTATIC ENLARGEMENT

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HYPOTHESIS / AIMS OF STUDY

The European Association of Urology (EAU) and the American Urological Association (AUA) guidelines recommend bipolar transurethral vaporization of the prostate (B-TUVP) for men with prostate volumes (PVs) of 30–80 ml but not for those with PV >80 ml. In contrast, holmium laser enucleation of the prostate (HoLEP) has broader indications for its use than B-TUVP. It is currently recommended for the treatment of moderate (PV 30-80 ml) and large (PV >80 ml) benign prostatic enlargement (BPE).

Recently, we introduced the second-generation B-TUVP using an oval electrode (Olympus, Japan) and demonstrated its efficacy and safety for large BPE (PV ≥100 ml). This confirmed the hypothesis that B-TUVP is an alternative treatment option for HoLEP in patients with moderate and large BPE.

This study was a retrospective review of two regional, high-volume centers that compared the efficacy and safety of second-generation B-TUVP against HoLEP in patients with moderate and large BPE, with the aim of evaluating and eventually establishing the future outlook of B-TUVP for BPE treatment.

STUDY DESIGN, MATERIALS AND METHODS

We retrospectively compared clinical data from two regional, high-volume centers employing second-generation B-TUVP and HoLEP for BPE treatment. All procedures were performed between September 2016 and October 2021. Patients with suspected impaired detrusor function, active urinary tract infection, prostate cancer, bladder cancer, urethral stricture, or dementia who were not able to complete outcome measurements were excluded from the study. The two centers shared the same surgical indications. Briefly, surgical indications were International Prostate Symptoms Score (IPSS) >7, maximum flow rate (Qmax) <10 ml/s, persistent or recurrent urinary retention or bladder stones, or post-void residual urine volume (PVR) >100 ml.

The B-TUVP and the HoLEP patient-oriented and treatment outcomes were then retrospectively compared. The main treatment outcomes were measured by IPSS and IPSS Quality of Life Index (IPSS-QoL) at preoperative baseline, then at 1and 3 postoperative months (POM).

RESULTS

This study enrolled 177 consecutive patients with BPE who underwent B-TUVP and 286 consecutive patients who underwent HoLEP. Thus 16 patients (7 with prostate cancer, 2 with bladder cancer, 4 with dementia and 3 in the terminal stages of non-prostate cancer) were excluded from the B-TUVP group. Because of no records of preoperative PV, 4 more patients from the B-TUVP group and 5 patients from the HoLEP group, were also excluded.

In uncatheterized patients with PV 30-80 ml from both the B-TUVP and HoLEP groups, total IPSS and IPSS-QoL scores significantly decreased after surgery (at 1 and 3 POM) compared to baseline within each group ($P<0.001$). Between B-TUVP and HoLEP groups, total IPSS was significantly lower in HoLEP than in B-TUVP at 1 and 3 POM. In catheterized patients with PV 30-80 ml, the rate of achieving catheter-free status after surgery was relatively higher in HoLEP than in B-TUVP but this was not statistically significant. A total of 2 cases in the B-TUVP group required a 2nd procedure for persistent LUTS after the initial session.

In uncatheterized patients with PV >80 ml in both B-TUVP and HoLEP groups, total IPSS and IPSS-QoL scores significantly decreased after surgery (at 1 and 3 POM) compared to baseline within each surgery group ($P<0.001$, Table 1). Between B-TUVP and HoLEP, total IPSS and IPSS-QoL were significantly lower in the HoLEP group than in the B-TUVP group at 1 and 3 POM. In catheterized patients with PV >80 ml, the rate of achieving catheter-free status after surgery was significantly higher in HoLEP than in B-TUVP. A total of 8 cases of B-TUVP required 2nd procedures to address persistent urinary retention, whereas 3 cases of HoLEP had to undergo repeat sessions owing to incomplete morcellation.

The incidence of postoperative fever was significantly higher in B-TUVP than in HoLEP in patients with a PV 30-80 ml but not in PV >80 ml (Table 2). There were 2 cases of septic shock needing catecholamine therapy and one postoperative cerebral cortex infarction (Clavien-Dindo Grade IVb) in a B-TUVP (PV >80 ml) patient. Postoperative urinary incontinence and complications associated with morcellation occurred only in the HoLEP group and all cases were treated conservatively (Clavien-Dindo GradeI). Both B-TUVP and HoLEP (PV >80 ml) groups had a case each which necessitated a resurgery for transurethral coagulation (Clavien-Dindo Grade IIIb).

INTERPRETATION OF RESULTS

This study was the first retrospective comparative study evaluating the short-term efficacy and safety of second-generation B-TUVP and HoLEP for moderate (PV 30-80 ml) and large (PV >80 ml) BPE. In uncatheterized patients, voiding symptoms and patients' QoL derived from IPSS and IPSS-QoL clearly and significantly improved after B-TUVP and HoLEP in both PV 30-80 ml and PV>80 ml, but these improvement rates were consistently greater in HoLEP than in B-TUVP.

In catheterized patients, both B-TUVP and HoLEP exhibited their efficacy through high rates of postoperative catheter-free status in this study. Particularly, for catheterized patients with PV >80 ml, the postoperative catheter-free rate was significantly higher in HoLEP than in B-TUVP with a similar trend seen in patients with PV 30-80 ml. These findings indicated that HoLEP has clinical advantages over B-TUVP in achieving catheter-free status for patients with urinary retention, especially in patients with PV >80 ml. B-TUVP may have less of an advantage in producing this outcome as it sometimes results in inadequate vaporization and residual adenoma compared to HoLEP in PV >80 ml.

The most common surgical complication of both B-TUVP and HoLEP was postoperative fever which was more frequent in B-TUVP than in HoLEP, especially in patients with PV 30-80 ml. One of the general drawbacks of HoLEP was its prerequisite for morcellation during surgery which subsequently leads to serious operative complications including bladder injury. Furthermore, the rate of postoperative incontinence was significantly higher in HoLEP than in B-TUVP. Urinary incontinence was well-documented as a major complication of HoLEP, with incidence rates at 10.7-16.2%. Most case of urinary incontinence were reported as transient and, in this study, all urinary incontinence was transient and ceased without any treatment within 6 months. The rate of hemoglobin reduction was lower in B-TUVP than in HoLEP suggesting that the bipolar system has a higher hemostatic capacity than holmium laser.

CONCLUDING MESSAGE

This is the first retrospective study investigating the short-term efficacy and safety of second-generation B-TUVP in comparison with HoLEP for moderate and large BPE.

For both uncatheterized and catheterized patients, improvement in LUTS, achievement of catheter-free status, and the non-necessity of a follow-up procedure were predominant in HoLEP, and these outcomes were more prominent in patients with large BPE of PV >80 ml.

However, B-TUVP resulted in less blood loss postoperatively, with shorter operative duration, and less urinary incontinence in both moderate and large BPE suggesting that B-TUVP is a well-tolerated surgical modality, irrespective of prostate volume, over HoLEP.

FIGURE 1

Table 1: Patient-oriented and surgical outcomes of bipolar transurethral electro vaporization of the prostate (B-TUVP) and holmium laser enucleation of the prostate (HoLEP) in patients with prostate volume >80 ml

		B-TUVP	HoLEP	P value
All patients		N = 82	N = 115	
Age(years-old)		74.4 ± 7.5	73.0 ± 6.6	0.157
Prostate volume (ml)		119.4 ± 44.9	111.2 ± 29.8	0.126
Operative time (mins)		120.28 ± 31.0	164.6 ± 43.0	< 0.001
Duration of post-operative catheter implantation (days)		3.0 ± 1.4	2.5 ± 1.2	0.009
Hospital stay period after operation (days)		6.8 ± 2.7	7.0 ± 2.8	0.213
Hemoglobin (g/dl)	Pre	13.5 ± 1.6	13.5 ± 1.8	0.856
	1POD	13.0 ± 1.6	11.4 ± 2.0	< 0.001
	Change rate (%)	96.0 ± 6.5	84 ± 10.6	< 0.001
Necessity of 2nd procedure		8 (9.8%)	3 (2.6%)	0.031
Uncatheterized patients		N=48	N=76	
Total IPSS	Pre	20.3 ± 8.6	22.3 ± 8.4	0.295
	1POM	13.8 ± 8.2	8.8 ± 6.2	0.001
	Change rate (%) at 1POM	86.0 ± 63.9	50.4 ± 64.2	<0.001
	3POM	10.6 ± 8.0	6.0 ± 5.0	0.002
	Change rate (%) at 3POM	62.2 ± 42.0	27.0 ± 20.0	<0.001
IPSS-QoL	Pre	4.9 ± 1.1	4.7 ± 1.3	0.581
	1POM	3.7 ± 1.7	2.5 ± 1.8	0.005
	Change rate (%) at 1POM	78.5 ± 33.0	58.5 ± 72.2	0.005
	3POM	2.9 ± 1.8	1.7 ± 1.5	0.002
	Change rate (%) at 3POM	63.3 ± 39.0	30.7 ± 30.8	0.001
Catheterized patients		N=34	N=39	
Achieving catheter free status after surgery		24 (71%)	39 (100%)	< 0.001

Table1

FIGURE 2

Table 2: Surgical complications of B-TUVP and HoLEP in patients with prostate volume of 30-80 ml and >80 ml

		B-TUVP	HoLEP	P value
PV 30-80ml	Number of cases	75	166	
	Post operative fever	14 (19%)	4 (2.4%)	< 0.001
	Bladder tamponade	1 (1.3%)	0	0.142
	Prostate capsule injury	0	1 (0.6%)	0.503
	Bladder neck perforation	0	2 (1.2%)	0.339
	Urethral stricture	1 (1.3%)	5 (3.0%)	0.442
	Post operative incontinence	0	9 (5.4%)	0.040
PV >80ml	Number of cases	82	115	
	Post operative fever	15 (18%)	11 (10%)	0.075
	Bladder tamponade	0	2 (1.7%)	0.220
	Bladder injury	0	2 (1.7%)	0.218
	Prostate capsule injury	0	1 (0.9%)	0.393
	Prostate neck perforation	0	1 (0.9%)	0.389
	Urethral stricture	0	1 (0.9%)	0.397
	Post operative incontinence	0	15 (13%)	< 0.001

Table2

Funding The authors have no COI to disclose **Clinical Trial** Yes **Public Registry** No **RCT** No **Subjects** Human **Ethics Committee** YKH21-69 and KSSH3219-07 **Helsinki** Yes **Informed Consent** Yes

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ENDOSCOPIC AND FUNCTIONAL RESULTS AFTER AQUABLATION FOR PATIENTS WITH BENIGN PROSTATIC HYPERPLASIA: A PRIMARY EXPERIENCE IN A TERTIARY CARE CENTER.

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HYPOTHESIS / AIMS OF STUDY
We report our clinical experience with Aquablation in terms of perioperative and 1-year functional outcomes, along with 3- months and 1-year endoscopic evaluation after the procedure.

STUDY DESIGN, MATERIALS AND METHODS
From 10/2018 to 09/2021, patients referred to our center with BPH-related LUTS, International Prostate Symptom Score (IPSS) $\geq$10, maximum urinary flow rate (Qmax) $\leq$12 mL/ s, and prostate volume $<$80 mL were enrolled in this prospective study to undergo Aquablation. Exclusion criteria were prostate cancer diagnosis, previous prostate surgery, indwelling catheter, urethral stenosis, bladder stones, prostatic calcifications. Demographics, perioperative data and complications (according to the Clavien–Dindo system) were collected. Functional outcomes were assessed at 1, 3, 6, and 12 months with IPSS, Sexual Health Inventory for Men (SHIM), Male Sexual Health Questionnaire for ejaculatory dysfunction (MSHQ-EjD), uroflowmetry and evaluation of post void residue (PVR). In addition, the patients underwent cystoscopy at 3 and 12 months after the surgical procedure. During the cystoscopy the presence of residual fluffy tissue or mucous flaps, the preservation of the veru montanum and the ureteral orifices as well as the presence of scar tissue at the level of the bladder trigone were evaluated. Moreover, the quality of the ablation at cystoscopy was rated according to a Likert scale (1-poor; 5-excellent).

RESULTS
68 patients were enrolled in the study, the mean BMI was 26.1. Before the surgery the median Qmax, IPSS, QoL score and mean PVR were respectively 8 (6-10), 22 (16-28), 4 (3-5) and 76 ml. The median ablation time was 5.12 (2.13) min. The median catherization time and hospital stay were 3 (3-4) and 4 (4-5) days, respectively. 13 postoperative complications were recorded (19.1%), of which 4 classified as Clavien-Dindo grade $>$ 2 (5.9%), namely 2 (2.9%) anemization requiring transfusions, 2 (2.9%) acute urinary retention after catheter removal. The mean (SD) Qmax at 1, 3, 6 and 12 months was 20.2 (10.8), 17.7 (3.4), 18.3 (6.2) and 17.3 (6.1) ml/s, respectively. The median IPSS urinary symptom score was 5 (2-8) after 1 month and further improved to 2 (1-4) one year after surgery.

INTERPRETATION OF RESULTS
The median IPSS QoL score and mean PVR reached 1 (0-1) and 17 ml (5,6) at 12th month. No patients developed postoperative erectile dysfunction, while 2 (2.9%) reported loss of antegrade ejaculation. At 3-month follow-up cystoscopy, no residual fluffy tissue, as well as no damage to the verumontanum, ureteral orifices or bladder trigone were recorded. In 19/68 (27.9%) patients non-obstruent mucosal flap was shown. The median quality of the ablation was 3 (3-4). All these findings were confirmed at 12-months cystoscopy.

CONCLUDING MESSAGE
Ablation is a feasible, safe and effective procedure for the treatment of benign prostatic hypertrophy. This is demonstrated by endoscopic and functional results one year after the procedure.

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LONGITUDINAL, ONE-YEAR OUTCOMES FOR URINARY CONTINENCE AND QUALITY OF LIFE AFTER NON-NERVE-SPARING ROBOT-ASSISTED RADICAL PROSTATECTOMY WITH ADVANCED RECONSTRUCTION OF VESICOURETHRAL SUPPORT

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HYPOTHESIS / AIMS OF STUDY

Robot-assisted radical prostatectomy (RARP) using the da Vinci surgical system has become the standard procedure for localized prostate cancer. RARP is considered a minimally invasive technique with a low complication rate, low transfusion rate, and short hospital stay. Unfortunately, however, a certain number of patients had a reduced quality of life (QOL) due to postoperative urinary incontinence. Various factors were reported to influence urinary incontinence RARP. In addition, techniques such as nerve sparing, bladder neck preservation, Retzius sparing, and the Hood technique have been devised for achievement of urinary continence. Advanced Reconstruction of Vesicourethral Support (ARVUS) is a technique reported in 2017 for achievement of urinary continence [1]. We had performed ARVUS in patients undergoing non-nerve-sparing RARP from 2019. The purpose of this study is to evaluate the effect of ARVUS on postoperative urinary continence in non-nerve-sparing RARP.

STUDY DESIGN, MATERIALS AND METHODS

Patients who underwent non-nerve-sparing RARP between October 2010 and December 2020 at our department for prostate cancer (stages cT1–cT3 N0 M0) were included in the present study. All patients consented after being fully informed in accordance with the ethics committee at our institution. All study data were analyzed retrospectively. Age, BMI, prostate-specific antigen (PSA), prostate volume (PV), membranous urethral length (MUL), Gleason score (GS), clinical stage were recorded. Cystography was performed to measure the distance from the symphysis pubis to the bladder neck and the posterior urethrovesical angle. IPSS, ICIQ-SF, QOL index, and number of pads used each day were evaluated before RARP and at 1, 3, 6, and 12 months after RARP. Data are presented as median value and interquartile range (IQR). To exclude possible influences on urinary continence after RARP other than ARVUS, 1:1 propensity score matching was conducted. Propensity scores were estimated by multivariable logistic regression using variables such as age, clinical stage, BMI, PV, and MUL. Demographic factors were evaluated using the Mann-Whitney U test, chi-square test. To identify factors associated with urinary continence using the PICOMB definition at 12 months postoperatively, multivariable logistic regression analysis was performed [2]. Values of $p < 0.05$ were considered significant. Statistical analyses were performed using EZR, which is a modified version of R Commander.

RESULTS

In Table 1 patients' characteristics are presented. The number of patients in non-ARVUS group was 41 and ARVUS group was 41. Median age, BMI, PV, and MUL for the ARVUS and non-ARVUS groups were 70.5 and 69 years, 23.2 and 24.1 kg/m^2, 24.2 and 26.6 ml, and 12.5 and13.8 mm, respectively. The distance from the symphysis pubis to the bladder neck at cystography was significantly shorter in the ARVUS group (median 10.9 mm vs. 17.6 mm, $p < 0.001$) and the posterior urethrovesical angle was significantly smaller in the AUVUS group (median 129.6 degrees vs. 145 degrees, $p < 0.001$). Table 2 showed ICIQ-SF total score, question 1, 2, 3, IPSS total score, and QOL index between two groups. In the ICIQ-SF, questions 1, 2, 3, and total scores were not significantly different at 1 and 3 months postoperatively, but the ARVUS group was significantly better at 6 and 12 months postoperatively. In terms of IPSS, the ARVUS group was significantly better than the non-ARVUS group after 3 months postoperatively. The QOL index was significantly better in the ARVUS group than in the non-ARVUS group at 6 months postoperatively, but there were no significant differences at other time points. Pad free rates were 9.1% and 6.8% in the non-ARVUS and ARVUS groups at 1 month, 20.5% and 15.9% at 3 months, 36.4% and 34.1% at 6 months, and 45.5% and 61.4% at 12 months postoperatively. In a multivariable logistic regression analysis with age, BMI, PV, MUL, and ARVUS performed as factors, MUL and ARVUS were significant factors in achieving PICOMB definition at 12 months postoperatively.

INTERPRETATION OF RESULTS

In the present study, postoperative urinary continence and QOL were both better with ARVUS group. The mechanism of ARVUS is to reinforce the vesicourethral anastomosis in a hammock-like shape, which is similar to the mechanism after urethral sling surgery, and is useful against urinary incontinence. In our study, postoperative cystography showed that the posterior urethrovesical angle in the ARVUS group was more sharply angled than in the non-ARVUS group. This was thought to be due to dorsal support of the urethra. In addition, for the evaluation of urinary continence, International Continence Society (ICS) recommended pad weight, not pad count, for the assessment of postoperative urinary incontinence after radical prostatectomy. The International Consultation on Incontinence Questionnaire-Short Form (ICIQ-SF) was developed as an international common questionnaire for the assessment of urinary incontinence symptoms and QOL [3]. In our study, there was no difference in pad free rate between the ARVUS and non-ARVUS groups, but the ARVUS group was significantly better in terms of urinary continence on the ICIQ-SF, suggesting that it is difficult to evaluate urinary incontinence by the number of pads used.

CONCLUDING MESSAGE

Our study suggests that ARVUS for patients who underwent non-nerve-sparing RARP may improve postoperative urinary continence. The limitations of this study were the small number of cases. If the number of cases is increased, a more detailed study will be possible in the future.

FIGURE 1

Table 1

Patients characteristics (non-ARVUS n=41, ARVUS n=41)

		median	IQR	*P-value*
Age (years)	non-ARVUS	69	65-72	0.153
	ARVUS	70.5	67-73	
BMI (kg/m^2)	non-ARVUS	24.1	20.7-25.8	0.45
	ARVUS	23.2	22.3-25.7	
PSA (ng/ml)	non-ARVUS	8.6	5.9-14.0	0.229
	ARVUS	8.4	5.8-11.1	
PV (ml)	non-ARVUS	26.6	22.6-39.2	0.796
	ARVUS	24.2	20.2-40.8	
MUL (mm)	non-ARVUS	13.8	11.1-15.1	0.922
	ARVUS	12.5	10.2-15.9	
cT stage T1c/T2/≥T3	non-ARVUS	1/28/12		0.98
	ARVUS	0/27/14		
Gleason score 6 / 7 / >8	non-ARVUS	0/17/24		0.906
	ARVUS	0/19/22		
NCCN risk Low / Intermediate / High	non-ARVUS	0/13/28		0.972
	ARVUS	0/14/27		
Total surgical time (min)	non-ARVUS	328.5	299.5-360.5	0.362
	ARVUS	320.5	265.5-364.0	
Console time (min)	non-ARVUS	250.5	220.0-281.5	0.12
	ARVUS	234	190.5-276.5	
Estimate blood loss (ml)	non-ARVUS	100	68.5-212.5	0.192
	ARVUS	130	100.0-235.0	

FIGURE 2

Table 2 Longitudinal outcomes for ICIQ-SF, IPSS ,and QOL index

	/ month	pre-RARP	1	3	6	12
ICIQ-SF Total score	non-ARVUS, median (IQR)	0.0 (0.0-3.5)	11.5 (8.0-15.5)	8.0 (5.0-11.0)	6.0 (4.0-9.0)	5.0 (3.5-7.5)
	ARVUS, median (IQR)	0.0 (0.0-1.5)	9.0 (7.0-13.5)	6.5 (4.0-9.0)	4.0 (0.0-6.5)	3.0 (0.0-6.0)
	P-value	0.171	0.098	0.218	0.017	0.013
ICIQ-SF Question 1	non-ARVUS, median (IQR)	0.0 (0.0-1.0)	4.0 (4.0-5.0)	4.0 (2.0-4.0)	2.0 (1.0-4.0)	1.5 (1.0-3.0)
	ARVUS, median (IQR)	0.0 (0.0-0.0)	4.0 (3.0-4.0)	3.0 (1.0-4.0)	1.0 (0.0-3.0)	1.0 (0.0-2.0)
	P-value	0.087	0.201	0.068	0.005	0.012
ICIQ-SF Question 2	non-ARVUS, median (IQR)	0.0 (0.0-2.0)	2.0 (2.0-4.0)	2.0 (2.0-2.0)	2.0 (2.0-2.0)	2.0 (2.0-2.0)
	ARVUS, median (IQR)	0.0 (0.0-0.0)	2.0 (2.0-4.0)	2.0 (2.0-2.0)	2.0 (0.0-2.0)	2.0 (0.0-2.0)
	P-value	0.193	0.211	0.106	0.02	0.016
ICIQ-SF Question 3	non-ARVUS, median (IQR)	0.0 (0.0-1.0)	5.0 (2.5-8.0)	2.0 (1.0-5.0)	2.0 (1.0-3.5)	1.0 (1.0-3.0)
	ARVUS, median (IQR)	0.0 (0.0-0.0)	3.0 (1.5-5.0)	2.0 (1.0-3.0)	1.0 (0.0-2.0)	0.0 (0.0-1.5)
	P-value	0.19	0.023	0.115	0.015	0.004
IPSS Total score	non-ARVUS, median (IQR)	8.0 (4.5-12.5)	15.0 (10.0-20.0)	11.0 (6.5-16.5)	7.0 (5.0-11.0)	8.0 (4.0-11.0)
	ARVUS, median (IQR)	7.0 (3.0-10.0)	12.0 (7.0-17.5)	6.5 (4.0-10.5)	5.5 (3.0-9.0)	4.5 (3.0-8.0)
	P-value	0.14	0.081	0.004	0.026	0.009
QOL Index	non-ARVUS, median (IQR)	3.0 (2.0-4.0)	5.0 (3.0-6.0)	4.0 (3.0-5.0)	3.0 (2.0-4.0)	2.5 (2.0-4.0)
	ARVUS, median (IQR)	2.5 (1.0-3.0)	4.5 (3.0-6.0)	3.0 (2.0-6.0)	2.0 (1.0-3.5)	2.0 (1.0-4.0)
	P-value	0.113	0.396	0.202	0.024	0.248

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IS PROSTATIC URETHRAL LIFT BENEFICIAL TREATMENT FOR PATIENTS WITH MULTIPLE COMORBIDITIES?

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HYPOTHESIS / AIMS OF STUDY

Prostatic urethral lift (PUL) can be performed in patients at high risk for general anesthesia due to multiple comorbidities, under local anesthesia. However, the clinical efficacy of PULs in patients with multiple comorbidities remains unknown. Therefore, this study aimed to evaluate the clinical efficacy of PUL in patients with multiple comorbidities by comparing the clinical efficacy in these patients with that in healthy individuals.

STUDY DESIGN, MATERIALS AND METHODS

We performed a retrospective observational cohort study, in which patients who underwent PUL between December 2016 and January 2019 at a single tertiary care center were categorized into two groups: healthy individuals who wanted to preserve sexual function (Group 1) and patients with high comorbidities who were at high risk for general anesthesia based on an American Society of Anesthesiologists (ASA) score of ≥ 3 (Group 2). The International Prostate Symptom Score (IPSS), maximum urinary flow rate (Qmax), post-void residual urine (PVR), International Index of Erectile Function-5 (IIEF-5), and Male Sexual Health Questionnaire for Ejaculatory Dysfunction Short Form (MSHQ-EjD) were obtained preoperatively and compared throughout the 2-year follow-up. This study was approved by Ethical Committee of the Korea University Hospital.

RESULTS

Sixty-six patients were included in this study, of whom 36 were stratified as healthy individuals who underwent PUL for preserving ejaculatory function (Group 1) and 30 as having high comorbidity and underwent PUL under local anesthesia (Group 2). There were significant differences in patient age (Group 1 vs Group 2: 60.7 ± 5.3 vs75.3 ± 8.1, $p < 0.001$) and comorbidities based on group classification characteristics; however, there were no differences between the groups regarding prostate volume, symptom severity, and deployed implants.

INTERPRETATION OF RESULTS

In Group 1, IPSS, IPSS quality of life (QoL), and Qmax were significantly improved and main-tained during follow-up, whereas in Group 2, improvements in these parameters were not maintained during follow-up, except for IPSS QoL (Table 1.). In both groups, there was no significant decline in ejaculatory and sexual parameters (assessed by IIEF and MSHQ scores) over the course of the 2-year and 1-year follow-up, respectively. Eleven patients (36%) in Group 2 required additional treatment for the recurrence of lower urinary tract symptoms.

CONCLUDING MESSAGE

Patients with multiple comorbidities had a low therapeutic effect after PUL, suggesting a high rate of treatment failure. This study suggests that comorbidity status should be considered when evaluating the expected benefits for PUL in preoperative counseling. Although PUL is a conceivable alternative in patients at a high risk for general anesthesia due to comorbidities, it should be recognized that severe and multiple comorbidities can lead to treatment failure after PUL. Future studies based on new concepts introduced in recent years should aim to determine whether other minimally invasive treatments are indeed beneficial for these patients.

FIGURE 1

Table 1. Paired outcomes after prostatic urethral lift in both groups.

Variable	1 month		3 months		6 months		12 months		24 months	
	Healthy individuals	High comorbidity	Healthy individuals	High comorbidity	Healthy individuals	High comorbidity	Healthy individuals	High comorbidity	Healthy individuals	High comorbidity
IPSS, n	31	30	34	30	32	30	30	26	23	18
Baseline, mean±SD	22±5.0	19.4±5.9	21.5±5.1	19.4±5.9	21.7±5.2	19.4±5.9	22.0±5.1	19.7±6.3	22.5±5.3	17.0±4.5
Follow-up, mean±SD	13.4±8.3	14.8±6.9	12.3±6.2	16.1±8.7	13.8±5.8	16.5±7.6	14.6±6.2	17.2±7.1	13.9±6.6	14.8±4.7
Change, mean±SD	-8.6±7.1	-4.7±6.7	-9.2±6.3	-3.3±8.5	-7.9±6.6	-2.9±7.1	-7.4±6.6	-2.6±3.1	-8.6±6.1	-2.2±4.5
Change P-value	<0.001*	0.001*	<0.001*	0.045*	<0.001*	0.03*	<0.001*	0.001*	<0.001*	0.054*
Comparison P-value	0.032		0.002		0.006		0.001		0.001	
QOL, n	31	30	34	30	32	30	30	26	23	18
Baseline, mean±SD	5.0±1.1	4.5±1.0	4.9±1.1	4.5±1.0	4.9±1.1	4.5±1.0	4.9±1.2	4.5±1.0	4.8±1.2	4.1±0.9
Follow-up, mean±SD	3.1±1.7	3.4±1.4	2.5±1.4	3.5±1.7	2.8±1.4	3.3±1.3	2.9±1.4	3.5±1.3	3.0±1.3	3.6±0.9
Change, mean±SD	-1.9±1.6	-1.1±1.4	-2.4±1.4	-1.1±1.8	-2.1±1.6	-1.2±1.5	-2.0±1.4	-1.2±1.4	-1.8±1.3	-0.6±1.1
Change P-value	<0.001†	0.001†	<0.001†	0.004†	<0.001†	0.001†	<0.001†	<0.001†	<0.001†	0.045†
Comparison P-value	0.039		0.002		0.022		0.038		0.002	
Qmax (mL/s), n	28	30	31	30	30	30	26	26	18	18
Baseline, mean±SD	9.7±4.2	8.0±4.6	10.1±4.3	8.0±4.6	10.3±4.2	8.0±4.6	9.1±3.9	8.4±4.8	10.0±3.9	9.5±5.3
Follow-up, mean±SD	14.0±7.5	10.7±6.0	15.9±6.2	10.3±5.2	14.4±6.9	9.4±5.7	12.8±5.8	9.2±4.7	13.3±6.2	10.4±4.7
Change, mean±SD	4.3±5.7	2.7±4.6	5.8±5.0	2.3±3.8	4.1±5.2	1.4±4.3	3.8±4.1	0.8±3.1	3.3±4.8	0.9±4.0
Change P-value	<0.001*	0.004†	<0.001*	0.002†	<0.001*	0.137†	<0.001*	0.469†	0.009*	0.325†
Comparison P-value	0.242		0.003		0.028		0.006		0.112	
PVR, n	28	30	31	30	30	28	25	26	17	20
Baseline, mean±SD	53.6±77.3	44.7±38.2	46.5±73.7	44.7±38.2	49.3±75.2	36.4±22.6	58.0±80.5	49.2±39.1	65.9±95.5	36.0±20.6
Follow-up, mean±SD	34.8±32.1	54.9±59.7	30.0±53.4	43.5±38.1	23.0±24.3	37.1±29.7	36.4±42.2	92.3±160.4	44.7±92.7	32.5±29.8
Change, mean±SD	-18.8±79.1	10.3±53.1	-16.5±59.3	-1.2±36.6	-26.3±67.1	0.7±30.7	-21.6±67.4	43.1±128.5	-21.2±78.7	-3.5±36.4
Change P-value	0.475†	0.841†	0.217†	0.509†	0.061†	0.498†	0.286†	0.651†	0.483†	0.153†
Comparison P-value	0.104		0.233		0.053		0.03		0.403	
IIEF-5, n	19	6	23	20	22	16	23	14	21	14
Baseline, mean±SD	16.9±5.8	16.7±1.0	16.4±6.0	9.4±6.8	16.3±6.2	11.4±6.2	16.1±6.1	13.0±4.6	16.5±6.1	13.0±4.6
Follow-up, mean±SD	15.6±6.9	16.7±1.0	15.5±6.1	9.8±6.6	16.8±5.6	11.9±5.5	16.4±6.2	13.3±3.5	16.2±5.7	13.0±5.2
Change, mean±SD			-1.3±3.6	0.4±2.2	0.5±4.0	0.5±2.6	0.3±4.4	0.3±2.6	-0.2±3.8	0.0±1.8
Change P-value	0.033†	1.00†	0.199†	0.497†	0.681†	0.691†	0.839†	0.874†	0.380†	0.794†
Comparison P-value			0.065		0.985		0.83			
MHSQ-function, n	15	6	15	16	10	12	19	12		
Baseline, mean±SD	10.5±4.0	9.0±1.5	12.1±3.1	9.7±3.3	12.6±3.0	9.3±3.5	11.2±3.8	9.3±3.5		
Follow-up, mean±SD	9.3±5.1	9.0±1.5	11.1±3.6	9.2±3.3	10.7±2.9	9.2±3.3	10.9±2.6	9.2±3.0		
Change, mean±SD			-1.1±3.3	-0.6±1.1	-2.8±4.1	0.1±3.2	-1.0±4.4	-0.2±2.0		
Change P-value	0.447†	0.914†	0.234†	0.058†	0.052†	0.959†	0.528†	0.776†		
Comparison P-value			0.167		0.081		0.544			
MHSQ-bother, n	15	6	15	16	10	12	19	12		
Baseline, mean±SD	1.6±1.5	1.7±0.5	1.1±0.9	1.5±0.7	0.9±0.9	1.5±0.8	1.4±1.3	1.4±0.8		
Follow-up, mean±SD	1.7±1.8	1.7±0.5	1.2±1.3	1.5±0.7	1.4±1.3	1.8±0.9	1.6±1.3	1.4±0.9		
Change, mean±SD			0.1±0.9	0.0±0.5	0.0±2.1	0.3±0.5	0.1±1.1	0.2±0.4		
Change p-value	0.829†	1.00†	0.589†	1.00†	0.301†	0.046†	0.357†	1.00†		
Comparison p-value			0.618		0.625		0.838			

SD, standard deviation; PSA, prostate-specific antigen; IPSS, International Prostate Symptom Score; QoL Quality of Life; Qmax, maximum urinary flow rate; PVR, post-void residual volume; IIEF-5, International index of erectile function, MSHQ-EjD; Male sexual health questionnaire ejaculatory dysfunction short form version (MSHQ-EjD)
* Paired Student's t-test, † Wilcoxon signed-rank test.

Table 1

Funding None **Clinical Trial** No **Subjects** Human **Ethics Committee** Institutional Review Board of Korea University Guro Hospital **Helsinki** Yes **Informed Consent** No

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444 | www.ics.org/2022/abstract/444

PROSTATIC URETHRAL LIFT (PUL) PROVIDES DURABLE SYMPTOMS RELIEF IN REAL-WORLD ANALYSIS OF PATIENTS WITH PROSTATE CANCER

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HYPOTHESIS / AIMS OF STUDY

Increased rates of post-operative events such as infection, bleeding, and incontinence associated with invasive techniques in patients previously treated for prostate cancer may influence BPH-associated LUTS treatment. In this analysis, we examine outcomes in patients with a prostate cancer diagnosis who were then treated with the minimally invasive PUL using the UroLift System.

STUDY DESIGN, MATERIALS AND METHODS

The Real-World Retrospective (RWR) database includes 3226 patients who underwent PUL after market clearance at 22 international sites. Patients were stratified according to those with a diagnosis of prostate cancer (n = 138), those with prostate cancer who received any form of treatment (n = 90), and those treated specifically with radiation (n = 74). These groups were compared through 36 months post-PUL with patients without a cancer diagnosis (n = 2174).

RESULTS

5.2 years passed on average between prostate cancer diagnosis and PUL procedure. Compared to non-cancer patients, cancer patients were older (74 y.o. vs. 69 y.o.) and had significantly higher baseline PSA levels (4.0 vs. 2.3). All studied cohorts demonstrated similar improvements in IPSS, Qmax, QoL and PVR through 24 months post-PUL. Excluding standard of care catheterization, post-procedural catheter-free rates were similar between treated cancer, radiation-treated cancer, and non-cancer groups. Within 1 year of treatment, incontinence rates were 2.6% in the non-cancer group and 7.8% in the treated cancer group; 2 of 3 had ongoing urge incontinence at last contact and the remaining 4 resolved in 64 days on average. Most AEs occurred within 3 months after the procedure; no differences in rates of UTI, stricture, or hematuria were found between groups. Retreatment rates were 8.08 for all subjects, 7.29 for cancer patients, 6.66 for prostate cancer patients treated with radiation, and 8.23 for non-cancer patients per 100 patient years.

INTERPRETATION OF RESULTS

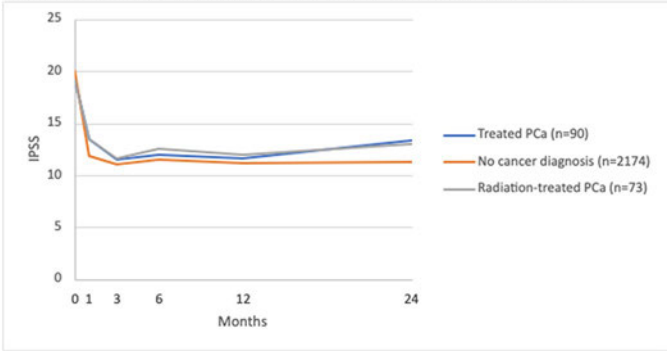
This analysis assessed outcomes of patients with prostate cancer who had a PUL procedure. All prostate cancer subgroups (diagnosed, treated, radiation-treated) improved similarly from baseline, with similar non-standard-of-care catheterization rates. Most adverse events were no different between those with baseline prostate cancer and those without, with the exception of increased incontinence in the treated cancer group, though most cases resolved in an average of 64 days post-PUL. In sum, real-world prostate cancer patients who underwent the PUL procedure experienced improvements and outcomes largely similar to non-cancer patients, without increased rates of most AEs or increased rate of retreatment.

CONCLUDING MESSAGE

The approach to BPH therapy in patients previously treated for oncologic disease must be informed by the risk of complications. This comprehensive analysis demonstrates that PUL provides durable LUTS improvement for real-world patients with prostate cancer.

FIGURE 1

Fig. 1 IPSS improvement is independent of previous oncologic therapy



Funding NeoTract Inc./Teleflex **Clinical Trial** No **Subjects** Human **Ethics Committee** Sterling IRB **Helsinki** Yes **Informed Consent** Yes

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EFFICACY AND SAFETY OF 'INVERTED OMEGA SYMBOL EN-BLOC' HOLMIUM LASER PROSTATE ENUCLEATION (HOLEP) FOR BENIGN PROSTATIC HYPERPLASIA: A SIZE-INDEPENDENT TECHNIQUE FOR SURGICAL TREATMENT OF LUTS

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HYPOTHESIS / AIMS OF STUDY
Lower urinary tract symptoms (LUTS) secondary to benign prostatic hyperplasia (BPH) is one of the most common diseases affecting the aging man, with almost 80% of men greater than 70 affected. Historically, transurethral resection of the prostate (TURP) has been considered the historical gold standard in the treatment of LUTS due to BPH for many years, contemporary literature indicates that holmium laser enucleation of the prostate (HoLEP) has replaced TURP and open simple prostatectomy as surgical gold standard for BPH treatment. This study was to evaluate the safety, efficiency, and size-dependency of 'Inverted omega symbol En-bloc' HoLEP in the treatment of BPH with LUTS.

STUDY DESIGN, MATERIALS AND METHODS
716 consecutive patients who underwent HoLEP by a single surgeon using 'Inverted omega symbol En-bloc' HoLEP technique to treat bladder outlet obstruction from 2014 to 2021 were retrospectively analyzed. Patients were divided into group 1 (<40 cc, mean 29.1 cc, n=339), group 2 (40-<60 cc, mean 48.1 cc, n=216), group 3 (≤ 60 cc, mean 84.5 cc, n=161). Perioperative parameters, safety and functional outcomes were assessed and analyzed.

RESULTS
Mean ages, body mass index, and comorbid diseases of 3 groups were no significant difference but showed a significantly higher median PSA level in larger prostate sizes ($p<0.01$). Perioperative parameters, such as enucleation time (45.8 ± 26.9 min), morcellation time (13.2 ± 47.5 min), and catheterization duration (1.6 ± 1.2 day) were significantly differed in favor of smaller prostate sizes ($p<0.01$). The significant improvements of IPSS (total, voiding, storage, and quality of life), PVR, and Qmax were showed from 3 months after HoLEP, and continued during the 1-year follow-up period in all groups ($p<0.01$). Postoperative complications were urethral stricture (1.5%), bladder neck contracture (1.7%), urinary incontinence (2.0%), and bladder injury by morcellator (0.6%). Bladder neck contractures occurred only in group 1. Postoperative surgical managements for complications were urethral sounding (1.3%), endoscopic internal urethrotomy (EIU) (0.3%), and Re-HoLEP for bladder neck contracture (1.7%). And Re-HoLEP for regrowing adenoma were 15 (2.1%). Postoperative medications for more than 6 months were α-blocker (3.1%), cholinergics (2.2%), anticholinergics (8.1%), antidiuretics (2.5%), and daily PDE5 inhibitor (5.3%). Postoperative incidental prostate cancers were 34 (4.8%).

INTERPRETATION OF RESULTS
The significant improvements of IPSS (total, voiding, storage, and quality of life), PVR, and Qmax were showed from 3 months after HoLEP, and continued during the 1-year follow-up period in all size of prostaes ($p<0.01$). Postoperative complications were also few and similar to those already reportted in other HoLEP studies. Some complications could be resolved with surgical treatment such as EIU or Re-HoLEP..

CONCLUDING MESSAGE
'Inverted omega symbol En-bloc' HoLEP technique is safe and effective for the treatment of bladder outlet obstruction. And also, 'Inverted omega symbol En-bloc' HoLEP is a size-independent and effective method in all size of prostate.

Funding No **Clinical Trial** No **Subjects** Human **Ethics Committee** Ethics committee of gyeong national university hospital **Helsinki** Yes **Informed Consent** No

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THE EFFECT OF THE MEDICATIONS BY ALPHA-1 BLOCKERS AND 5 ALPHA REDUCTASE INHIBITORS FOR CHRONIC PROSTATIC INFLAMMATION.

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HYPOTHESIS / AIMS OF STUDY
Chronic prostatic inflammation is well known as an important factor to exacerbate the condition of benign prostatic hyperplasia (BPH). The urine reflux into the prostatic stroma has been thought to be one of the key factors to worsen the magnitude of prostatic inflammation.

Alpha 1 blockers and 5 alpha-reductase inhibitors (5ARIs) have been used for BPH therapy, and several reports demonstrated that alpha 1 blockers and 5ARIs suppressed prostatic inflammation. However, the effect of these medications on prostatic inflammation is still controversial and the mechanisms of these anti-inflammatory effects are still unclear. It is thought that the reduction of urine reflux by reducing bladder outlet obstruction (BOO) would be the main mechanism of this anti-inflammatory effect.

Androgen signaling is also an important factor in the pathogenesis of BPH. 5ARIs inhibit the conversion of testosterone to dihydrotestosterone (DHT), which has anti-inflammatory effects by inhibiting nuclear factor kappa B (NF-κB) [Ref. 1].

Lymphocytes recognize high endothelial venule-like vessels (HEV-like vessels) at the inflamed sites and are recruited there. The HEV-like vessels are thus essential for the development of chronic inflammation, and they are a reliable marker of the magnitude of chronic inflammation [Ref 2]. Here, we investigated the therapeutic effect of alpha 1 blockers and dutasteride on patients with BPH in terms of the magnitude of prostate inflammation as assessed by the number of HEV-like vessels.

STUDY DESIGN, MATERIALS AND METHODS
The analysis of human prostate tissues was approved by the Ethics Committee of our institution and informed consent was performed on all patients. Tissue samples were obtained from 148 BPH patients who underwent transurethral resection of the prostate (TURP) or holmium enucleation of the prostate (HoLEP). Thirty-three of the patients had been treated with dutasteride prior to surgery. The magnitude of prostatic inflammation was quantified histologically by the number of HEV-like vessels. HEV-like vessels were detected by the immunohistochemistry of MECA-79 [Ref 2].

We assessed the affection of alpha 1 blockers or dutasteride on the magnitude of chronic prostatic inflammation and the parameters of the international prostate symptom scores (IPSS) and urodynamic study (UDS).

RESULTS
We observed that 126 of the 148 cases harbored HEV-like vessels. 143 patients have treated with alpha 1 blockers and 31 patients were with dutasteride. 113 patients were treated with alpha 1 blocker monotherapy, 30 cases with a combination of alpha 1 blockers and dutasteride, and only one case took monotherapy with dutasteride. 4 cases have never taken any medications for BPH.

The duration of alpha 1 blockers' administration was significantly negatively correlated with the number of HEV-like vessels (correlation coefficient = -0.194, p = 0.030, Fig. 1). When the study was limited to the alpha 1 blocker monotherapy group only, there was no significant correlation between the duration of administration and the number of HEV-like vessels (correlation coefficient = -0.109, p = 0.180). On the other hand, the number of HEV-like vessels was significantly positively correlated with the duration of dutasteride treatment (correlation coefficient = 0.501, p = 0.001, Fig. 2).

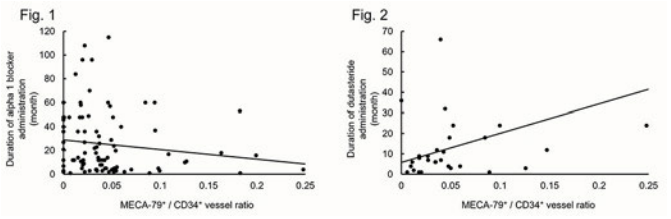
Focusing on the relationships between the UDS parameters and these drugs, the duration of alpha 1 blockers' administration was significantly negatively correlated with BOOI (correlation coefficient = -0.270 p = 0.029). Meanwhile, the duration of dutasteride administration was not significantly correlated with BOOI.

Next, we evaluated the impact of alpha 1 blockers and dutasteride combination therapy versus alpha 1 blockers alone on LUTS. Regarding the subjective parameters, the total IPSS score, voiding subscore, storage subscore, and QOL score of the group of combination therapy were significantly lower than those of the alpha 1 blocker monotherapy (total score 20.154 vs 14.350, p = 0.002; voiding subscore 9.154 vs. 6.095, p = 0.003; storage subscore 10.736 vs. 8.429, p = 0.033; QOL score 4.476 vs. 3.700, p = 0.017).

INTERPRETATION OF RESULTS
These results indicated that alpha 1 blockers could contribute to the suppression of chronic prostatic inflammation whereas dutasteride would enhance the magnitude of chronic prostatic inflammation. However, the combination therapy of these drugs would contribute to relieving the subjective LUTS.

CONCLUDING MESSAGE
The present analysis revealed that there would be the opposite effect on chronic prostatic inflammation between alpha 1 blockers and 5ARIs. At the same time, dutasteride would bring improvement of subjective LUTS to patients with severe BPH.

FIGURE 1



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Funding None **Clinical Trial** No **Subjects** Human **Ethics Committee** the **Ethics Committee** of the Faculty of Medical Sciences, University of Fukui **Helsinki** Yes **Informed Consent** Yes

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SESSION 29 - CONSERVATIVE MANAGEMENT

Abstracts 447-458
09:35 - 11:05, Hall N
Chairs: Paula Igualada Martinez (Spain), Katharina Meller (Austria)

447 | www.ics.org/2022/abstract/447

EVALUATING A DIGITAL INTERVENTION FOR OVERACTIVE BLADDER: OAB PILOT STUDY

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HYPOTHESIS / AIMS OF STUDY
Overactive Bladder Syndrome (OAB) is defined by urgency, frequency, and nocturia, with or without urgency urinary incontinence in the absence of pathological causes of these symptoms. This condition affects patients worldwide and can have a great effect on their quality of life. This study aims to investigate the feasibility, acceptability, and preliminary efficacy of a digital intervention, the OAB App, for the conservative management of overactive bladder syndrome. Particularly, this study looks at if the intervention improves the symptoms experienced by patients with overactive bladder syndrome. Furthermore, this study looks at if the participants experience any decrease in the degree of bother on participants due to these symptoms and if there is any improvement in participants' quality of life. Finally, this study will help to determine the most appropriate outcomes for the OAB app use in a future definitive RCT and the effect size for future sample size calculations.

STUDY DESIGN, MATERIALS AND METHODS
Participants were selected from clinic waiting lists at each study site. The consultant at each site reviewed patient referral letters from their general practitioner and selected patients that fit the trial inclusion and exclusion criteria (Figure 1). The clinic contacted the patient on behalf of the trial team. An email was sent with a brief description of the study, a recommendation to participate and an online 'consent to be contacted' form. If participants were interested in hearing more about the trial or participating, they completed the 'consent to be contacted' form. This provided their contact details to the study team who then contacted the participant inviting them to participate in the trial. The email contained a participant information leaflet and an informed consent form as an online link. If participants had any questions about the trial, they either replied to the email or requested a phone call from a member of the study team.

All participants that agreed to participate and completed the informed consent form downloaded the OAB app. They then completed an 8-week programme; The app guided the participants through 8 evidence-based modules. Each week a new module was made available to the participants. Participants were asked to do bladder retraining with the use of urge suppression techniques and delayed toileting. They also were guided through low-risk physical exercises including pelvic floor exercises, walking, stretching, and body weight strengthening activities. There were also elements of cognitive behaviour therapy they engaged in such as journaling, behaviour retraining, and goal setting.

Participants completed three study surveys weeks 1, 4, and 8. These surveys contained validated measures to assess the study outcomes and demographic measures to describe the study population. The app collected usage data throughout the 8-week programme. At weeks 1 and 8 participants were prompted by the app to complete a Bladder Diary using the app.

Outcomes measured included the mean voids in 24 hours, followed through the in-app bladder diary. Patient-reported urgency, frequency of urination, symptom bother and symptom impact on quality of life were also evaluated through the International Consultation on Incontinence Questionnaire Overactive Bladder (ICIQ-OAB) (1) and the International Consultation on Incontinence Questionnaire Overactive Bladder Quality of Life (ICIQ-OAB-QoL) (2) validated questionnaires. Programme adherence was measured through website analytics based on the percent of the programme completed and programme acceptability was measured through an acceptability questionnaire based on the Patient Global Impression Improvement (PGI-I) (3).

RESULTS
Overall, 100% of our participants reported a reduction in their OAB symptoms and 82% reported an improvement in their quality of life. Paired samples t-tests were conducted as Shapiro-Wilk tests demonstrated that the distribution of the differences in the ICIQ-OAB and ICIQ-OABqol scores was normal. A Bonferroni correction was applied to control for multiple comparisons. The alpha level was adjusted to .017. The intervention significantly reduced patients' OAB symptoms in 4 weeks and this reduction was maintained to 8 weeks. There was a significant difference in ICIQ-OAB scores between baseline ($M = 7.13$, $SD = 2.53$) and week 4 ($M = 5.19$, $SD = 2.46$; $t(15) = 3.78$, $p = .002$, $d = .78$) and between baseline and week 8 ($M = 5.00$, $SD = 2.52$; $t(16) = 5.28$, $p < .001$, $d = .8$'). The intervention significantly improved patients' quality-of-life scores at 4 weeks and this change was maintained to 8 weeks. There was a significant difference in ICIQ-OAB-QoL scores between baseline ($M = 84.45$, $SD = 20.50$) and week 4 ($M = 69.06$, $SD = 22.14$; $t(15) = 3.12$, $p = .007$, $d = .72$) and between baseline and week 8 ($M = 62.41$, $SD = 31.28$; $t(16) = 3.52$, $p = .003$, $d = .78$).

Behavioural data were collected from participants in week 1 and week 8 through the in-app digital bladder diary. Participants logged the number of times they went to the toilet daily to create the variable Frequency of Urination. Paired samples t-tests were conducted as a Shapiro-Wilk test demonstrated that the distribution of the differences in Frequency of Urination scores was normally distributed. There was a significant difference in the Frequency of Urination between baseline and week 8 ($t(6) = 3.28$, $p = .017$, $d = .1.07$). Participants experienced a significant reduction in the number of times they went to the toilet with the average dropping from 10.19 visits per day at week 1 ($SD = 3.41$) to 6.71 visits at week 8 ($SD = 1.25$).

Participants also logged the number of incontinence episodes they experienced. Although it was not possible to conduct paired samples t-tests on this data as the Shapiro-Wilk test demonstrated that the distribution of the differences at baseline and week 8 was not normally distributed, participants experienced a reduction in episodes of incontinence with the average dropping from 10 ($SD = 15.17$) at baseline to 3.57 at week 8 ($SD = 4.58$).

INTERPRETATION OF RESULTS
The use of the OAB app over an 8 week period lead to significant improvements in participants' ICIQ-OAB scores. Lower scores are equivalent to improvements in patients' symptoms of frequency, nocturia, urgency, incontinence, and symptom bother. After the 8 week intervention, lower ICIQ-OABqol were also noted; this indicates improvements in participants' quality of life concerning their OAB symptoms and experiences. This questionnaire also encompasses an evaluation of participants' self-confidence and any relationship or mental strain placed on them due to their OAB symptoms. The variable Frequency of Urination, calculated from behavioural data from weeks 1 and 8, also showed a significant decrease between the beginning and end of the intervention. Finally, there was a notable decrease in the average number of incontinence episodes experienced by participants between weeks 1 and 8.

CONCLUDING MESSAGE
Overactive bladder syndrome has a significant effect on the lives of patients experiencing it. The symptoms of urgency, frequency, and nocturia not only bother patients but also affect their capacity to fulfil daily activities without advanced planning and preparation. This is particularly true in the setting of incontinence. Furthermore, these symptoms may also affect the patients' views of themselves and their interpersonal relationships. The use of the OAB app has a significant and positive effect on the outcomes measured through the ICIQ-OAB and ICIQ-OABqol validated questionaries. Its use can, therefore, be beneficial in the conservative management of patients with OAB. Furthermore, this intervention can also be implemented to conservatively manage patient symptoms while they are awaiting appointments for clinics.

FIGURE 1

Inclusion criteria	Exclusion criteria
1. On waiting list 2. Referred for OAB from general practitioner 3. Symptoms of OAB to include at least one of the following: urgency of urination, frequency of urination or urge incontinence 4. Female 5. Own a smartphone	1. Active/Recurrent urinary tract infection 2. Urinary retention 3. Bladder Pain Syndrome/ interstitial cystitis 4. Pelvic/gynae cancer 5. Pregnant 6. Dementia 7. Kidney problems 8. Stroke 9. Have/had a neuro-stimulation implant for treatment of OAB

Inclusion and Exclusion Criteria

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Funding Enterprise Ireland **Clinical Trial** Yes **Registration Number** ClinicalTrials.gov, Identifier: NCT05170100 **RCT** No **Subjects** Human **Ethics Committee** Galway Clinical Research **Ethics Committee**, Rotunda Hospital Research **Ethics Committee**, National Maternity Hospital Research **Ethics Committee**, **Helsinki** Yes **Informed Consent** Yes

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ONLINE HEALTH INFORMATION ON POP LACKS ADEQUATE INFORMATION ABOUT TREATMENT OPTIONS

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HYPOTHESIS / AIMS OF STUDY

Online health information is becoming increasingly popular among patients. However, concerns have been raised since the quality of information varies and may lead to misinformation, distress and even adversely affect the patient-physician relationship. This investigation aimed to identify differences in the content and quality of online health information of pelvic organ prolapse depending on the utilized source.

STUDY DESIGN, MATERIALS AND METHODS

The platforms Google search, LinkedIn, YouTube, Instagram and Facebook were searched between March to June 2021 for the keyword “pelvic organ prolapse”. The first 30 search results were used for analysis. Results were categorized as useful, misleading, advertising, and personal experience. Useful was defined if the content contained scientifically accurate information about any aspect of the disease. In contrast, misleading content contained advertisements, jokes, or job postings. Data were categorized by website organization into individual health care professionals, professional organizations, industry, patients, and individuals. Medical content was analyzed and classified as pathophysiology, diagnosis, and treatment.

The readability score, Alexa score, and HealthOnTheNet-toolbar were analyzed for Google searches. Descriptive analysis was performed. Univariate analysis was performed to assess heterogeneity with respect to the distribution of information as a function of source. A p-value <0.05 was considered significant. Statistical analysis was performed using SPSS 16.

RESULTS

There were significant differences between the source and the occurrence of useful content, advertising, and personal experiences. The source with the highest quantity of useful content was Youtube, whereas advertising and misleading content were most common on LinkedIn. The source with the highest quantity of personal experience was Instagram. The most common organization on Google search [n = 24 (80%)], Facebook [n = 17 (56.7%)] and LinkedIn [n = 9 (30%)] were professional organizations. Healthcare professionals were the most common organization in Youtube [n = 29 (96.7%)] and Instagram [n = 13 (43.3%)].

Regarding medical content, pathophysiology was most frequently addressed on YouTube [n = 22 (73.3%)], whereas diagnostics and surgical treatment was most frequently addressed on Google. Youtube and Google provided the greatest variety of medical content. However, a lack of adequate comprehensive content covering all aspects of POP repair has been identified for all sources.

The most frequent reported secondary diseases related to pelvic organ prolapse were birth trauma, faecal incontinence, sexual dysfunction, or sleep disturbances. OAB or SUI were only reported in up to 36.7%

For Google searches, the mean Alexa score was 360039, and 12 (40%) were HON-qualified. The mean readability score was 10.4.

INTERPRETATION OF RESULTS

Besides the popular search engine Google, Youtube has been identified as a valuable source of online content on POP. Although Google search for pelvic organ prolapse is very popular according to Alexa ranking, only 40% of the websites were HON qualified. Furthermore, the readability score was challenging, limiting the accessibility for patients and leading to misinformation. Nevertheless, there is a lack of aeaquate presentation of all available treatment option of POP.

CONCLUDING MESSAGE

Urogynecological association may contribute to improve patient information by providing online health information which is complete and easy to understand.

FIGURE 1

Source / Treatment	Facebook	Google	Instagram	LinkedIn	YouTube	p-value
Conservative						
Pessary, *n (%)*	11 (36.7)	22 (73.3)	1 (3.3)	0	11 (36.7)	<0.001*
Pelvic floor exercises, *n (%)*	18 (60.0)	25 (83.3)	27 (90.0)	1 (3.3)	16 (53.3)	<0.001*
Surgical						
Route, *n (%)*						
vaginal	9 (30.0)	18 (60.0)	0	0	8 (26.7)	<0.001*
abdominal	4 (13.3)	16 (53.3)	0	0	12 (40.0)	<0.001*
Robotic assisted surgery, *n (%)*	3 (10.0)	10 (33.3)	0	0	8 (26.7)	<0.001*
Laparoscopic surgery, *n (%)*	3 (10.0)	15 (50.0)	0	0	11 (36.7)	<0.001*
Native-Tissue vaginal, *n (%)*	0	7 (23.3)	0	0	7 (23.3)	<0.001*
Native-Tissue abdominal, *n (%)*	0	4 (13.3)	0	0	7 (23.3)	<0.001*
Mesh-augmented surgery, *n (%)*	9 (30.0)	14 (46.7)	0	0	6 (20.0)	<0.001*
Uterine sparing technique, *n (%)*	4 (13.3)	10 (33.3)	0	0	11 (36.7)	<0.001*
Sacrocolpopexy, *n (%)*	3 (10.0)	11 (36.7)	0	0	7 (23.3)	<0.001*
Colpocleisis, *n (%)*	0	15 (50.0)	0	0	3 (10.0)	<0.001*
Colporrhaphy, *n (%)*	3 (10.0)	15 (50.0)	0	0	6 (20.0)	<0.001*

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CULTURAL HUMILITY RATHER THAN COMPETENCY: A QUALITATIVE STUDY EXPLORING THE DIFFERENCES IN CLINICAL REASONING AND DECISION MAKING BETWEEN THE UK AND KSA PHYSIOTHERAPISTS WHILE ASSESSING AND TREATING PATIENTS WITH URINARY INCONTINENCE.

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HYPOTHESIS / AIMS OF STUDY

The objective of the study is to understand the similarities and differences between pelvic health physiotherapists (PHPTs) clinical reasoning (CR) processes and decision-making in the United Kingdom (UK) and the Kingdom of Saudi Arabia (KSA) while assessing and treating patients with urinary incontinence (UI). Comparing between PHPTs reasoning and decision-making (DM) in two different countries with different individual and organisational cultures may contribute toward the understanding of the influence of cultures on physiotherapists' decision making and clinical reasoning while managing patients with UI. There are limited studies that explore the influence of culture on physiotherapists' DM and clinical reasoning in the UK and other countries. In a recent review of the literature to understand how physiotherapists consider patients' culture in management decisions. The authors found that there is limited consideration of patients' culture in physiotherapists' goal setting and management plans (Yoshikawa et al. 2020). Incontinence has a negative impact on patients' emotional, social, and quality of life. Patients with UI may avoid physical activities because they might be worried about leaking or odour after exercises. The culture of secrecy, sense of shame and self-blame for UI limit help-seeking for UI in women from ethnic minorities. Some Muslim women may be hesitant to undertake Uro-gynecological tests because there are customs that demand that women should expose certain body parts to their husbands only. It can be assumed that the lifestyles women have will affect how UI is experienced. It is therefore likely that women in different countries and cultures experience and perceive incontinence differently. It is also possible therefore that PHPT DM and CR may vary in different cultures. Moreover, most of the research on physiotherapy CR has been conducted in Western democratic countries. Relatively little is known about CR in other cultures or how culture may shape CR. It cannot be assumed that CR in Western countries will be equivalent to that used in other cultures. This premise is explored in this study by including participants from two different countries, i.e., the UK and KSA.

STUDY DESIGN, MATERIALS AND METHODS

Using a qualitative design, PHPTs' were interviewed with semi-structured topic schedules guiding conversations on their thinking processes while managing patients with UI. Focus groups to discuss factors influencing PHPTs' decision-making were undertaken with experienced PHPTs in the UK and KSA. Participants from the UK were invited via the Pelvic Obstructive Gynaecology Physiotherapy association, the area representative of the UK pelvic health physiotherapists. While, the KSA participants were invited via the Saudi Physical Therapy Association, the area representative of KSA pelvic health physiotherapists. Recruitment continued until no new key themes arose for two consecutive interviews and in focus groups, the research was considered to be addressed sufficiently. The interviews and focus groups were transcribed verbatim. A framework analysis approach was used to interpret the data for the exploration of the CR models and the factors that affect the DM of PHPTs. Data collection took place between September 2018 and December 2019.

RESULTS

Forty-eight participants from across both countries took part in interviews and focus groups in each country. The main themes were found; contextual factors (individual and organisational culture), and sense-making theory to understand physiotherapists' clinical reasoning processes. There were key similarities and differences between KSA and the UK. The impact of these factors on DM and CR varied slightly between the UK and KSA participants due to differences in the cultural and religious context, and organisational culture. The culture was the biggest differentiation between the two countries. UK participants living in culturally diverse places were aware of the significance of considering culture in their management decisions, based on their training, knowledge and experiences of working within a multicultural context. Some participants in the UK also attended a cultural competency program. However, they questioned the benefit of that programme in helping them deal with different ethnicities. Compared to the UK, religion plays a dominant role in KSA culture, which in turn influences healthcare delivery. In the UK however, the religious background of patients does influence how PHPTs decide to provide healthcare to certain patients. The findings suggest that some patients from different ethnic groups or religious backgrounds might be sensitive to digital palpation, and the way PHPTs ask questions might vary due to different beliefs or understandings.

INTERPRETATION OF RESULTS

A novel finding of this research is that individual and organisational cultures were more influential in CR than had previously been considered in the general physiotherapy clinical reasoning and DM literature. This finding regarding the importance of individual and organisational cultures was made possible by comparing the UK and the KSA. National and regional identity, as well as religion, shaped patients' individual cultures in both countries, but there was also the organisational or institutional culture that shaped the physiotherapist's identity and influenced how they made decisions in the face of uncertainty. This was evident in the findings of the current study, which demonstrated that participants in both countries exhibited different understandings and incorporation of culture into their management plans. Some of them did implement this, while others were only showing awareness of those cultural needs and beliefs without considering the impact on management. The present study is the first study to explore the influence of culture on PHPTs' CR while treating UI patients in different countries. 'Cultural humility', introduced by Tervalon and Murray-Garcia (1998), gives a different and deeper perspective on cultural competence through a continuous reflection of one's self and acknowledgement of the power imbalances between patient and healthcare providers and the challenges of institutional-level barriers. Also, it takes into account the fluidity of culture and challenges both individuals and institutions to address health inequalities (Fisher-Borne, Cain and Martin, 2015). It is not about a certain ethnicity, race, behaviour or belief, but about integrating cultural perspectives into management decisions. It requires physiotherapists to be open about patients' identities, giving it more weight than their own experience. There is a growing body of literature that has challenged the explicit and implicit assumptions of cultural competency. Some limitations of the cultural competency approach include an over-emphasis and rigidity when it comes to an individuals' health practitioners' own opinions. This approach fails to wholly and comprehensively value and incorporates the needs and wishes of an individual patient from a different cultural background. Most of the UK participants were aware of cultural competency as a method of understanding patients' needs from different ethnicities, but only a few PHPTs were using cultural humility instead. However, cultural competency does not provide a completely tailored solution that fully encompasses and incorporates an individual's culture, so an increased awareness and understanding of cultural humility among PHPTs may be necessary to help resolve this issue.

CONCLUDING MESSAGE

This is the first study in PHPTs that explores in-depth CR and DM in two different cultures. The differences identified between the CR of PHPTS in the two countries led to the identification of new findings that recognises the critical impact of individual and organisational culture on PHPTs' sense-making and CR processes. There is an urgent need to consider individual and organisational cultures in any attempts to introduce new evidence or implement clinical guidance, especially among Muslim women and other minor ethnicities. It is highly recommended to implement cultural humility rather than competency in physiotherapists' management of patients of minor ethnicity.

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TOOLS FOR TEACHING INTIMATE EXAMINATIONS TO MEDICAL STUDENTS: A SYSTEMATIC REVIEW

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HYPOTHESIS / AIMS OF STUDY
Genital and rectal examinations are challenging intimate examinations for medical students to learn. This is often related to a lack of content in the curriculum, poor training or difficulty in gaining access to practice these skills in a comfortable environment for both student and patient. The aim of this study is to identify studies that utilised different educational tools for teaching intimate examinations and assess their efficacy in terms of student competence and confidence following the intervention.

STUDY DESIGN, MATERIALS AND METHODS
PubMed, Embase and Cochrane Library were searched for English language published articles which evaluated teaching tools for rectal, gynaecological and testicular examinations to medical students. Risk of bias was assessed according to Cochrane Risk of Bias Tool and ROBINS-I. The GRADE tool was used to determine a level of effectiveness for each teaching modality.

RESULTS
In total, 5619 articles were screened and 26 were ultimately eligible for inclusion in the study, enrolling 2456 students. All (n = 21) of the studies looking at the use of teaching associates saw an increase in student competence. Following teaching with a teaching associate, 93% (n = 14) saw an increase in student confidence. One study assessed the effect of real patients on student competence and one study on confidence. There was an increase in student competence and confidence respectively. One study showed an increase in student confidence following teaching with real patients. When comparisons were made between teaching with teaching associates and models 80% (n = 4) showed a significant superiority in favour of teaching associates regarding student competence and 100% (n = 3) regarding student confidence. Two studies (67%) comparing teaching associates with the use of real patients saw a significant increase in student competence. One study (33%) comparing teaching associates with real patients saw a significant increase in student confidence; the remaining studies showed no significant difference. One study (50%) comparing the use of models with use of lectures saw a significant increase in student competence. The other showed the reverse; a significant increase in student competence in favour of lecture-based teaching. With regards to student competence when comparing model and lecture-based teaching, 100% (n = 1) saw no significant difference.

INTERPRETATION OF RESULTS
Intimate genital examination education should be adopted into the medical school curriculum. Several educational tools have been developed. In the studies eligible for inclusion, it appears that the use of teaching associates is the most effective teaching method.

CONCLUDING MESSAGE
Whilst the use of Teaching Associates appears to be the most effective teaching method for genital examinations, further trials directly comparing teaching methods need to be conducted.

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ASSESSMENT OF LOWER URINARY TRACT FUNCTION IN PATIENTS WITH SYMPTOMS OF DYSFUNCTION OR PAIN: IS OBTAINING AN ACCURATE OBJECTIVE DIAGNOSIS A PRIVILEGE OF SOME PATIENTS OR A RIGHT (WITH POSSIBILITY TO REFUSE) OF ALL PATIENTS?

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HYPOTHESIS / AIMS OF STUDY
Symptoms of lower urinary tract dysfunction (LUTD) are very prevalent. A person LUT symptoms will enter the health care system when the level of bother has exceeded her, or his personal threshold. A first–line physician will subsequently use knowledge of the specific patient's epidemiological background, medical history and a physical examination to obtain a provisional diagnosis. Subsequent treatment has acceptable outcomes for many diseases and dysfunctions, especially in primary care.

Questions arise however, when the management, based on the initial diagnosis, fails. Was the diagnosis correct? Was the treatment dose sufficient? Should lifestyle be more severely adapted? Or: Is a more invasive treatment needed? Ultimately if concerns persist, possibly after trying a second treatment, a proportion of patients turns to second-line care.

Second-line care is often in-hospital care and has a dual purpose, invasive or complex treatments are (better) possible and there are ample possibilities to obtain an objective diagnosis. Regarding LUTS-LUTD, guidelines recommend using non-invasive objective testing and also, recommend considering objective assessment for most symptom syndromes (LUTS-BPO; SUI-s(yndrome); UUI (or OAB)-s; ICBPS. The guidelines do however, not specify which arguments should lead to invasive testing and or how log trial and error should continue. Medical practice guidelines (in general) for syndromes, usually provide a series of 'red flags' leading to specific considerations, but the guidelines for LUTD-syndromes lack these. It is thus left to the discretion of the treating physician whether trial and error management is continued or, whether objective assessment is ordered. With this ambiguity in our guidelines, the decision of an individual physician becomes leading.

With the patient perspective in mind it is although, not clear whether or not objective assessment is a patient right or, a privilege depending on the physicians view. This is a narrative of the ethical dilemmas surrounding the rights of the patient to be precisely informed about the nature of their dysfunction.

STUDY DESIGN, MATERIALS AND METHODS
Ethical principles, guidelines for good clinical practice and statements about patient rights, are used as the background for these considerations.

RESULTS
Patients that experience symptoms of signs of dysfunction are worried about the cause. It is not unlikely that their concerns further increase when an initial management fails. Anxiety about disease in the diagnostic phase is very prevalent and e.g. fear of malignant disease is a good example.(PMID: 21369377) Declarations concerning patient-rights state that patients have the right to [cited from AMA e.g.,] 'receive information from their physicians and to have opportunity to discuss the benefits, risks, and costs of appropriate treatment alternatives, including the risks, benefits and costs of forgoing treatment. Patients should be able to expect that their physicians will provide guidance about what they consider the optimal course of action for the patient based on the physician's objective professional judgment.' Most relevant seems: 'information….treatment' and 'course of action'. This AMA statement is followed by the right 'to ask questions about their health status'. Most patient rights statements (e.g.UK-NHS; EU–Directive 2011/24/EU) predominantly focus on the information that the treating physician should provide about treatment. Little is included about the required precision of and, transparency about the diagnosis before treatment. One guideline from the Indian Ministry of Health(1) includes: [cited] 'Every patient has the right to know what is the illness that they are suffering, its causes, the status of the diagnosis, provisional or confirmed, expected costs of treatment'. This statement implies openness about the diagnosis beiing provisional or presumed, if that is the case.

Opinions about health information vary between more paternalistic/Confucian societies/healthcare systems versus those that support individual autonomy although, not specifically regarding diagnosis.(3) Disclosure of diagnosis, or the decision to not disclose, may be subject to debate in palliative care, malignancy or psychiatric illness (PMID: 26420014, PMID: 34562324) but not clearly in benign potentially treatable dysfunctions.

Contemporary ethical principles are potentially relevant to consider whether objective assessment is a patient's right or privilege: the normative (deontological) ethics; the utilitarianism and the discourse ethics. The normative ethics asks 'us' to do good, to do our best. Regarding openness and information there seems no discrepancy in ethical statements; physicians acknowledge that patients need (want or deserve) information. It implies that diagnostic information is presented sufficiently precise and clear to the patient, but this is not stated very clearly and specific and, contrasting with the recommendations to provide precise and complete information about the proposed treatment(s) and alternatives. According to the statements it seems therefore not 'wrong' to not disclose a precise diagnosis, but probably this shows the lack of patient's input in the statements. Utilitarianism, the theory of morality that advocates actions that foster happiness or pleasure and oppose actions that cause unhappiness or harm, may be an argument for physicians to avoid actions when these are thought to cause unhappiness. Invasive diagnostics, requiring punctures, injections or catheters are unpleasant, or carry risks. Failed invasive therapy also causes unhappiness. A quick and simple route to management may causes immediate (physician and patient-) happiness. And not invasive diagnostic tests are preferred over infvasive tests if they can give reliable information. A trial and error route with persisting diagnostic uncertainty will however certainly not increase quality of life of the patient and the 'uncertainty is the worst illness' may become predominant (PMID: 21369377). Utilitarian maximalization may also strive to do the good for the 'most of the people'. Equality and limited resources (time, money) may play a role. If a treatment or a diagnostic test is (very) expensive the availability will be limited to a proportion of patients, but also: expenses for diagnostics should outweigh the information gained with it, including its relevance for management.

Regarding the discourse ethics perspective; Weighing of all elements: Our guidelines appear to contain some implicit arguments; Invasive diagnostic tests for LUTD are: risky, painful and not relevant for management. This is not explicitly stated, also not evidence based and certainly little supported from the patient perspecive, however this implicit opinion seems to direct the recommendations. That trial and error management may be frustrating for the patient and causing anxiety because of uncertainty, or may be costly is also not stated nor specifically demonstrated in reliable studies. None of the managements however, available for the syndromes lead to a (nearly) perfect cohort-outcome and, the common 60-70% 'good' outcomes are not an indicator of absolute success. Treatment, based on the patient's individual precise staged and graded pathophysiology, thus better individualized management, may lead to better outcome but this is insufficiently acknowledged in our LUTD guidelines.

INTERPRETATION OF RESULTS
The lack of discussion about (or lack of inclusion) the patient's view or expectations and, especially the implicit (utilitarian) 'diagnostic risk minimization' from the physicians perspective has probably led to the fact that objective diagnosis has become a privilege for patients.

CONCLUDING MESSAGE
Ethical issues regarding patient information regarding diagnosis are discussed. Ethical principles and patient perspective, as well as scientific evidence should be used and balanced to recommend practice. Not many (ethical) arguments seem to exist, to suport that confirmed objective diagnosis is only a patient's privilege. Given the statements about patient rights and the normative 'do good' it seems, within the ethical discourse frame, necessary to adapt our guidelines and, to at least inform our patients whether management is based on a provisional or a confirmed diagnosis.

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ASSESSMENT TOOLS AND THE CHARACTERISTICS OF FEMALE PELVIC FLOOR MUSCLE CONTRACTION: AN INTEGRATIVE REVIEW

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HYPOTHESIS / AIMS OF STUDY
Identify instruments that assess contraction of the female pelvic floor muscles to characterize them in terms of pressure, strength, activation, location, and caudo-cranial and/or laterolateral displacements.

STUDY DESIGN, MATERIALS AND METHODS
An integrative review was conducted, based on five steps to ensure adequate methodological rigor (1): problem formulation; data collection, data evaluation, data analysis and interpretation; and public presentation.

Using the PICo (Population-Interest-Context) strategy for non-clinical research, we asked: what are the instruments used to evaluate the contraction of female pelvic floor muscles (PFM) that can provide a pattern of contraction of these muscles? We included articles that contained the adult female pelvic floor - which, for this study should be understood as the anatomical-specific, biologically defined floor - with or without urogynecological dysfunctions, objective measurements of PFM - pressure in mmHg or cmHg or cmH2O; force in Newton (N); activation (muscle recruitment) by electromyography or electroneuromyography root mean square (RMS) in microvolts (μV); and/or contractile localization and displacement by ultrasonography, tomography, and magnetic resonance imaging (mm or cm), full text in Brazilian Portuguese, Spanish, or English published within the last 20 years (2000-2020) in the Medline, Embase, Lilacs, Scopus, Web of Science, PeDRO, or Cochrane Library databases. Studies exclusively involving pregnant women, children, male pelvic floor, or pelvic pain were excluded. All grey literature was also disregarded for this article.

The data were evaluated using the MMAT - Mixed Methods Appraisal Tool, capable of evaluating quantitative, qualitative, and mixed studies, to which a scoring system of 25%, 50%, 75%, and 100% quality was associated, with no exclusion. Data were collected and organized according to the collection tool validated by Ursi (2005) (2). Two reviewers independently graded the articles and discussed discrepancies when necessary. When consensus was not reached, a third reviewer, blinded to the other two, performed the ranking as a tie-breaker.

The results were categorized according to similar quantitative data, according to the measuring instrument used for measuring the PFM.

RESULTS
The search strategy yielded 982 articles and followed the PRISMA criteria used for systematic reviews (Figure 1). In the end, were included 54 articles. Methodological evaluation by MMAT and classification resulted in 9 (16.67%) articles with a score of 25%, 19 (35.19%) of 50%, 13 (24.07%) of 75%, and 13 (24.07%) of 100%.

It was verified that fifteen studies (27.7%) used the manual assessment of PFM concomitantly with other methods. Of these, thirteen (86.6%) used the PERFECT scheme and nine (60%) were studies from Brazil. The mean strength was 2.74 (0.64) considering the studies analyzed. Manometry was the measure most used by the studies for measurements related to PFM. The most used equipment was the Peritron (Cardio Design Pty Ltd, Australia), being used in nineteen studies (63.3%) of the thirty (55.5%) found. Of these, eleven (36.6%) are exclusively Brazilian and two (6.66%) are in partnership with Norway. In addition, five studies (16.6%) from Norway used the Camtech AS device, developed in Norway. Among the studies that used Peritron, the mean peak pressure was 31.81 (16.97).

Eight studies (14.81%) used dynamometry, two articles (25%) most recent (2020) are Canadian, one of them being in partnership with New Zealand, used the Montreal Dynamometer. Three Brazilian studies (37.5%) were located, two of which, used the EMG System do Brasil equipment, model DFV 020101/10 (2015 and 2016). The other study is from 2011 and describes a speculum for measurement, without brand and measurement unit.

Electromyography was used in nineteen studies (35.18%), twelve (63.18%) of these Brazilian articles: four (21.05%) used EMG: EMG System do Brasil LTDA software and intracavitary electrode (Chattanooga Group, Hixson, USA); two (10.52%), more recent (2019, 2021) used MyoTrac® G, Montreal, Canada, and one (5.26%) older (2007) describes only Myotrac 3G, the others (52.65%) used Miotool 400 and 200 system (Miotec) and Physio-Med Services® vaginal probe and two (10.52%) did not describe the equipment.

Ultrasonography was used in eight studies (14.81%), two articles (25%) exclusively Brazilian, and one (12.5%) in partnership with Australia. Two studies (25%) are Norwegian, one Australian (12.5%), one Canadian (12.5%) and African (12.5%). The equipment most used was the GE Voluson ultrasound system (Norway or Austria), but the description of this equipment does not clearly state that it is the same measuring device. The South African study used the PhillipsTM HDIIXE equipment.

INTERPRETATION OF RESULTS
Through the evaluation of the PFM, the physiotherapist prepares the diagnosis and care of his patient, so understanding the state of the art on the measurement and functionality data of this musculature becomes important.

Arnold Kegel, in his works between 1948 and 1950, revolutionized the study and rehabilitation of the pelvic floor with proposals for intervention on these muscles. After 50 years, science continues to improve the knowledge about PFM and with the technological advances and accumulated knowledge, it has been making possible a better dialogue between subjectivity and practical issues.

A point in common among all the analyzed equipment was the prevalence of Brazilian studies, evidencing the growth of research in the area of women's health in the last 20 years. Through manual evaluation, we identified that the major reference for this evaluation is the PERFECT Scheme, described by Laycock and Jerwood (2001), which recommends the introduction of only one finger into the vaginal canal, with the evaluation of the right (at 4:00 am) and left (at 8:00 am) walls (3). Despite referring to such references, the descriptions of the way to evaluate are mostly unclear, indicating that the necessary evaluative rigor is not maintained.

Manometry, for historical reasons of availability, scientific basis, and cost-effectiveness, is the most used, and the Peritron device is the most prevalent. Electromyography was the second most used equipment by the researchers and presented the greatest equipment variability. This is possibly because it is a technology developed to evaluate muscles in general, and was then adapted by the companies to measure the PFM, using intracavitary probes and data collection programs.

Dynamometry and ultrasonography were less used. It is verified that dynamometry presents a history of research centers developing its equipment, also generating variability of devices, not always commercialized. Ultrasonography is a more expensive technology and depends on a specialized professional to collect and analyze the image data.

It was not possible to verify a pattern of contraction and the characteristics of PFM with the different instruments analyzed, due to the large population variability of the studies and the equipment used. However, it was possible to verify by the PERFECT scheme an average force of 2.74 (0.64) among women in the selected studies, and by the Peritron the average peak pressure was 31.81 (16.97) with an average pressure of 15.81 (9.97).

CONCLUDING MESSAGE
It was not possible to verify a pattern of PFM contraction due to the heterogeneity of the measurement instruments found - which can be directly associated with the cost-benefit of each collection tool associated with the complexity of its use -, collection protocol, data processing, and methodological rigor. The prevalence of Brazilian studies demonstrates the relevance of the area rising in the country, with a future perspective of growth. Possibly more studies on data collection standardization methods related to the respective instruments found may improve the understanding of the functionality of PFM.

FIGURE 1

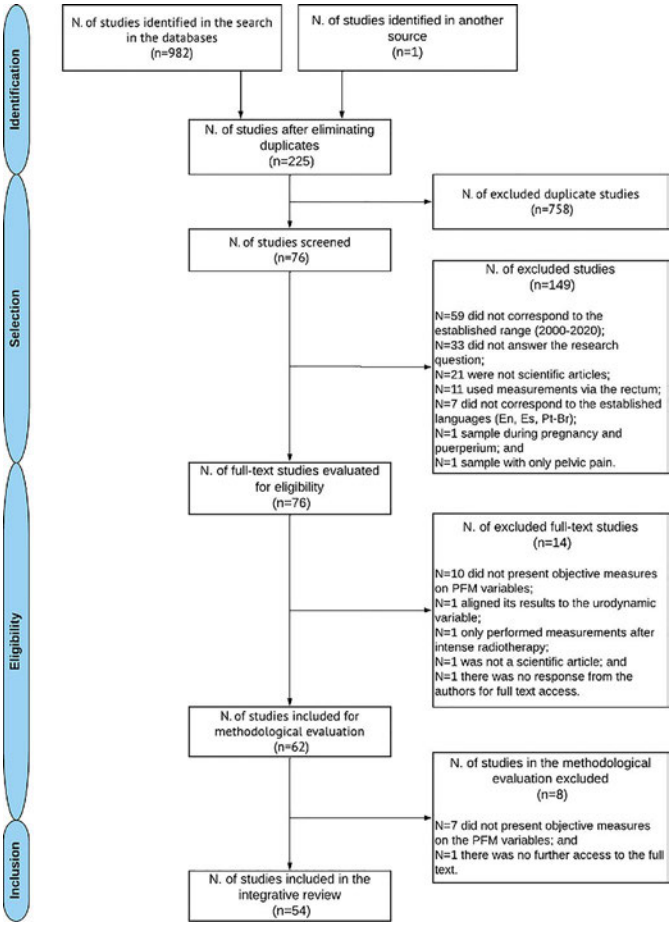

Figure 1. PRISMA Flowchart. Legend: N = number

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DIFFERENCES IN HELP-SEEKING BEHAVIOUR BETWEEN MALES AND FEMALES HAVING MULTIPLE PELVIC FLOOR SYMPTOMS

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HYPOTHESIS / AIMS OF STUDY

Pelvic floor symptoms, i.e. lower urinary tract symptoms (LUTS), defecation problems, sexual dysfunction, pelvic pain, and pelvic organ prolapse (POP) in females are common and frequently co-occur, and are associated with a negative impact on an individual's quality of life. There are several treatment strategies for these symptoms. However, many patients with pelvic floor symptoms do not seek help and therefore do not start any treatment. Most studies assessing help-seeking behaviour are focused on one symptom at the time, predominantly urinary incontinence (1,2). As we are interested in help-seeking behaviour when multiple pelvic floor symptoms occur, the aim of this study is to explore the contributing factors of, and barriers to help-seeking behaviour in both males and females with two or more pelvic floor symptoms.

STUDY DESIGN, MATERIALS AND METHODS

Males and females aged ≥16 years were invited to fill in a questionnaire on pelvic floor symptoms for a cohort study conducted in a municipality in the Netherlands. Presence of symptoms was defined using the following questionnaires: LUTS: the International Consultation on Incontinence Modular Questionnaire (ICIQ)-male and female (ICIQ-MLUTS/FLUTS). Defecation problems: the combined Wexner score (Wexner incontinence score plus Wexner constipation score, based on the Groningen Defecation and Fecal Continence (DeFeC) questionnaire. Sexual dysfunction males: having erectile and/or ejaculation problems and/or pain during intercourse or ejaculation; females: having orgasmic dysfunction and/or orgasmic problems and/or vaginismus and/or vaginal dryness and/or pain during intercourse (based on the Pelvic Organ Prolapse/Incontinence Sexual Questionnaire, IU-GA-Revised (PISQ-IR) and Sexual Health in the Netherlands questionnaire). POP: four out of six items of the Pelvic Organ Prolapse Distress Inventory 6 (POPDI-6) answered with yes. Pelvic pain: Presence of pain in the pelvic region (yes).

Participants with two or more pelvic floor symptoms, and willing to take part in sub-studies of the cohort study were pre-selected based on their type of symptoms and age, and invited for this interview study. The local ethical committee approved the study and all participants of this current study provided informed consent for both the questionnaire (cohort) study and the interviews.

Two female interviewers conducted the semi-structured interviews by telephone, using an interview guide compiled based on literature. They had no prior relationship with the participants. Interviews were performed until saturation was reached and no longer new themes were introduced. The audio-recorded telephone interviews were transcribed and analysed thematically.

Two researchers separately encoded the transcripts using Atlas.ti. First, the person who interviewed the participants coded the interviews. Subsequently, the other interviewer continued with the codes of the first researcher. All interviews with males were conducted first, then all interviews with females. Codes from the male interviews were used as a starting point for coding of the female interviews.

RESULTS

In total 13 males (mean age 68.7 ± 12.1 years) and 12 females (mean age 63.4 ± 9.5 years) were interviewed. Most prevalent clusters in males were LUTS and defecation problems (n = 7, with or without other symptoms as well), and LUTS and sexual dysfunction (n = 6, with or without other symptoms as well). Most prevalent clusters in females were: LUTS and defecation problems (n = 8, with or without other symptoms as well), and LUTS and pelvic pain (n = 7, with or without other symptoms as well). Four males and five females sought help for all their symptoms, five males and five females did not seek any help and four males and two females sought help for some, but not all of their symptoms.

Figure 1 illustrates the themes found in this study for seeking help and not seeking help. Since help seeking is a process in which multiple factors play a role, there can be more than one theme or subtheme applicable for one participant. The associations between themes and subthemes are illustrated in the figure.

Factors that influence help-seeking behaviour (both as a facilitator and as a barrier) are duration, severity and type of the symptoms, and the impact of the symptoms on (activities in) daily life. Other overlapping themes were the influence from someone else in their surroundings, and the role of their doctor (i.e. relation/connection with their health care provider). Themes specific for not seeking help were: the conception that it is useless (nothing to do about it, age-related, and part of life), having a negative earlier experience when looking for help for their symptoms, feelings of shame or embarrassment, finding it difficult to discuss the symptoms, and practising self-help (e.g. using incontinence pads). Facilitators for seeking help were having a specific question for a health care professional, and experiencing emotional distress because of the symptoms.

Differences between males and females

Although most themes apply for both sexes, we found some specific themes for males and for females. Males generally do not quickly seek help for their symptoms. Furthermore, males specifically mentioned sexual complaints (type of symptom), either as a reason to seek help, or as a barrier to seek help. For females, having pelvic pain or prolapse symptoms were specific reasons to seek help. Furthermore, having no trust in, or having a negative relation with their general practitioner prevented females from seeking help. Furthermore, females do not seek help when they experience their symptoms as being part of the female sex and therefore, in their opinion, nothing can be done about it.

INTERPRETATION OF RESULTS

Our results are in agreement with the findings of other studies. However, what makes our study of particular interest is the fact that we included males and females having multiple pelvic floor symptoms, where some patients did seek help for some of their symptoms, but not for all of their symptoms. This adds information to the current knowledge of help-seeking behaviour for pelvic floor symptoms in both males and females.

CONCLUDING MESSAGE

Although most themes apply for both sexes, showing similarities in help-seeking behaviour when having multiple pelvic floor symptoms, we found some specific themes for males and for females.

FIGURE 1

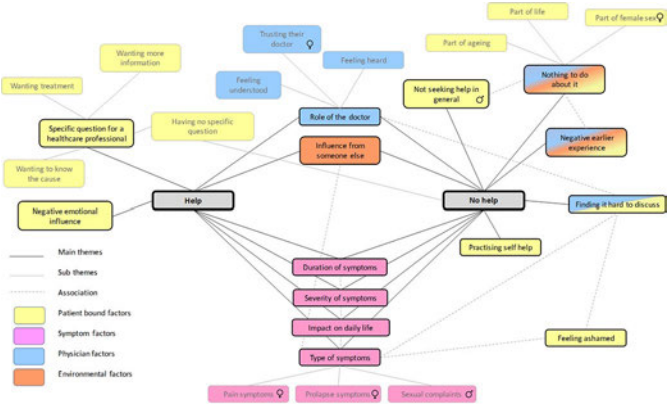

Figure 1. Schematic overview displaying main themes, sub themes and associations in help-seeking behaviour for pelvic floor symptoms

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Funding Netherlands Organisation for Health Research and Development ZonMw (Gender and Health 849200004). **Clinical Trial** Yes **Registration Number** ClinicalTrials.gov, number NCT03558802. **RCT** No **Subjects** Human **Ethics Committee** Medical Ethical Committee University Medical Center Groningen (METc UMCG) **Helsinki** Yes **Informed Consent** Yes

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A RANDOMIZED CONTROLLED TRIAL OF VAGINAL CRYOTHERAPY FOR THE TREATMENT OF PELVIC FLOOR MYOFASCIAL PAIN

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HYPOTHESIS / AIMS OF STUDY

Pelvic floor myofascial pain (PFMP), defined as tenderness and trigger points in the levator ani (LA) and obturator internus (OI) muscles, is prevalent among women with pelvic floor disorders. Current management options are associated with side effects and are not always accessible or covered by insurance. Cryotherapy has been shown to improve myofascial pain elsewhere in the body; therefore, vaginal cryotherapy may be a promising alternative treatment for PFMP. In the present pilot randomized controlled trial, we sought to determine the effect of vaginal cryotherapy on PFMP and pelvic floor symptoms.

STUDY DESIGN, MATERIALS AND METHODS

Following a standardized PFMP screening exam, eligible participants with a pain score $\geq 4/10$ in ≥ 1 of 4 muscle groups were invited to participate in a randomized controlled trial, comparing cryotherapy (15 mL centrifuge tube prepared with 10 mL tap water and 5 mL 70% isopropyl alcohol) to a control (empty 15 mL centrifuge tube at room temperature). Participants in both arms could select to participate in a one-time in-office treatment, an at-home two-week daily treatment, or both. Participants in the in-office group were instructed to place the assigned tube intravaginally for 10 minutes and were immediately reexamined. At-home therapy participants were instructed to perform the intervention daily for 10 minutes for 2 weeks or until their follow-up appointment. T-tests and Wilcoxon rank-sum tests were used to compare changes in pain scores between arms. At-home participants completed baseline and follow-up Urogenital Distress Inventory-19 (UDI-19), Pelvic Floor Distress Inventory short form (PFDI-20) comprised of Pelvic Organ Prolapse Distress Inventory (POPDI-6), Urogenital Distress Inventory (UDI-6), Colorectal-Anal Distress Inventory (CRADI-8), and Patient Global Impression of Improvement (PGI-I).

RESULTS

Between 3/2019-9/2021, 164 participants were enrolled and randomized: 81 to cryotherapy and 83 to control. A total of 64 (30 cryotherapy; 34 control) completed the in-office treatment and 56 (32 cryotherapy; 24 control) completed the at-home, two-week treatment. Most participants identified as Caucasian (85.4%) with mean age of 53.6 ± 15.1 years and reported lower urinary tract symptoms (LUTS) (90.2%, mean baseline UDI score $= 111 \pm 56.3$). In the in-office comparison, mean pain scores decreased significantly in both arms: cryotherapy (5.00 vs 3.99; $p = 0.02$) and control (5.69 vs 4.84; $p < 0.01$), with a similar magnitude of reduction between arms ($p = 0.61$). In the at-home comparison, mean pain scores decreased significantly in the cryotherapy arm (6.31 vs. 4.72; $p < 0.01$), and non-significantly in the control arm (5.50 vs. 4.74; $p = 0.06$), resulting in a non-significant difference in mean pain score change between arms ($p = 0.14$; table1.0). At-home cryotherapy participants reported an overall improvement in UDI-19, PFD-20, and PGI-I scores, with significant differences between arms noted for POPDI-6 (-12.9 vs. 2.4; $p = 0.03$; table 2.0) and PGI-I scores (3 (a little better) vs. 4 (No change); $p \leq 0.01$).

INTERPRETATION OF RESULTS

PFMP pain scores improved following both short-term cold and room temperature intravaginal therapy, as well as following two weeks of cryotherapy. Interestingly, two-week cryotherapy participants reported improvement in LUTS and prolapse symptoms. Whether these findings reflect a therapeutic effect of both cold and room temperature intravaginal therapy, or a placebo effect is unclear but should be explored in larger studies.

CONCLUDING MESSAGE

Vaginal cryotherapy is a readily available treatment option with the potential to improve pelvic floor myofascial pain on palpation and associated pelvic floor disorder symptoms. Whether these findings reflect a therapeutic or a placebo effect is unclear but should be explored in larger studies.

FIGURE 1

Table 1.0 Change in mean pain scores from baseline after at-home vaginal cryotherapy and control

Site	Control (N=24) Baseline	Follow- up	P-Value††	Cryotherapy (N=32) Baseline	Follow -up	P-Value††	Change in mean pain score Control	Cryo	P-Value‡
Individual sites									
ROI	5.92	5.33	0.43	6.35	4.68	**<0.01**	0.58	1.68	0.20
RLA	4.54	3.79	0.26	6.23	4.39	**<0.01**	0.75	1.84	0.21
LLA	5.21	4.63	0.31	5.42	4.39	**0.07**	0.58	1.03	0.58
LOI	6.33	5.21	0.06	7.23	5.42	**<0.01**	1.13	1.81	0.39
Sites Combined									
Right	5.23	4.56	0.22	6.29	4.53	**<0.01**	0.67	1.76	0.11
Left	2.77	4.92	0.06	6.32	4.90	**<0.01**	1.00	7.42	0.38
LA	4.88	4.21	0.19	5.82	4.39	**<0.01**	0.75	1.44	0.28
OI	6.13	5.27	0.09	6.79	5.50	**<0.01**	0.75	1.74	0.16
Mean score:	5.50	4.74	0.06	6.31	4.72	**<0.01**	0.76	1.58	0.14

Cryo, Cryotherapy; ROI, Right obturator internus; RLA, Right levator ani; LLA, Left levator ani; LOI, Left obturator internus; Right, Both right obturator internus and levator ani; Left, Both left obturator internus and levator ani; LA, Both right and left levator ani combined; OI, Both right and left obturator internus combined
†P-value comparing baseline pelvic floor myofascial pain score on standardized exam to follow-up pelvic floor myofascial pain score on standardized exam within arm. Calculated using paired t-test.
‡P-Value comparing mean change in pelvic floor myofascial pain scores on standardized exam between arms using T-test and Wilcoxon rank-sum test as appropriate.
†Bolded p-values represent statistical significance.

FIGURE 2

Table 2.0 Change in patient reported outcome measures of pelvic floor disorder symptoms from baseline after at-home vaginal cryotherapy vs. control

	Control (N=19) Baseline	Follow-up	P-Value††	Cryotherapy (N=30) Baseline	Follow -up	P-Value††	Change in mean score Control	Cryo	P-Value‡†
UDI-19*	112.5	101.6	0.30	117.7	100.4	**0.05**	-10.9	-17.3	0.60
PFDI-20*	171.5	170.8	0.96	180.1	161.2	0.10	-0.6	-18.9	0.32
POPDI-6*	63.4	76.5	**0.04**	75.3	68.8	0.11	2.4	-12.9	**0.03**
UDI-6*	70.0	63.5	0.44	66.8	64.0	0.66	-6.4	-2.9	0.75
CRADI-8*	51.5	51.0	0.93	53.0	44.6	0.13	-0.5	-8.5	0.34

Cryo, Cryotherapy; UDI, Urogenital Distress Inventory long form; PFDI-20, Pelvic floor distress Inventory short form; POPDI-6, Pelvic Organ Prolapse Distress Inventory; UDI-6, Urogenital Distress Inventory short form; CRADI-8, Colorectal-Anal Distress Inventory.
*Questionnaires were scored according to published protocols as described by the original authors.
†P-value comparing change in mean scores from baseline after two weeks of intervention within arm. Calculated using paired T-test.
‡P-value comparing mean change in scores after two weeks of intervention between arms. Calculated using T-test and Wilcoxon ran-sum test as appropriate.
†Bolded p-values represent statistical significance.

Funding #T32 DK120497-01A1 **Clinical Trial** Yes **Registration Number Clinical Trial**s.gov, NCT03885791 **RCT** Yes **Subjects** Human **Ethics Committee** Washington University Institutional Review Board **Helsinki** Yes **Informed Consent** Yes

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IS A FLUID AND CAFFEINE INTAKE MODIFICATION EFFECTIVE AT RELIEVING OVERACTIVE BLADDER SYMPTOMS IN ADULTS: A SYSTEMATIC REVIEW

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HYPOTHESIS / AIMS OF STUDY

Overactive bladder (OAB) is symptomized by urinary urgency. It is usually accompanied by increased daytime urinary frequency or nocturia, with or without urinary incontinence (UI) [1]. The prevalence of OAB increases with age and in older adults, and lifestyle modifications should be simple and sustainable [2].

This study aimed to review and summarize available scientific evidence on the effect of modification of fluid and caffeine intake on OAB in community-dwelling people.

STUDY DESIGN, MATERIALS AND METHODS

A systematic review of randomized controlled trials (RCTs) and uncontrolled studies was conducted to evaluate fluid or caffeine intake modification interventions on OAB in adults.

Studies published up to February 2022 were searched using PubMed, Embase, CINAHL, Scopus, the Cochrane Library, KoreaMed, and RISS. The keywords used in the search were (OAB OR UI OR LUTS) AND ("fluid intake intervention" OR "caffeine intake management").

The inclusion criteria for this study were as follows: RCT or quasi-experimental studies; studies with OAB patients with adults as participants; studies that performed conservative interventions, including fluid or caffeine intake modification, without using pharmaceutical drugs or surgery; and studies that reported the urgency, frequency, UI episodes or amount of urine leakage, nocturia, and quality of life (QoL) as outcome variables. The exclusion criteria were as follows: studies including people with UI after surgery and presently admitted to a health institution; studies including people with a urinary disorder as a symptom of another disease; and studies that included pharmacological, surgical, or orthopedic treatment.

Cochrane's tool for assessing the risk of bias (ROB 2.0) was used to assess the methodological quality of the selected studies [3]. Two authors independently assessed and co-checked the results and reached an agreement through discussion if there were any disagreements or misunderstandings.

Because of the heterogeneity among the included studies, quantitative analyses combining the outcomes of different studies were not performed.

RESULTS

A total of 5,900 articles were identified through the database searches. Four thousand six hundred ninety-two articles, excluding duplicates, were screened by title, leaving 124 articles. Twelve articles were selected through abstract screening. After reviewing the full text of the 12 articles, seven articles were selected, and one article was discovered through a review-article's citation. Finally, eight papers were included in the systematic review, and the data were narratively synthesized. Seven were RCTs, and one was a quasi-experimental study. Four studies had a high risk of bias, and the other four had a low risk of bias.

Urgency was assessed in four studies, and caffeine restriction was effective in significantly reducing it. Increasing fluid intake had no significant effect on urgency compared to the control or decreased fluid intake groups. Frequency was reported on in five studies. They found that caffeine reduction and decreased fluid intake were effective for reducing the frequency of symptoms. An increased fluid intake resulted in more frequent episodes. The number of UI episodes was assessed in six studies. Caffeine reduction resulted in fewer UI episodes, but there were no significant differences between the intervention and control groups. UI symptoms were also improved by modifying caffeine and fluid intake. Nocturia was evaluated in two studies. They found that the caffeine-reduction only group and the caffeine and fluid intake modification group were more effective at reducing nocturia than the control group. QoL was reported on in five studies with various measurements. Although all five studies showed improvement in QoL in the intervention group, only two reported statistically significant improvement by managing both fluid and caffeine consumption.

INTERPRETATION OF RESULTS

Caffeine restrictions should first be considered to manage OAB symptoms as all outcome variables improve as a result. Fluid management was also effective, and reducing fluid intake is more effective than increasing it. Where both caffeine and fluid intake were managed, a decrease in both was more effective at improving urgency, frequency, wetting episodes, and QoL, than increasing fluid intake.

CONCLUDING MESSAGE

While there were a limited number of studies, our systematic review demonstrated that modifying fluid and caffeine intake is effective in relieving OAB symptoms in adults. Therefore, when managing OAB symptoms, fluid and caffeine regulation should be included in the intervention. Additional research is needed to determine the long-term effects of increased or decreased fluid intake on OAB because most results are based only on short outcomes. Moreover, more related studies should be conducted to allow for a more comprehensive meta-analysis.

FIGURE 1

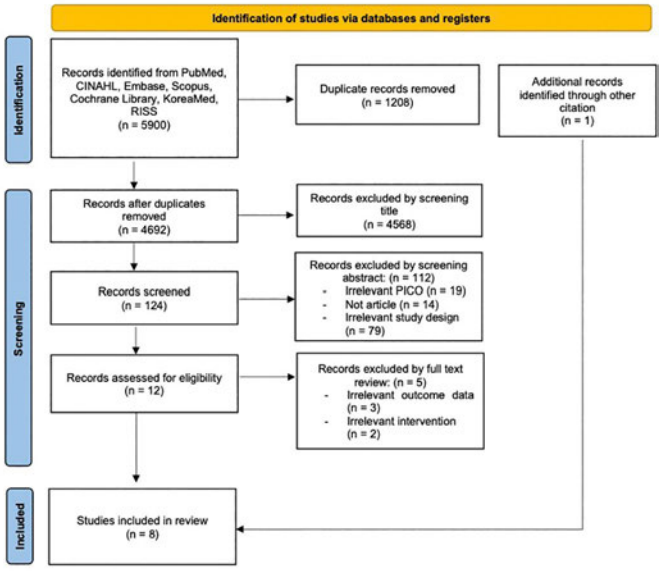
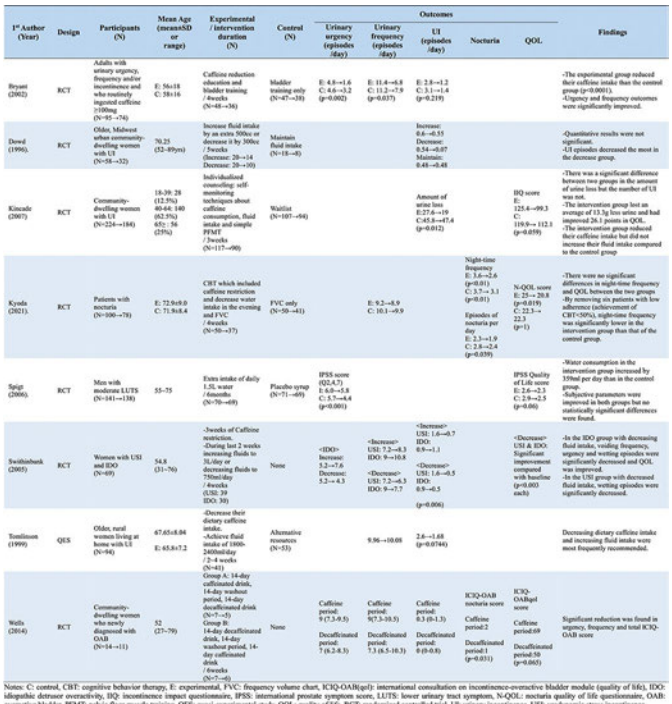


Figure 1. PRISMA flow diagram

FIGURE 2



1st Author (Year)	Design	Participants (N)	Mean Age (mean±SD or range)	Experimental / intervention duration (N)	Control (N)	Outcomes					Findings
						Urinary urgency (episodes /day)	Urinary frequency (episodes /day)	UI (episodes /day)	Nocturia	QOL	
Bryant (2002)	RCT	Adults with urinary urgency, frequency and/or incontinence and who routinely ingested caffeine ≥100mg (N=95→74)	E: 56±18 C: 58±16	Caffeine reduction education and bladder training / 4weeks (N=48→36)	bladder training only (N=47→38)	E: 4.8→1.6 C: 4.6→3.2 (p=0.002)	E: 11.4→6.8 C: 11.2→7.9 (p=0.037)	E: 2.8→1.2 C: 3.1→1.4 (p=0.219)			-The experimental group reduced their caffeine intake than the control group (p<0.0001). -Urgency and frequency outcomes were significantly improved.
Dowd (1996).	RCT	Older, Midwest urban community-dwelling women with UI (N=58→32)	70.25 (52–89yrs)	Increase fluid intake by an extra 500cc or decrease it by 300cc / 5weeks (Increase: 20→14 Decrease: 20→16)	Maintain fluid intake (N=18→8)			Increase: 0.6→0.55 Decrease: 0.54→0.07 Maintain: 0.48→0.48			-Quantitative results were not significant. -UI episodes decreased the most in the decrease group.
Kincade (2007)	RCT	Community-dwelling women with UI (N=224→184)	18-39: 28 (12.5%) 40-64: 140 (62.5%) 65↑: 56 (25%)	Individualized counseling: self-monitoring techniques about caffeine consumption, fluid intake and simple PFMT / 3weeks (N=117→90)	Waitlist (N=107→94)			Amount of urine loss E:27.6→19 C:45.8→47.4 (p=0.012)		IIQ score E: 125.4→99.3 C: 119.9→ 112.1 (p=0.059)	-There was a significant difference between two groups in the amount of urine loss but the number of UI was not. -The intervention group lost an average of 13.3g less urine and had improved 26.1 points in QOL. -The intervention group reduced their caffeine intake but did not increase their fluid intake compared to the control group
Kyoda (2021).	RCT	Patients with nocturia (N=106→78)	E: 72.9±9.0 C: 71.9±8.4	CBT which included caffeine restriction and decrease water intake in the evening and FVC / 4weeks (N=50→37)	FVC only (N=50→41)		E: 9.2→8.9 C: 10.1→9.9		Night-time frequency E: 3.6→2.6 (p=0.01) C: 3.7→ 3.1 (p=0.01) Episodes of nocturia per day E: 2.3→1.9 C: 2.8→2.4 (p=0.039)	N-QOL score E: 25→ 20.8 (p=0.019) C: 22.3→ 22.3 (p=1)	-There were no significant differences in night-time frequency and QOL between the two groups -By removing six patients with low adherence (achievement of CBT<50%), night-time frequency was significantly lower in the intervention group than that of the control group.
Spigt (2006).	RCT	Men with moderate LUTS (N=141→138)	55–75	Extra intake of daily 1.5L water /6months (N=70→69)	Placebo syrup (N=71→69)	IPSS score (Q2,4,7) E: 6.0→5.8 C: 5.7→4.4 (p=0.001)				IPSS Quality of Life score E: 2.6→2.3 C: 2.9→2.5 (p=0.06)	-Water consumption in the intervention group increased by 359ml per day than in the control group. -Subjective parameters were improved in both groups but no statistically significant differences were found.
Swithinbank (2005)	RCT	Women with USI and IDO (N=69)	54.8 (31–76)	-3weeks of Caffeine restriction. -During last 2 weeks increasing fluids to 3L/day or decreasing fluids to 750ml/day / 4weeks (USI: 39 IDO: 30)	None	<IDO> Increase: 5.2→7.6 Decrease: 5.2→ 4.3	<Increase> USI: 7.2→8.3 IDO: 9→10.8 <Decrease> USI: 7.2→6.3 IDO: 9→7.7	<Increase> USI: 1.6→0.7 IDO: 0.9→1.1 <Decrease> USI: 1.6→0.5 IDO: 0.9→0.5 (p=0.006)		<Decrease> USI & IDO: Significant improvement compared with baseline (p=0.003 each)	-In the IDO group with decreasing fluid intake, voiding frequency, urgency and wetting episodes were significantly decreased and QOL was improved. -In the USI group with decreased fluid intake, wetting episodes were significantly decreased.
Tomlinson (1999)	QES	Older, rural women living at home with UI (N=94)	67.65±8.04 E: 65.8±7.2	-Decrease their dietary caffeine intake. -Achieve fluid intake of 1800-2400ml/day / 2–4 weeks (N=41)	Alternative resources (N=53)		9.96→10.08	2.6→1.68 (p=0.0744)			Decreasing dietary caffeine intake and increasing fluid intake were most frequently recommended.
Wells (2014)	RCT	Community-dwelling women who newly diagnosed with OAB (N=14→11)	52 (27–79)	Group A: 14-day caffeinated drink, 14-day washout period, 14-day decaffeinated drink (N=7→5) Group B: 14-day decaffeinated drink, 14-day washout period, 14-day caffeinated drink / 6weeks (N=7→6)	None	Caffeine period: 9 (7.3-9.5) Decaffeinated period: 7 (6.2-8.3)	Caffeine period: 9(7.3-10.5) Decaffeinated period: 7.3 (6.5-10.3)	Caffeine period: 0.3 (0-1.3) Decaffeinated period: 0 (0-0.8)	ICIQ-OAB nocturia score Caffeine period:2 Decaffeinated period:1 (p=0.031)	ICIQ-OABqol score Caffeine period:69 Decaffeinated period:50 (p=0.065)	Significant reduction was found in urgency, frequency and total ICIQ-OAB score

Notes: C: control, CBT: cognitive behavior therapy, E: experimental, FVC: frequency volume chart, ICIQ-OAB(qol): international consultation on incontinence-overactive bladder module (quality of life), IDO: idiopathic detrusor overactivity, IIQ: incontinence impact questionnaire, IPSS: international prostate symptom score, LUTS: lower urinary tract symptom, N-QOL: nocturia quality of life questionnaire, OAB: overactive bladder, PFMT: pelvic floor muscle training, QES: quasi-experimental study, QOL: quality of life, RCT: randomized controlled trial, UI: urinary incontinence, USI: urodynamic stress incontinence

Table 1. Characteristics of selected studies

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EFFECTIVENESS OF PLANNED TEACHING PROGRAM ON BOWEL AND BLADDER CARE IN TERMS OF KNOWLEDGE AND PRACTICE AMONG THE CAREGIVERS OF SPINAL CORD INJURY PATIENTS IN LOW AND LOWER MIDDLE INCOME COUNTRIES.

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HYPOTHESIS / AIMS OF STUDY

This is the original research work done to overcome the practical difficulties of spinal cord injury patients in low and lower middle income countries. Many of the consequences associated with spinal cord injury with incontinence of bowel and bladder do not result from the condition itself, but from inadequate medical care and rehabilitation services. Patients with spinal cord injury are totally dependent on their caregivers initially after being discharged from hospital. Caregivers are usually from their family members and loved ones; to reduce the treatment cost (1). Patient's and caregiver's education is necessary for the safe, effective rehabilitation in terms of activities of daily living and quality of life.

The objectives of the study were to develop and validate a planned teaching program (PTP) on bowel and bladder care of spinal cord injury patients and to assess the level of knowledge and practice and to access the specialized skills in rehabilitation services.

H-I: The mean post-test knowledge score of the caregivers is significantly higher than their mean pre-test knowledge score after administration of planned teaching program on bowel and bladder care of SCI patients.

H2: The mean post-test practice score of the caregiver is significantly higher than their mean pre-test practice score after administration of PTP on bowel and bladder care of SCI patients.

STUDY DESIGN, MATERIALS AND METHODS

Patients often get discharged with bowel and bladder problems and they need care during their rehabilitation at home. Hence the caregivers play a vital role in caring for these patients in their home environment and they can apply their knowledge gathered during patient's hospital stay to practice bowel and bladder care (2).

The Demographic pro-forma for the caregiver regarding age, gender, educational qualification, occupation, any previous experience of caring of SCI patients, exposure to other sources regarding bowel and bladder care after SCI and relationship with the patient was collected.

The conceptual framework of the study was based on System Model. Convenient sampling technique was used to obtain 40 male spinal cord injury patients with the caregivers as the sample. Structured interview schedule and observation checklist were used to collect data before and after the planned teaching program with a practical knowledge observation. The scale Short Form 36 (SF-36) was used to assess Health Related Quality of Life (HRQOL) and the Caregivers Burden Scale (CB Scale) for care burden.

Review of the related literature is regarding bowel and bladder care of SCI patients and effect of planned teaching program on bowel and bladder care in terms of knowledge and practice among caregivers of spinal cord injury (SCI) patients. The review of literature facilitates the investigator in designing and conducting the study. Literature also helped to establish the need for the study, to develop a conceptual framework, adopt a research design, develop tools and decide on plan of data analysis.

RESULTS

The findings revealed that the mean post-test knowledge score (17.2) and practice score (21.4) are higher than the mean pre-test knowledge score (6.5) and practice score (14.6). The mean differences in both the cases are true differences as evident from paired t test values ['t' (39) = 23.26 $p < 0.001$ and 't (39) = 6.12, $p < 0.001$ respectively]. Thus the null hypothesis was rejected and research hypothesis was accepted (3).

INTERPRETATION OF RESULTS

Interpretation of data obtained through demographic pro-forma, structured knowledge questionnaire and observation checklist to assess the effectiveness of planned teaching program on bowel and bladder care among the care givers of spinal cord injury patients.

CONCLUDING MESSAGE

The research validates and concludes that the planned teaching program for care giver is effective in increasing knowledge and enhancing practice for the relatives and loved one form home and reduce the treatment cost (3). Statistically significant association was found between pre-test knowledge score and educational qualification. The study has several implications to access the ongoing health care, health education and products to reduce risk of secondary conditions and improve quality of life. The scope of the study can be enhanced if it could be conducted across a diverse population.

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ACUTE EFFECTS OF USING PELVIC FLOOR MUSCLE EXERCISE WITH LOCAL VIBRATION AND VISUAL FEEDBACK IN HEALTHY WOMEN

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1. Hiroshima university

HYPOTHESIS / AIMS OF STUDY

Japan's population is aging rapidly compared to other countries, with the aging rate reached 28.4% in 2020. Under this situation, there is an urgent need to tackle the various health issues that are expected in an aging society. One of the biggest health problems is pelvic floor muscle dysfunctions, such as urinary incontinence (UI). According to an epidemiological survey over 40 years old in Japan, 21.7% of women were reported to have UI symptoms. There has been a lot of discussion about prevention strategies for UI, and pelvic floor muscle training has been noted to be useful to prevent UI. Pelvic floor muscle exercises are recommended to practice at home, but the contraction of the pelvic floor muscle cannot be visualized. Therefore, it is difficult for UI patients to be aware of the contraction sensation by themselves, and to make exercise a habit. These days, there are many ways to help people get a contraction sensation. The previous study that conducted pelvic floor muscle exercise using the cushion to provide vibration stimulation and visual feedback has shown that the muscle activity of the pelvic floor muscles was improved (1). However, the target population of the previous study was men, and the effect on women, who have a higher prevalence of the disease than men, is still unclear. This study is the first study to confirm whether the exercise of the pelvic floor muscle with vibration stimulation and visual feedback using the cushion is effective in increasing muscle activity of the pelvic floor muscle group in women. The hypothesis was that the pelvic floor muscle activity would be higher after the exercise task with the vibration stimulus and visual feedback than after the normal exercise task.

STUDY DESIGN, MATERIALS AND METHODS

Nine healthy women participated in this study (age: 22.9 ± 0.6). All subjects performed three exercise tasks: control, vibration stimulation, and visual feedback. Each exercise task was a 5-minute exercise of the pelvic floor muscle group; six 10-second sustained contractions of the pelvic floor muscle group were performed, with a 40-second rest period between the 10-second contractions. The participants maintained the seated posture on a cushion (kyuttoburu, Dream Co.) with the hip and knee joints bent at approximately 90 degrees during the exercise task. The vibration terminal is embedded in this cushion. Also, the pressure sensor is designed to contact the pelvic floor muscles, and the participant can get visual feedback by checking the pressure gauge at hand. The maximum voluntary contraction (MVC) of the pelvic floor muscle was measured three times for 5 seconds before and after each exercise task, and the muscle activity of the pelvic floor muscle was recorded by surface electromyography (P-EMG plus, Oisaka Electronic Equipment Ltd.). The electromyogram (EMG) was measured by attaching a blue sensor (P-00-S, Ambu) to the midline of the perineum at two points on the right and left sides to record the muscle activity of the pelvic floor muscle. For comparison of the RMS pre and post the exercise task in each condition, the corresponding t-test was used when normality was followed, and the Wilcoxon signed rank-sum test was used when normality was not followed. Comparison of muscle activity (post/pre) between conditions was performed by Kruskal-Wallis test and Bonferroni as post-test. The effect size (Cohen's d) was calculated for the RMS of pre and post-task exercise in each condition. The level of significance was set at $p < 0.05$.

RESULTS

Table 1 shows the results of RMS pre and post the exercise in each condition. Comparing the muscle activity of the pelvic floor muscle before and after the exercise task, there was a significant increase in muscle activity of 78.28% in the condition with vibration stimulation, 46.42% in the visual feedback condition ($p < 0.05$), indicating a moderate to high effect size ($d = 0.89, 0.81$). In the control condition, no significant changes in muscle activity were detected before and after the exercise. Table 2 shows the results of the muscle activity ratio (post/pre). In the comparison between the conditions, the muscle activity ratio was significantly higher in the condition with vibration stimulation than in the control condition ($p < 0.01$). The visual feedback condition also showed a higher muscle activity ratio than the control condition ($p < 0.05$).

INTERPRETATION OF RESULTS

This is the first study to show that exercise with vibration stimulation and visual feedback by the cushion can cause an acute increase in muscle activity in the pelvic floor muscle of women. First, we mentioned the increase in muscle activity after exercise with vibration stimulation. The tonic oscillatory reflex induced by vibration stimulation has been reported to be involved in the increase in muscle activity during exercise, and the increase in muscle output after exercise (2). When a vibration stimulation is applied to skeletal muscles, α-motoneurons are excited and muscle contraction is observed due to centrifugal impulses generated by α-motoneurons. At the same time, centrifugal impulses generated by γ-motoneurons cause afferent impulses in the fibers of muscle spindles, which pass through the spinal monosynaptic reflex circuit and induce muscle activity via α-motoneurons. In this study, we suggested that the pelvic floor muscles may have been activated by the same mechanism. Second, it was discussed the reasons for the increase in muscle activity after the exercise using visual feedback. A variety of descending nerve tracts are involved in the voluntary control of muscles. Corticospinal tracts, one of the descending nerve tracts, are related to voluntary control of skeletal muscles such as the pelvic floor muscles, and it has been suggested that motor control is better with visual feedback than without it. A previous study of an exercise intervention in UI patients, using a probe inserted into the vagina to provide visual feedback of pressure during pelvic floor muscle exercises, found that muscle activity in the pelvic floor muscle increased after the exercise intervention (3). In this study, the simple visual feedback by checking the pressure gauge of the cushion helped to exercise the pelvic floor muscle smoothly, and it is inferred that the muscle activity increased after the exercise task with visual feedback compared with the control condition.

CONCLUDING MESSAGE

The results of this study showed that the exercise interventions in the vibration stimulation and visual feedback conditions immediately increased the muscle activity and muscle activity ratio (post/ pre) of the pelvic floor muscle in healthy women. Exercise intervention for the pelvic floor muscle group using vibration stimulation and visual feedback by the cushion may be one of the effective exercise methods to stimulate the pelvic floor muscle group, which is considered difficult to obtain contraction sensation.

FIGURE 1

Table 1. The comparison of RMS of the pelvic floor muscle pre and post exercise in each condition

RMS (mv)	Pre	Post	Effect size (d)
Control	23.11 ± 10.57	24.17 ± 14.28	0.00
Vibration stimulation	21.22 ± 9.55	37.83 ± 21.01**	0.89
Visual feedback	21.78 ± 15.49	31.89 ± 28.32*	0.81

Mean ± SD. RMS: root mean square. *: p<0.05 (vs pre). **p<0.01 (vs pre).

FIGURE 2

Table 2. The comparison of muscle activity ratio of the pelvic floor muscle between each condition

	Muscle activity ratio (post/ pre)
Control	1.00
Vibration stimulation	1.79**
Visual feedback	1.42*

Mean ± SD. *: p<0.05 (vs control). **: p<0.01 (vs control).

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ABDOMINOPELVIC EXERCISE PROGRAM VS ABDOMINOPELVIC EXERCISE PROGRAM AND POSTURAL INSTRUCTIONS ON PELVIC FLOOR MUSCLE FUNCTION IN WOMEN WITH STRESS URINARY INCONTINENCE. A RANDOMIZED CONTROLLED TRIAL

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HYPOTHESIS / AIMS OF STUDY
Urinary incontinence (UI) can cause loss of autonomy and quality of life, feelings of distress, loss of self-esteem; and social isolation. It can be treated effectively with conservative interventions such as pelvic floor muscle training (PFMT), which is the first line treatment of this condition. A relationship between posture and UI might exist: several studies state that specific postures may predispose UI or other pelvic floor muscle (PFMs) disorders. As such, rehabilitation programs including postural exercises combined with PFMT are commonly used by clinicians for the management of PFMs dysfunction. Nevertheless, the evidence regarding the efficacy of adding postural exercises to PFMT remains scarce.

The aim of this randomized controlled trial with two parallel groups was to investigate whether the addition of postural instructions to a 12-week abdominopelvic exercise program is superior to an abdominopelvic exercise program alone, in terms of PFMs function and symptoms in climacteric women with stress UI (SUI).

STUDY DESIGN, MATERIALS AND METHODS
Climacteric women aged between 40-75 years old who presented with SUI were included in this parallel study. All participants were randomly assigned in a 1:1 ratio to one of two groups: 1) a group performing an abdominopelvic exercise program (AEP); or 2) a group performing the same intervention with the addition of postural instructions (AEPPI). Both groups performed one 40-minutes session per week for 12-weeks. Electromyographical activity (EMG) and strength (through the Oxford Grading Scale) of PFMs were quantified during a maximal voluntary contraction. SUI symptoms were assessed using a 3-day bladder diary. Outcomes were collected at baseline, immediately after intervention, and 3-months after the intervention.

Sample size was calculated using G*Power software. Assuming an analysis of variance (ANOVA) of repeated measurements, a medium effect size (d = 0.5; ηp2 = 0.06), α = 0.05, power = 0.90, and a correlation among repeated measurements of 0.5, a total sample size of 36 subjects was needed to achieve an appropriate power level for this research.

RESULTS
A total of 47 women were included in the study (AEP [n = 23], AEPPI [n = 24]). Between-group analysis showed significant differences for post-intervention EMG and strength values, showing higher values for the AEPPI compared to the AEP group. At 3-months follow-up, statistically significant differences were only obtained in strength, with higher values in the AEPPI group. No significant differences were obtained in terms of UI symptoms.

INTERPRETATION OF RESULTS
A hypothesis that could explain the positive effect of the posture-based program combined with abdominopelvic training lies on the effect of body position on muscle recruitment. PFMs and/or abdominal muscle contraction may be facilitated by the postural input. It is also possible that changes in spinal curvature and pelvic orientation could modify vector forces within the abdomen and influence intra-abdominal pressure management.

A program including abdominopelvic exercises combined with postural instructions may be beneficial to improve moderate symptoms of SUI as well as PFMs activation and strength in women with SUI. Nevertheless, it is crucial to consider the importance of language and meaning when giving postural instructions, which should be implemented from an active rather than a protective point of view. Overly alarmist messages may generate hypervigilance, apprehension, and distortions in body image, with insights into behavioral and muscular responses.

CONCLUDING MESSAGE
A 12-session AEP supplemented with postural instructions is superior than an AEP alone in terms of voluntary PFMs activation and strength in women with SUI. When analyzing changes over time, PFMs activation and strength were improved in all subjects, regardless of receiving postural instructions or not. These findings should be considered with prudence due to the small size of our study.

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SESSION 31 - CHILDREN & TRANSITIONAL CARE

Abstracts 482-493
11:30 - 13:00, Hall K
Chair: Ms Ashani Couchman (Australia)

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BEST IN CATEGORY PRIZE: PAEDIATRICS

IMPACT OF DELAY IN SURGICAL INTERVENTION ON FUNCTIONAL OUTCOMES IN CHILDREN WITH UNILATERAL URETEROPELVIC JUNCTION OBSTRUCTION

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HYPOTHESIS / AIMS OF STUDY
Uretero-pelvic junction obstruction (UPJO) is the most common cause of obstructive uropathy in children. However, the timing of surgical intervention is debatable and the effect of delayed surgical intervention is also not well-understood. For example, COVID-19 pandemic has led to institutional delays and surgical shutdowns in all medical fields worldwide. Therefore, we aimed to identify the effect of delay in surgical intervention on renal function in cases of of unilateral UPJO and factors that may affect it.

STUDY DESIGN, MATERIALS AND METHODS
In a retrospective study, database of children who underwent pyeloplasty for unilateral UPJO in a tertiary center from January 2016 to October 2020 was reviewed. Patients who had a delay in pyeloplasty for more than 3 months from the time of diagnosis were identified. Patients for whom 3 renograms were performed at the time of surgical decision, immediately before surgery and within one year postoperatively were included in the study. Deterioration was defined as 5% or more decline in the split renal function (SRF) between 2 consecutive renograms. Patients were then categorized into 2 groups; group of preserved renal function (group 1) and group of deteriorated renal function (group 2) based on the difference in preoperative renograms. Both groups were compared regarding the preoperative and postoperative Antero-posterior diameter (APD), grading of hydronephrosis (HN), percent of change of HN, change in SRF and duration of delay in months.

RESULTS
A total 46 children were included in the study; 30 patients had preserved renal function (group 1), while 16 patients had significant deterioration of SRF (group 2). Group 2 showed higher percent increase of APD and more delay in the surgical intervention on univariate analysis, p value = 0.016 and 0.001, respectively (Table 1). On multivariate analysis these factors showed significant difference between both groups. However, other factors did not show any significant difference between the two groups. None of the patients who had surgery within 6 months showed functional deterioration.

INTERPRETATION OF RESULTS
In our study, children who underwent pyeloplasty for unilateral UPJO, were divided into 2 groups; group 1 had preserved renal function, while group 2 had significant deterioration of SRF. The group of deteriorated SRF significantly showed higher percent increase of APD and more delay in the surgical intervention. However, other factors did not show any significant difference between both groups. On the other hand, none of the patients who had delayed surgery within 6 months showed functional deterioration.

CONCLUDING MESSAGE
Delaying of surgical intervention for less than 6 months may not lead to functional deterioration. Moreover, worsening of HN might precede functional deterioration.

FIGURE 1

Table 1: Effect of delay in surgical intervention on functional outcome in children with unilateral UPJO

Variables	Group 1 (N = 30)	Group 2 (N = 16)	P-value
Preoperative APD at time of diagnosis, cm, mean ± SD	3.17 ± 1.54	2.45 ± 1.2	0.13
Preoperative APD at time of intervention, cm, mean ± SD	2.34 ± 1.04	3.22 ± 2.01	0.22
Postoperative APD, cm, mean ± SD	1.76 ± 1.14	2.29 ± 1	0.11
Preoperative percent of change of APD, %, median (range)	- 6.67 (-50 to 42.86)	21.05 (-25.17 TO 83.49)	**0.016**
Postoperative percent of change of APD, %, median (range)	- 28.75 (-70 to 16.67)	- 60.43 (-29.63 to - 93.33)	0.38
Grading of hydronephrosis at time of diagnosis, mean ± SD	3.23 ± 0.77	3.5 ± 0.81	0.32
Grading of hydronephrosis at time of intervention, mean ± SD	2.51 ± 0.84	3.6 ± 0.67	0.31
Grading of hydronephrosis postoperatively, mean ± SD	2.29 ± 1	2.15 ± 0.9	0.76
Preoperative SRF at time of diagnosis, %, mean ± SD	37 ± 17.5	43.8 ± 15.7	0.21
Preoperative SRF at time of intervention, %, mean ± SD	37.8 ± 17.4	34.2 ± 16.9	0.51
Postoperative SRF, %, mean ± SD	37.7 ± 16.7	37.6 ± 11.4	0.98
Preoperative change in SRF, %, median (range)	-0.035 (-4.32 to 12.21)	-7.5 (-24.93 to - 5.25)	**0.001**
Postoperative change in SRF, %, median (range)	-0.12 (-4.27 to 14.4)	5.17 (-2.03 to 10.23)	0.13
Surgical intervention delay duration, months, mean ± SD	10.6 ± 4.34	16.1 ± 5.5	**0.001**

Table 1: Effect of delay in surgical intervention on functional outcome in children with unilateral UPJO

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PREDICTORS OF RESOLUTION OF HYDRONEPHROSIS AFTER PYELOPLASTY IN CHILDREN: WILL IT GO AWAY?

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HYPOTHESIS / AIMS OF STUDY

Pyeloplasty is the gold standard surgical intervention for ureteropelvic junction obstruction which entails removal of this obstruction. However, hydronephrosis (HN) may persist despite adequate surgical techniques, such as patent, water-tight and tension-free anastomosis. Resolution of HN is still not well understood and time to HN resolution varies greatly among individuals. As a result, postoperative follow-up protocols are different worldwide.

STUDY DESIGN, MATERIALS AND METHODS

In a retrospective study, data of children who are younger than 15 years and underwent pyeloplasty at a tertiary center between January 2015 and October 2019 were reviewed. Patients who underwent redo pyeloplasty and those with missing data were excluded from the study. Resolution of HN was defined as decrease of the antero-posterior diameter (APD) to less than 10 mm or >50% reduction of the preoperative APD. Analysis of survival using Kaplan Meier`s curve was performed with adjustment to perioperative and clinical data.

RESULTS

A total of 256 children were included in the study. Resolution of HN rate was 74.6%, 87.3%, 93.7% and 97% at 1, 2, 3 and 4 years of follow-up, respectively (Figure 1). Univariate analysis showed no difference in resolution neither between patients with preoperative APD <2, 2-4 and >4 cm (p= 0.15) nor between different HN grades (p=0.38). No difference was found among patient age groups <1, 1-5, 5-10 and >10 years old (Log rank 0.21). Bilateral cases and those with poorly functioning kidneys (<20% split renal function) did not show any difference in resolution of HN (Log rank 0.2 and 0.7 respectively). However, patients with solitary kidneys had less resolution rates (Log rank 0.03). On the other hand, cases with percent of improvement of APD (PIAPD) more than 10% within the initial visit showed significantly better resolution rates (Log rank 0.0001) (Figure 2). Both were significant in cox regression analysis.

INTERPRETATION OF RESULTS

Resolution of HN rate was more than 90% within 3 years of follow-up after pyeloplasty. There was no significant difference in resolution neither between patients with different preoperative APD nor between different grades of HN. No significant difference was also found among patient with different age groups. Bilateral cases and those with poorly functioning kidneys did not show any significant difference in resolution of HN. However, patients with solitary kidneys had less resolution rates. On the other hand, cases with PIAPD more than 10% within the initial visit showed significantly better resolution rates.

CONCLUDING MESSAGE

HN tends to resolve within 3 years after pyeloplasty in more than 90% of cases. Patients with decrease in APD more than 10% from the preoperative value have higher rates of resolution of HN, however, patients with solitary kidneys have lower rates of resolution of HN.

FIGURE 1

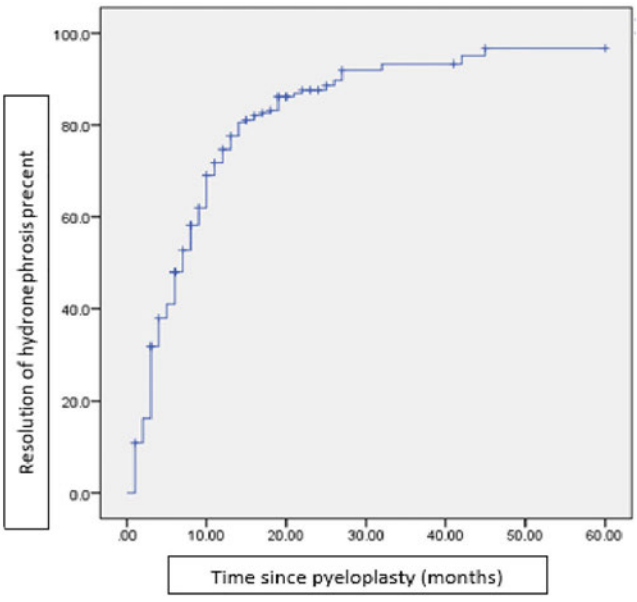

Figure 1: Kaplan Meier curve of resolution of hydronephrosis.

Figure 1: Kaplan Meier curve of resolution of hydronephrosis.

FIGURE 2

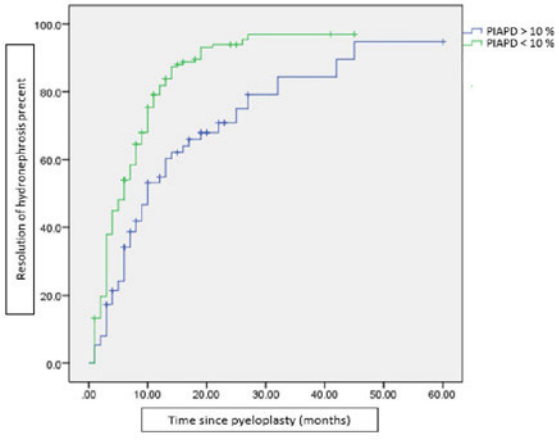

Figure 1: Kaplan Meier curve of resolution of hydronephrosis among children with different PIAPD.

Figure 2: Kaplan Meier curve of resolution of hydronephrosis among children with different PIAPD.

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DOES PYELOPLASTY FOR UNILATERAL URETEROPELVIC JUNCTION OBSTRUCTION IN RENAL UNITS WITH MORE THAN 40% SPLIT FUNCTION IMPROVE THE SURGICAL OUTCOMES IN PEDIATRICS?

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HYPOTHESIS / AIMS OF STUDY
Pyeloplasty for ureteropelvic junction obstruction (UPJO) in pediatrics has traditionally been selected for cases of impaired renal drainage or renal function (RF) deterioration. However, there is a risk of possibly irreversible renal damage if RF deterioration occurs before pyeloplasty. Therefore, we evaluated the surgical outcomes of pyeloplasty for UPJO in well-functioning renal units with more than 40% split renal function (SRF).

STUDY DESIGN, MATERIALS AND METHODS
In a retrospective study, pediatric patients with unilateral UPJO who underwent open Anderson-Hynes pyeloplasy were included. Patients with solitary kidneys, bilateral UPJO or associated anomalies were excluded. All patients were divided in 2 groups according to preoperative SRF; group 1 (SRF >40%) and group 2 (SRF ≤40%). Renal ultrasonography and renographic images were reviewed to evaluate preoperative baseline characteristics and analyze postoperative anatomical and functional outcomes at 6 and 12 months. Antero-posterior diameter (APD), parenchymal thickness (PT), degree of hydronephrosis (HN) as defined by Society for Fetal Urology (SFU) grading system and SRF were measured. A decline of SRF by more than 5% was considered to be deterioration.

RESULTS
A total of 103 patients were included in the study; 45 patients (44%) had SRF >40%, while 58 patients (56%) had SRF ≤40%. Their mean ages were 4.72 ± 0.15 years. At baseline, both groups had comparable APD, PT and SFU grading of HN (Table 1). The group of SRF >40% showed lower degrees of HN by SFU grading (1.91 ± 1.06 vs. 2.46 ± 0.96, p =0.04) and higher SRF (38.49 ± 13.1 vs. 22.59 ± 13.93, p =0.03) at 6-month follow up and less APD (1.47 ± 0.71 vs. 2.41 ± 1.08, p =0.01) at 12-month follow up relative to the other group. However, both groups did not develop significant change of preoperative SRF after 12 months (Table 1).

INTERPRETATION OF RESULTS
In our study, 103 pediatric patients with unilateral UPJO were divided into 2 groups according to their SRF, either >40% or ≤40%. Both groups had comparable APD, PT and SFU grading of HN. The group of SFR >40% (group 1) significantly showed lower degrees of HN by SFU grading and higher SRF at 6-month follow up and less APD at 12-month follow up relative to group 2. On the other hand, both groups did not develop significant change of preoperative SFR after 12 months of follow up.

CONCLUDING MESSAGE
Pyeloplasty for UPJO in well-functioning renal units with more than 40% SRF might improve anatomical and functional surgical outcomes. Yet, further prospective studies are recommended.

FIGURE 1

Table 1: Results of preoperative and postoperative APD, PT, SFU grading of HN and SRF between both groups

Variables, mean ± SD		Group 1 (n = 45)	Group 2 (n = 58)	P value
APD	Baseline	4.18 ± 1.97	4.19 ± 1.74	0.98
	6-month	1.77 ± 0.36	2.37 ± 1.25	0.45
	12-month	1.47 ± 0.71	2.41 ± 1.08	*0.01*
PT	Baseline	0.63 ± 0.19	0.62 ± 0.25	0.97
	6-month	1.63 ± 0.21	0.98 ± 0.42	0.05
	12-month	1.11 ± 0.31	1.10 ± 0.51	0.94
SFU grading of HN	Baseline	3.40 ± 1.34	3.75 ± 0.46	0.5
	6-month	1.91 ± 1.06	2.46 ± 0.96	*0.04*
	12-month	2.12 ± 0.81	2.17 ± 1.10	0.84
SRF	Baseline	49.92 ± 15.9	27.64 ± 7.79	*<0.001*
	6-month	38.49 ± 13.1	22.59 ± 13.93	*0.03*
	12-month	33.13 ± 7.51	26.17 ± 11.47	0.32
	Change in SRF	-10.76 ± 4.17	-1.04 ± 0.18	0.16

*The italic values refer to the statistically significant results (p <0.05). Group 1 = SRF >40%, while group 2 = SRF ≤40%. APD, Antero-posterior diameter; HN, Hydronephrosis; PT, Parenchymal thickness; SFU, Society for fetal urology; SRF, Split renal function. *student's t-test.*

Table 1: Results of preoperative and postoperative APD, PT, SFU grading of HN and SRF between both groups

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OUTCOMES OF EXTRAVESICAL ROBOTIC ASSISTED LAPAROSCOPIC URETERAL REIMPLANTATION (ERALUR) IN PEDIATRIC PATIENTS WITH VESICO-URETERAL REFLUX AND BLADDER AND BOWEL DYSFUNCTION SYNDROME.

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HYPOTHESIS / AIMS OF STUDY

Bladder and bowel dysfunction syndrome (BBD) is reported to have no impact on success rate after open ureteral reimplantation (OUR). However, Bladder dysfunction (BD) and urinary retention is reported to be one of the complications after OUR, especially when it is done bilaterally. The aim of this study is to report the preliminary outcome of initial experience with robotic ureteral reimplantation in pediatric patients with VUR and BBD.

STUDY DESIGN, MATERIALS AND METHODS

We retrospectively reviewed all pediatric patients who underwent ERALUR. We identified 29 patients between July 2018 and December 2021. We excluded 3 patients who did not have at least 3 months follow. Out of the remaining 26 cases, a total of 23 patients/24 ureters were found to have preoperative BBD. All patients received an average of 6 weeks of preoperative standard Urotherapy.

RESULTS

Patients' mean age is 6.1 years (SD 2). Most patients (50%) had grade 3 reflux. Only one patient underwent bilateral reimplantation. Mean operative time is 155 min (SD 27). Blood loss was minimum. The average tunnel length was 3.2 cm (SD 0.4). No reported intraoperative complications. Hospital stay was less than 24 hours in 22 (95.7%) patients and one patient was discharged after 48 hours. One postoperative complication was reported in a bilateral reimplantation, as patient had urinary extravasation that required stent placement. Subsequent evaluation showed complete healing with no long-term consequences. Postoperative ultrasound was normal in all patients except one who showed improvement of the preexisting hydronephrosis but not complete resolution. Postoperative VCUG was done in 21 patients (22 ureters) and showed resolution of reflux 20 patients/21 ureters (95%) and one patient showed improvement from grade 4 down to 1. Also, 3 patients (14.3%) developed de novo contralateral grade 1 reflux. All patients showed stable or improved BBD without any case of urinary retention.

INTERPRETATION OF RESULTS

We are reporting results of outcome following ureteral reimplantation via extravesical approach using robotic approach in pediatric patients who also suffer from bladder and bowel dysfunction. Results of this approach in this group of patient in our series showed that bladder and bowel dysfunction did not negatively affect success rate of the surgery using robotic approach, with similar success rate to open approach.

CONCLUDING MESSAGE

Our preliminary data suggests that robotic approach is a safe option for ureteral reimplantation in BBD patients, with high success rate, like those reported in open series. . Further studies with larger number and long-term outcomes are needed to reach a solid conclusion.

FIGURE 1

Number of Patients	23
Number of Ureteral Units	24
Age years, *(mean, SD)*	6.1 (1.97)
Gender *(no., %)*	
Female	19 (82.6%)
Male	4 (17.4%)
Laterality *(no., %)*	
Left	13 (56.5%)
Right	9 (39.1%)
Bilateral	1 (4.3%)
Duplex system *(no., %)*	4 (17.4%)
Grade of reflux *(no., %)*	
G1	0
G2	5 (20.8%)
G3	12 (50%)
G4	7 (29.2%)
G5	0
Operative time (minutes) *(mean, SD)*	155 (27)
Length of the tunnel (cm) *(mean, SD)*	3.2 (0.4)
EBL (cc) *(median, range)*	Minimum
Postoperative complications	
No	22 (95.7%)
Yes	1 (4.3%)
Hospital-stay *(no., %)*	
<24 hr	22 (95.7%)
<48 hr	1 (4.3%)
Postoperative PVR (cc) *(median, range)*	2 (0-79)
30-dyas readmission *(no., %)*	1 (4.3%)
Post-operative US *(no., %)*	
No Hydronephrosis	22 (95.7%)
Improved Hydronephrosis	1 (4.3%)
Persistent hydronephrosis	0
Post-operative VCUG *(no., %)*	
Resolution of ipsilateral VUR	20 (95.2%)
Improved ipsilateral VUR	1 (4.7%)
Newly developed contralateral VUR	3 (14.3%)
No new contralateral VUR	18 (85.7%)

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ONABOTULINUM TOXIN A LONG-TERM SAFETY, EFFECTIVENESS AND ADHERENCE TO TREATMENT IN PEDIATRIC POPULATION: 25 YEARS PERSONAL EXPERIENCE WITH 230 PATIENTS.

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HYPOTHESIS / AIMS OF STUDY
Onabotulinum toxin A (BONTA) (Botox, Irvin USA) changed completely the management of neurogenic bladder dysfunction (NBD)in adults and then in children. A 48-week prospective, multicenter, randomized, double-blind phase 3 study, including our center, ruled out in more than 100 children (age 5–17 years) with NDO and incontinence demonstrated how BONTA injections is safe, well tolerated, effective. According to these results FDA approved Botox bladder injections, in children 5 years and older with neurogenic detrusor overactivity with no response or intolerance to anticholinergics, with a max dosage of 200U or ≤ 6U/kg. Intradetrusor Botox injections are a highly effective therapy for refractory NDO, but in adults approximately 40% of the patients discontinue treatment over time, for a lack of clinical and/or urodynamic response or because the patients preference. Pediatric data on long-term safety, efficacy, adherence are lacking. For these reasons we present our 25 years experience with 230 pediatric patients.

STUDY DESIGN, MATERIALS AND METHODS
All records of patients treated with bladder botox injections since 1997, in our Institution has been evaluated, Botox has been always considered an off-label second line treatment, and suggested after failure of standard treatment (anticholinergics and clean intermittent catheterizations) or where CIC was not accepted or anticholinergics not tolerated . A written consent has been always signed before evaluation and treatment.

From 2007 a standard protocol has been defined and still used, but for the new patients treated in the period of prospective, multicenter, randomized, double-blind phase 3 study. Our protocol , approved by our Ethical Committee, includes endoscopic bladder wall biopsy for edema, inflammation, fibrosis control.

Data regarding age, pathologies, clinical and UD data, histhologic have been recorded during time as number of injections, lapse time between injections, complications , adherence.Botox has been used in the past commonly at 10UI/kg max 300 UI, with a dosage reduction after approval in adult population (max 200 UI) in 2011. Data have been evaluated considering 3 period: a) 1997-2007, b) 2008-2011, c) 2011 until 2021.In order to define outcome measures we considered success when patients reported own satisfaction plus amelioration of 50% between : leaking episodes per day (number and degree),Number of pads replaced per day, Post void residual decrease, N° of intermittent catheterism per day, UTI frequency reduction. Kidney ultrasound, UD, serum creatine have been monitored. In this study focus has been established on safety, long term effectiveness and adherence, not reporting urodynamic or histology records that will be considered for future studies.

RESULTS
230 patients aged 1-18 yrs, mean age 8,5 yrs at first injection, 112 males, 118 females, have been treated in our hospital , since 1997 to 2021. 38 pts were treated between 1997-2007, 63 between 2008-2011, 129 from 2012 until December 2021. 45 pts had only 1 injection during time, 49 pts had 2 injections, 40 pts had 3 injections, 26 pts had 4 injections, 15 pts had 5 pts injections, 13 pts had 6 injections, 10 had 7 injections, 16 pts had 8 injections, 3 pts had 9 injections, 8 had 10 injections, 5 pts have been injected more then 10 times (11-22 injections). 70 pts have been injected more then 5 Times. Lapse between repeated injections has been 6-13 months. 127 pts were treated for Spina Bifida (SB) (62 myelomenyngocele, 40 occult spinal dysraphism, 13 lipomenyngocele, 12 caudal regression syndrome), 18 traumatic SCI , 11 iatrogenic injury, 8 post oncological, 9 myelitis, 46 cerebral palsy and others central injury, 11 valve bladder. Regarding safety in 916 injections performed in 230 pts no severe intraoperative surgery and anesthesia complications have been reported. All patients have been treated in inpatient regimen, with scheduled postoperative antibiotic, intravenous saline solution hydration, indwelling catheter for 12 hours. In 15 cases, injections, persistent hematuria has been described.5 patients described either limb weakness or generalized fatigue following Botox injection,Effectiveness has been evaluated at 70%, with high success rate, 78% in SCI and SB, lower for CP and posterior urethral valves, 50%. About 230 pts , 31 have been lost at the follow-up. Part of them shifted to other treatment, 32 choose to come back to anticholinergics, In other cases there was a request of definitive solution, and for this reason 49 pts performed bladder augmentation, 39 were shifted to sacral neuromodulation and 9 pts died for primary disease complications . Considering adherence (> 5 treatment) in the remaining 70, is interesting to note the highest adherence value in SCI, 50%, then SB 33%, with the low data in CP, 20%.

INTERPRETATION OF RESULTS
Intradetrusor Botox injections are a highly effective therapy for refractory NDO. Despite the high percentage fo success there is an high rate of low adherence, where patients require other treatment, less or more invasive. The literature data, 40% of the patients discontinue treatment over time, is light higher respect to our pediatric experience, where we have consider not only the lack of clinical and/or urodynamic response but the choice to choose another treatment, despite efficacy, could be related to the fact to avoid repeated anesthesia. Different hypothesis have been done to explain discontinuation rate, first of all primary and secondary failure. Some mechanisms have been hypothesized to explain long-term failure: formation of neutralizing antibodies and histological modification of the bladder wall. We don't tested antibodies but

little data exist on the risk o BONTA neutralizing antibodies after bladder injections. Regarding bladder fibrosis induced during the time of consecutive injections may prevent the normal spread of toxin into the bladder wall and explain secondary failure , our previous data on the histological changes induced by BONTA intradetrusor injections would suggest that BONTA reduces fibrosis. A critical point remain to establish a correct information with patients and relatives, in order to well explain the advantageof BONTA treatment. In a large series of our patients, BONTA was not able to avoid baller augmentation , performed during time, but has been able to postpone it , after puberty.

CONCLUDING MESSAGE
On long-term intradetrusor BONTA injections demonstrated to be safe and effective in pediatrics. Neverthless an high percentage of the patients discontinue treatment over time. A careful follow-up seems useful but BONTA treatment and may be optimized (indication, scheduled injections, etc) . Avoid repeated UD control, in presence of a clinical response, could be useful too with a specific therapeutic education of children and caregiver. Adolescence remains a critical point for low adherence severity of NDO appears to be a significant risk factor for failure, because unsatisfying relatives's expectations.

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SACRAL NEUROMODULATION IN PEDIATRIC POPULATION: WHAT WE LEARNED AFTER 65 IMPLANTS.

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HYPOTHESIS / AIMS OF STUDY
Up to now more than 400,000 patients have been implanted worldwide and sacral neuromodulation (SNM) has become an established minimally invasive therapy for refractory overactive bladder, non-obstructive urinary retention, and fecal incontinence. Experiences in pediatric population are limited and safety and effectiveness have not been established. In children urological treatment under the age of 16 yrs, for patients with neurological disease origins, or for bowel control under the age of 18, SNM is not approved . For these reasons ICCS and ICI reported a low level of recommendations, while an increasing pediatric studies reported improvement of bladder/bowel function in children. Different factors influenced on SNM outcome, where no specific factor, responsible for the success or failure of implanting, has been defined. For this reason hereby we present our results in 65 pediatric patients implanted, presenting our protocol for selection , implant and follow-up.

STUDY DESIGN, MATERIALS AND METHODS
SNM has been considered in our Division a third line treatment. According to this statement a protocol has been defined and approved by our Hospital Scientific Committee in 2008. All patients have been evaluated and treated after a written consent has been signed and all other treatment failed. Considering the pediatric age all patients have been informed about the off-label condition for SNM. All patients have been treated according to a protocol: a) preoperative, b) surgical, c) post-op and follow-up.

A)Preoperatively all patients performed: a new clinical evaluation , taking again patient's history and physical examination,Urinalysis and blood exams, checking 48 hrs urinary and bowel diaries, sacrum X-ray, renal/ bladder ultrasound , a no invasive urodynamic studies (FLW,EMG, PVR if micturition present), UD + VCUG or VUD, Neurophysiological test, Psychological evalution, QoL. Patients with renal function impairment or dilatation of urinary tract > 10 mm, or VUR or mental impairment have been excluded. In order to define clear outcome measures, we defined success when patients reported own satisfaction plus amelioration of 50% of one or more between : leaking episodes per day (number and degree), Number of pads/day , Post void residual decrease, N° of intermittent catheterisms per day,Episodes of faecal incontinence per day ,Number of defecation per day

B) Surgery: all patients have been treated with a 2 stage technique. Advanced test (using quadripolar electrode instead PNE) has been used in all. Second stage, implant has been performed after a successful control period of 2-8 weeks, on the basis of clinical improvement, patient's satisfaction, excluding worsening of renal function and upper urinary tract. UD test have been reported but not considered as main outcome. During surgical procedure fluoroscopy control has been used in all. Choice between local or general anesthesia has been discussed with patients above 14 yrs old. All patients have been treated in inpatient regimen, with antibiotics treatment for 7 days in each procedure.

C) Control and follow-up have been performed regularly at 1,4,12,36, 52 weeks and then twice/year.

Patients with a minimum of 12 months follow-up have been included.

RESULTS
72 patients between 2008-2021 have been operated, aged 11-19 yrs. 3 pts have been exclude because limited follow-up, < 6 months. 4 pts performed test , first stage, but non presented criteria for second stage.About 65 its, 39 presented neurogenic bladder dysfunction, 15 non neurogenic idiopathic urinary retention (NNIUR), 8 overactive bladder with urgency, frequency and urinary incontinence, 6 presented bowel dysfunction as main symptom, fecal incontinence. Implants have bene always performed in lee damaged neurological side, , prep evaluation, but 5. Overall success rate has been 70% at 12 months and 65% later, maintaining during time. Early surgical complications have been observed in 5, 1 intraoperative electrode breaking during removal, 4 infection, 2 electrode removal. All required reoperation, Later complications have been observed in 9 cases: electrode breaking during time in 5, battery dislocation in 5 , 4 of them followed by infection and skin erosion, with reimplant of new battery in contralateral side. Regarding neurogenic bladder dysfunction, overall success has been 65%, iatrogenic injury 80%, peripheral neuropathy 90%, myelomeningocele or lypomeningocele 0%, complete SCI 0%, occult spinal dysraphysm 50%. 15 pts removed device for resolution of symptoms.

INTERPRETATION OF RESULTS
According to our results a careful selection seems to be useful either for the choosing correct indication (neurological lesion) either the side for implant. In our opinion some disease seems to offer best chance for positive response, as iatrogenic injury or peripheral lesion (incomplete damage) versus others with complete damage (SCI or MMC) all without response. Sharifiaghdas evaluated SNM's effectiveness for managing refractory neuropathic lower urinary tract infection in children and adolescents: 61,53% of patients had positive test phase. Positive response was achieved in 85% at a mean follow-up of 14 months, and reported not difference in efficacy between patients with different pathologies.This data is contrasting with our experience. Complications rate seems high in our experience , where a younger age, as suggested seems to offer a better response, but presenting an highest complications rate due probably to height grow-up and variation in body mass index(BMI). In 2017 study identifying preoperative factors which associated with postoperative complications after SNM , others concluded, that there is no association between age, gender and BMI and postoperative complications. Regarding UD usefulness , Mason observed greater improvement in pts with uninhibited detrusor contractions. This is confirmed by our experience where underactive detrusor responding well too, where UD usefulness seems more relevant in preoperative period.

In 2021, Boswell reported the long-term results (2002-2019) of reoperation after SNM in one center. There were 154 total secondary surgeries in a 187 pediatric patients. There were 83 device revisions, with 89% of revisions for a non-functioning device, 8% for pain, and 2% for infection. In their cohort of children 68% carried a high reoperation rate. Critical point in our view are occult spinal disraphysm, where maybe different architectural configuration and ultrastructural properties of sacral plexus in these patients could justify discrepancies in results (van Der Jagt 2012).

CONCLUDING MESSAGE
SNM activity in pediatric population is increasing during time, because reported effectiveness and MRI compatible device. Furthermore rechargable devices are now available. SNM in pediatric is presenting some critical points to be considered: a) patients selection ad role of Sacral abnormalities (sacral roots and foramen) , b) Optimal age for implant ? (early stimulation versus risk of dislocation and trauma in younger), c) to define common outcome measures, d) electric field parameters for neuromodulation (Hz, V, used) that are scantly reported complicating evaluation of different series. According to 7th-ICI , SNM in pediatrics must be considered carefully because is Not approved in children, small study populations in different series with heterogenic pathologies but high complications rate. Good clinical response rate for neurogenic bladder and urinary functionally disorders are reported as well as seems to be effective in bowel bladder dysfunction, refractory constipation or faecal incontinence, but level of evidence remains low..

Cost effectiveness is debated, but is better considering in a 5 years period (normal activity of no rechargable battery) and not for single surgical procedure versus onabotulinum toxin A (less expensive but to repeat every 6-8 months). SNM in pediatrics must be used only in very few high level selected center, with a multidisciplinary team and high rate volume activity (minimum of 5 implants/year).

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STEP-BY STEP CORRECTION OF BLADDER DYSFUNCTION AFTER POSTERIOR URETHRAL VALVE ABLATION.

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HYPOTHESIS / AIMS OF STUDY
Posterior urethral valves (PUV) constitute the most common infravesical urinary obstruction in boys. PUV are often accompanied by severe consequences to the lower urinary tract. High voiding pressures are seen in infants around the ablation of the valves. Detrusor overactivity, which is frequent in infancy, has a tendency to become underactive with age. Accordingly, hypocontractibility and myogenic failure have been reported in older children. Successive increase in bladder capacity is suspected to be accompanied by a risk for overdistention. This concept of changing urodynamic patterns leads to the need to assess the possibility of using drugs that reduce detrusor pressure and determine other recovery tactics.

STUDY DESIGN, MATERIALS AND METHODS
42 boys after PUV ablation in infancy were followed up for 10-16 years. In 24 of them, the upper urinary tract was mainly retracted compared to the primary valve resection in others. Thus, the temporary or permanent decrease in bladder volume that was observed in these patients with defunctionalized bladder may have been secondary due to the diversion of the cutaneous ureterostomy. In 18 patients PUV were accompanied by VUR, in 24 there were besides nonobstructive megaureter. Diagnostic based on US, VCUG, DMSA and MAG3 scintigrapy investigations. Staged urodynamic studies were conducted on all boys 3-5 times at different ages.

RESULTS
Initially, all patients have high pressure in the bladder.

INTERPRETATION OF RESULTS
Only 2 of them recorded a decrease in urinary pressure during the first months spontaneously after the PUV incision. Most patients required primary postoperative treatment with oxybutynin (19), adrenergic blockers (35), and botulinum therapy of detrusor was performed in 3 patients.

To the age of 3-4 years old following the release of the valvular obstruction urodynamic patterns in patients with PUV were as follows: detrusor overactivity with median cystometric bladder capacity (CBC) of 42 ml (range 15 to 72) and maximal detrusor pressure during voiding (Pmax det) 112 cm H2O (range 40 to 331). – in 25 boys, low bladder compliance with mean bladder volume 35ml (20-42ml) – in 13, myogenic failure (detrusor underactivity with poor detrusor reflex or completely without it) – in 4.

This led to the need for prolongation of anticholinergic therapy in 29 boys and botulotoxin injections in 12, which led to an increase of residual urine in 50% of patients (20). At the same time, the addition of biofeedback therapy and noninvasive tibial neuromodulation made it possible to achieve good results of emptying the bladder in 28 boys of elder ages without oxibutinin.

Finally in teenagers, the 5 patients came to CIC without any additional medication therapy, 3 – have done CIC accompanied by oxibutinine, 7 need to prolog medication therapy with adrenergic blockers for improving the micturition, others were completely rehabilitated.

CONCLUDING MESSAGE
Lower urinary tract dysfunction (LUTD) is known to be common in PUV patients. It is worth thinking about and being wary of the use of m-anticholinergics and botulinum toxin in this category of patients, since most of them programmatically develop detrusor underactivity and violation of bladder emptying, which can be aggravated by these drugs. Urotherapy, neuromodulation and biofeedback therapy are the useful tools in management of patients with PUV and must be used widely.

Funding no **Clinical Trial** Yes **Public Registry** No **RCT** Yes **Subjects** Human **Ethics Committee** Local RNCRR **Helsinki** Yes **Informed Consent** Yes

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DOES EARLY ULTRASOUND INFLUENCE THE MANAGEMENT OF PATIENTS WITH ACUTE URINARY RETENTION?

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HYPOTHESIS / AIMS OF STUDY
Acute urinary retention, is a relatively rare entity in children, associated with multifactorial etiology, necessitate bladder decompression to relieve discomfort. Role of early urinary tract ultrasound (US) in the workup of these patients is controversial and no clear indication and patients selection is available in literature to manage pediatric patients with urinary retention in an emergency setting. We tested the hypothesis that early US provides important information.

STUDY DESIGN, MATERIALS AND METHODS
Retrospective study of pediatric patients admitted to the emergency unit for acute urinary retention between 01/2010 and 12/2020. Neonates, and patients with post-operative acute urinary retention or known (urological, neurological, or mental) disorders were excluded. Palpable bladder was identified in all patients after physical examination and, transabdominal ultrasound (US) was performed us a diagnostic toll of acute urinary retention.

Bladder hyperdistention alone was not considered an abnormal US finding.

RESULTS
193 patients presenting with acute urinary retention were identified. Median (range) age was 3 (2-16) year-old. US evaluation was performed in 129/193 (66.8%) patients, more commonly <5-year-old (73.6%vs 26.4, $p<0.01$). US detected urinary tract abnormalities in 16 patients including upper urinary tract dilatation in 10 [eventually diagnosed with vescico-ureteral reflux ($n=6$), tethered cord ($n=1$) and posterior urethral valves ($n=3$)]; bladder wall thickened in 2 patients, eventually diagnosed with neurogenic nonneurogenic bladder]; urinary stones in 2; and bladder suspended echoes in 2 patients with urinary tract infections only. In 13 additional patients, US showed a distended rectum consistent with fecal impaction or constipation. In the remaining 100/129 (78%) patients the US was normal.

Children with history of previous emergency access for Acute urinary retention, had less probability to underwent US evaluation. No variable, including gender and associated symptoms, was able to predict the risk of an abnormal US.

INTERPRETATION OF RESULTS
In our experience, US provided relevant urological information in less than 15% of patients with acute urinary retention, but allowed detecting clinically relevant conditions. We were unable to identify possible factors to select patients warranting US evaluation probably related to different bias such us, presence or the absence of others urological symptoms and conditions, or, the experience of the pediatrician managing patients with urinary tract retention in the emergency.

No clear indication for US in an emergency setting was identified. In our opinion history taken is good complimentary evaluation for the decision-making.

CONCLUDING MESSAGE
Urinary tract ultrasound is un import diagnostic tool in the management of patients with urinary tract retention, useful to urological pathologies identification and better patients management. Standardization is needed to define the steps and indication to ultrasound evaluation managing children with acute urinary retention

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ACUTE URINARY RETENTION IN CHILDREN: IS THE BLADDER CATHETERIZATION ALWAYS NECESSARY?

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HYPOTHESIS / AIMS OF STUDY
Acute urinary retention is uncommon in children and can be due to several causes. Bladder catheterization seems to play an important role in the initial management

We aimed to assess common causes and initial management of acute urinary retention at a tertiary center, focusing particularly on the role of bladder catheterization in the early emergency setting.

STUDY DESIGN, MATERIALS AND METHODS
We retrospectively analyzed all consecutive children admitted to the emergency department with acute urinary retention from 2010 to 2020. We evaluate the results considering the subgroup analyses of patients with more, and less than 5 years old. All children included in the study achieved urinary continence and be toilet trained. Exclusion criteria were: post-operative acute urinary retention, neonatal age, mental disability and known urological or neurological disorders. All patients received medical treatment initially including enemas and local anti-inflammatory depending on the identified cause of acute urinary retention.

RESULTS
193 patients were included. Median age was 3 (2-16) years; 53.4% were girls. The majority (124/193; 64.2%) were managed without catheterization. These patients were significantly younger than the remainder (median ager 3- vs 4-year-old, $p < 0.01$) and the most common diagnosis was external genitalia inflammation (53%). Of the remaining 69 patients, the most common diagnoses were external genitalia inflammation (35%), urinary tract infection (17%) and idiopathic acute urinary retention(13%). Of these 69 patients, 34 (49%) restored spontaneous micturition after a single catheterization, instead, the remining 35 (51%; 18% of all the 193 patients), required admission due to failure to re-establish micturition. In half of the latter (18/35), a previously unknown urological condition was diagnosed. Patients requiring admission were more commonly males (63%, $p = 0.01$), with higher incidence of abnormal ultrasound (33% vs 7%, $p < 0.001$).

INTERPRETATION OF RESULTS
Acute urinary retention is commonly due to external genitalia inflammation particularly in patients < 5-year-old and these patients can generally be managed without catheterization. When no clear cause of retention based on history taken, physical examination, laboratory assessment or imaging was available, hospitalization should be a choice for additional evaluations. No clear indication for catheterization was available in this study.

In our experience, 18% of patients required hospital admission, due to the need for prolonged catheterization and half of these were diagnosed with a urological condition previously unknown.

CONCLUDING MESSAGE
Bladder catheterization is a treatment option of pediatric patients with acute urinary retention, and can be placed when spontaneous micturition is not achieved after others less invasive strategies. Hospitalization should be avoided and performed only when suspect of urological conditions or when additional evaluations are necessary.

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OVERNIGHT FREE DRAINAGE HELPS RESOLVE UTIS IN CHILDREN WITH ABNORMAL URINARY TRACTS AND SECONDARY VESICOURETERIC REFLUX

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HYPOTHESIS / AIMS OF STUDY
Recurrent urinary tract infections (UTIs) in children with congenital abnormalities of the kidneys and urinary tract (CAKUT) with secondary vesicoureteric reflux are likely to result in renal scarring as well as multiple episodes of illness, often requiring admission for intravenous antibiotics. Increasing antibiotic resistance is also a major concern as the antibiotic options typically decrease with each infection. There are many management options including prophylactic antibiotics, non-medicinal products such as D-mannose, clean intermittent catheterisation (CIC), anticholinergics and bladder washouts/instillations. When such interventions fail, management options are limited. The aim of this abstract is to report successful use of overnight free drainage of the bladder to control recurrent UTIs.

STUDY DESIGN, MATERIALS AND METHODS
A retrospective case note review was undertaken for 5 patients, aged 21 months, 2, 3, 6 & 10 years each of whom had recurrent febrile urinary tract infections with increasing antibiotic resistance. Underlying pathology included 3 with neuropathic bladder secondary to spinal dysraphism, 1 boy with bilateral grade 5 VUR and detrusor failure and 1 girl with bilateral ectopic insertion of ureters in association with a frozen abdomen from neonatal pathology and a refluxing reimplantation. Creation of a vesicostomy was considered in all of the patients as an alternative to overnight free drainage but kept in reserve as a 'bail out' option due to the potential for the patients to need major urinary tract reconstruction at a later date. Overnight drainage was established via a urethral catheter in 4 patients and via a suprapubic catheter in the boy with VUR & detrusor failure as he was sensate and did not tolerate urethral catheterisation. Daytime bladder management was by spontaneous voiding in the girl with ectopic insertion of ureters, intermittent SPC drainage or CIC.

RESULTS
UTIs resolved completely in the 3 patients with spinal dysraphism within 2 months of commencing overnight free drainage. Subsequent break-through infections have been rare, <1/year; one patient has had no further UTIs at all over a 5 year period. The girl with ectopic insertion of ureters had previously had multiple admissions, following commencement of overnight catheterisation the UTIs became infrequent and could be managed at home with regular bladder washouts and instillation of GAG-layer replacements. She has been infection free for 2 years. UTIs persisted in the boy with VUR & detrusor failure until he was established on 24 hour free drainage and fortnightly instillation of GAG-layer replacement, he has been infection free for 17 months.

INTERPRETATION OF RESULTS
The range of abnormalities included within CAKUT is broad and there is no 'one-size-fits-all' solution to managing recurrent UTIs. Paediatric urologists have a broad armamentarium of options which are often selected according to how each patient and their family will manage the therapies. Overnight catheterisation dramatically improved the need for antibiotic therapy for UTIs and reduced the number of hospital admissions. Whilst not formally assessed, quality of life was also improved through prevention of hospital admissions.

CONCLUDING MESSAGE
Patients with challenging recurrent urinary tract infections in the setting of secondary VUR and an abnormal bladder require individualised solutions. Overnight bladder drainage prevented more invasive management options in these patients. Providing a low pressure 'empty' urinary tract for 12 hours can minimise damaging UTIs.

Funding N/A **Clinical Trial** No **Subjects** Human **Ethics not Req'd** it is a retrospective patient report **Helsinki** Yes **Informed Consent** No

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TOLERANCE OF MEDICATIONS PRESCRIBED IN CHILDREN FOR DAYTIME LOWER URINARY TRACT SYMPTOMS IN CHILDREN

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HYPOTHESIS / AIMS OF STUDY

Introduction

Lower urinary tract symptoms (LUTS) are prevalent in the paediatric population. If symptoms are not adequately controlled with urotherapy and management of underlying conditions then medication is often required. Anticholinergics are the mainstay of medical therapy though mirabegron is used in selected patients, usually when anticholinergic options have been exhausted. In the United Kingdom, oxybutynin is the first line drug therapy as it is licensed for children from the age of 5 years. However, oxybutynin is a broad spectrum anticholinergic, the downside of which is a broad side effect profile. In our experience a large number of children do not tolerate this medication. Subsequent prescribing is almost entirely off license even though more specific anticholinergics, such as solifenacin, and mirabegron are better tolerated in adults.

AIMS:

To determine reported side effects for anticholinergics and mirabegron in children attending a specialist urology nurse led clinic. To look in depth at the proportion of children who discontinue oxybutynin, as well as the time to and reason for discontinuation.

STUDY DESIGN, MATERIALS AND METHODS

Methods

The electronic patient record database at a single tertiary children's hospital was searched for children aged 5 and over who were seen in the specialist urology nurse service from June 2016 – April 2021. A retrospective review of the records of children who had at least one visit to the urology nurse clinic which included medication review was undertaken. Children with neuropathic bladder were excluded. Data was analysed using χ^2 test, Fisher's exact test, and linear regression.

RESULTS

175 children (128 (73%) female) were included in the data analysis (Figure 1). In the entire cohort, the most common symptoms reported were incontinence (158, 90%), urgency (144, 82%) and frequency (89, 51%). During the period of the study 129 children were prescribed oxybutynin, 82 were prescribed tolterodine, 70 were prescribed solifenacin and 33 were prescribed mirabegron; a number of children were prescribed more than one medication on a sequential basis and 8 received combination therapy with solifenacin and mirabegron. One patient was prescribed trospium and was excluded from the review. Table 1 shows the side effects reported. Children prescribed Solifenacin had significantly fewer side effects when compared to Oxybutynin ($p = 0.018$) and Tolterodine ($p = 0.037$). Whilst the side effects reported with mirabegron were comparable to solifenacin, i.e. fewer reported side effects than both oxybutynin and tolterodine, the number was not statistically significant in this patient cohort ($p = 0.082$).

Out of 129 children who were prescribed Oxybutynin, 100 (78%) discontinued the medication. The reasons documented for discontinuation are given in Table 2. Linear regression analysis showed correlation between time to discontinuation of oxybutynin and age, older patients discontinuing the medication more quickly than younger children ($p = 0.0102$).

INTERPRETATION OF RESULTS

Oxybutynin is prescribed in the majority of patients yet this medication is associated with a high rate of side effects. In this review 71% of patients discontinued the medication, almost 40% due to side effects. The equivalent data for other medications is currently being captured. In our practice, tolterodine is the second line medication since there is a dosing schedule in the British National Formulary for children (BNFc) although it is not licensed for use in children. The rate of reporting side effects was very similar to oxybutynin, despite the increased selectivity of tolterodine for the urinary bladder. In keeping with their more selective nature, both solifenacin and mirabegron were associated with fewer reported side effects.

The time to discontinuation of oxybutynin ranged from 8-35 weeks. The data analysis thus far does not allow interpretation of whether the side effect was present soon after commencing the medication but not reported / tolerated because of a benefit to symptoms or whether the side effect developed after a prolonged period of time. Of note, older children stopped taking the medication more quickly. This is most likely to be due to an increased likelihood that they would recognise and report a side effect. However, the treatment alogorithm followed in our centre limits the age at which solifenacin and mirabegron can be considered, requiring consultant input which is also likely to influence the timing of medication changes . Younger patients are more likely to be offered alternate formulations of oxybutynin (such as modified release tablets or patches) before moving to the next medication in the pathway.

CONCLUDING MESSAGE

Oxybutynin is the most commonly prescribed anticholinergic but is highly likely to be discontinued due to side effects. More specific medications such as solifenacin and mirabegron are better tolerated and future research should aim to establish such medicines as first line medical therapy for LUTS in children.

FIGURE 1

	Oxybutynin (n=129)	Tolterodine (n=82)	Solifenacin (n=70)	Mirabegron (n=33)
Mood changes	13	11	2	
Rash	2	2		1
Headache	7	5	4	2
Abdominal pain	3	6	6	2
Lethargy	6	2		
Dry mouth	2	3		
Nausea	6		2	
Constipation	2			
Blurred vision	1			
Hot flushes	1		1	
Loose stools			1	
Total number of children	41 (32%)	25 (35.7%)	11 (15.7%)	5 (17.9%)

Table 1: Side effects reported according to medication prescribed

FIGURE 2

	Oxybutynin (n=129)	Discontinued (n=100)	Time to discontinuation/ days
Ongoing	26 (29%)		
Lost to follow up	2 (1.5%)		
Non compliant	1 (0.8%)		
Discontinued	100 (77.5%)		
• Symptoms resolved		22 (22%)	610 (357-909)
• No change		17 (17%)	267 (220-459)
• Initial improvement but no resolution		18 (18%)	422 (231-939)
• Deterioration of symptoms		4 (4%)	169 (109-509)
• Side effect		39 (39%)	191 (56-247)

Table 2: Outcome of oxybutynin prescriptions

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EFFECTIVENESS OF PHYSIOTHERAPY IN URINATION DISORDERS OF CHILDREN WITH URINARY TRACT MALFORMATION REFRACTORY TO MEDICATION: AN ANALYSIS OF MEDICAL RECORDS

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HYPOTHESIS / AIMS OF STUDY
The aim of the study was to investigate the effectiveness of physiotherapy in children with voiding disorders and malformation of the urinary tract refractory to medication. Also, establish the minimum number of sessions required to observe the perception of improvement.

STUDY DESIGN, MATERIALS AND METHODS
It is a quantitative, descriptive, observational, and retrospective study based on the analysis of medical charts of patients treated at the Children's Pelvic Physiotherapy Outpatient Clinic of a University Hospital. The effectiveness of the treatment was based on the percentage (%) of improvement reported by the patient and/or guardian during or at the end of the treatment, with the data collected during the sessions being attached to the evolutions and, in turn, to the medical record. After analyzing the data, it was considered worsening when the urinary symptoms persisted at the same intensity or worsened, small improvement when the patient presented between 0-39% of improvement in symptoms, moderate improvement when the patient presented 40-79% of improvement in symptoms. improvement of symptoms and significant and/or complete improvement when the patient presented 80-100%.

RESULTS
Twenty-three medical records were included, with 60.86% of the sample consisting of male patients, with a mean age of 5.95 for both sexes (± 3.22).

INTERPRETATION OF RESULTS
Evaluating the malformations and clinical variables, it was found that the most common malformation among the studied sample was the posterior urethral valve (17.39%), followed by pyelocaliceal dilation (13.04%). As the main complication of the malformation, the occurrence of hydronephrosis was observed in 56.52% of the sample. Regarding the clinical characteristics, the most frequently reported voiding symptoms were urinary tract infection (73.91%), urinary incontinence (60.85%), and voiding urgency (47.82%). The vast majority (91.30%) of these signs and symptoms were not associated with the patient's emotional state. Furthermore, complaints and symptoms of constipation were found in 30.43% of the patients in the sample. As for the physical therapy intervention performed, it was observed that all patients received initial instructions and parasacral electrostimulation with parameters of 10 Hz frequency, 700 us of pulse width, and varying intensity, according to the subject's tolerance, for a period of 30 minutes, 1 time a week. Home exercises were also a frequent intervention, present in 56.52% of patients. Other treatments, such as kinesiotherapy, biofeedback, bladder emptying maneuvers, abdominal exercises, and programmed urination were also interventions present in the medical records, but to a lesser extent. Finally, analyzing the characterization of the number of sessions, the onset of improvement reported and the percentage of improvement reported, it can be observed that most patients (55.52%) underwent 6 to 10 intervention sessions, with the onset of improvement reported between the first 5 sessions (65.21%), with a report of significant and/or total improvement in 65.21% of the analyzed sample.

CONCLUDING MESSAGE
We concluded that Pelvic Physiotherapy is an effective alternative for the treatment of voiding disorders in children diagnosed with urinary tract malformations, in which the previous pharmacological treatment was not successful, with the majority having, significant and/or complete improvement in voiding symptoms (80-100% reported improvement) for 65.21% of the population studied, with rapid responses to treatment (1st to 5th session), also in 65.21% of the sample.

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Funding None **Clinical Trial** No **Subjects** Human **Ethics Committee** College of Medicine Of University of Brasilia - 2.481.442 **Helsinki** Yes **Informed Consent** No

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SESSION 32 - SEXUAL FUNCTION AND UROGENITAL PAIN

Abstracts 494-505
11:30 - 13:00, Hall G
Chair: Dr Marie-Eve Clermont (Canada)

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DYSPAREUNIA ONE YEAR POSTPARTUM. A HIDDEN BURDEN?

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HYPOTHESIS / AIMS OF STUDY
Dyspareunia is a special form of pelvic pain. It belongs to the pelvic floor disorders and still is rather unnoticed hence undertreated. Dyspareunia negatively affects women's relationship, physical health and quality of life (1). Vaginal delivery with its sequelae like episiotomies and perineal injuries which include I° and II° and especially III°/ IV° perineal tears, summarized as obstetric anal sphincter injuries (OASIS) are known to have an influence on postpartum dyspareunia. There are still few data which analyze if postpartum dyspareunia still is a burden one year after.

The aim of this study was to look for the frequency of dyspareunia one year postpartum in relation to possible influencing factors like mode of delivery, e.g. spontaneous vaginal delivery versus vacuum assisted delivery, birthing methods, e.g. bed versus water delivery, perineal lesions as episiotomies and perineal injuries in a cohort of primiparae after vaginal deliveries of singletons in cephalic presentation.

Our hypothesis: Vacuum assisted deliveries (VAD), episiotomies and obstetric anal sphincter injuries are related to a higher frequency of dyspareunia one year postpartum.

STUDY DESIGN, MATERIALS AND METHODS
In a cohort of 3298 primiparae we retrospectively compared the frequency of dyspareunia one year postpartum in the following birthing methods and mode of deliveries:

1. spontaneous bed delivery (SBD), 2. spontaneous water delivery (SWD), 3. spontaneous vaginal delivery other than bed or water, 4. vacuum assisted deliveries (VAD). And we compared the frequency of the following perineal lesions: 1. intact perineum / no perineal lesion, 2. episiotomies, 3. I° perineal tears, 4. II° perineal tears and 5. OASIS.

Objective and subjective data were immediately collected in a specially designed questionnaire. One year after delivery the specially designed questionnaire was sent out; and checked for dyspareunia.

Inclusion criteria: primiparae, ≥ 37 0/7 weeks of gestation, singleton, cephalic presentation, waterbirth with complete delivery of the baby under water, bedbirth, other spontaneous vaginal deliveries (e.g birthing chair) in different positions and vacuum assisted delivery.

Exclusion criteria: preterm birth < 37 0/7 weeks of gestation, cesarian section, multiparae, breech presentation.

The delivery management by the medical staff was identical in all mode of deliveries, e.g., fetal heart rate monitoring, indication for use of oxytocin, restrictively used episiotomies.

For pain relief epidural anesthesia was offered for all deliveries, except for spontaneous water birth.

Episiotomies and perineal tears I° and II° were treated by residents mostly. The diagnosis of OASIS was made by a consultant of obstetrics and gynecology and then treated by them. For all perineal injuries pain management was offered with antiinflammatory analgetics. After OASIS stool regulation was recommended.

Maternal age, fetal birth weight, duration of the delivery were recorded in the questionnaire.

Subgroup analysis to look for the influence between the birthing method/ mode of delivery and the perineal injury was performed.

Data were captured and analysed using the IBM SPSS Statistics software 24. Overall p-values were calculated by Pearson's chi-square or Fisher's exact test for categorical data. A p-value < 0.05 was considered as significant. The confidence interval was 95%.

RESULTS
In the cohort of 3298 primiparae 1210 women had a spontaneous bed delivery, 1148 had a spontaneous water delivery, 421 women had a spontaneous delivery other than bed or water and 519 had a vacuum assisted delivery. In 765 women an intact perineum was reported, 797 women had episiotomies, 530 I° perineal tears, 780 II° perineal tears and 191 OASIS. In 235 women the information about the perineal lesion was not available out of the questionnaire so they weren't included in the perineal lesion groups.

Birthing method and dyspareunia: A year after delivery dyspareunia was reported by 189 (15.6%) women after spontaneous bed delivery, 139 (12.1%) women after spontaneous water delivery, by 55 (13.1%) women after vaginal deliveries in different positions and by 94 (18.1%) women after vacuum assisted delivery. The spontaneous water delivery group had a statistically significant lower frequency of dyspareunia compared to spontaneous bed deliveries and vacuum assisted deliveries, $p = 0.008$, $p < 0.001$ respectively. The difference between spontaneous bed delivery and vacuum assisted delivery as well as between spontaneous other delivery didn't reach significance, $p = 0.113$, $p = 0.234$, respectively.

Perineal lesions and dyspareunia: 765 women had an intact perineum, 797 women had an episiotomy (mostly mediolateral), 530 women suffered from I°, 780 from II° perineal tears and 191 women suffered from OASIS (III° and IV° perineal tear).

Primiparae with intact perineum showed a significantly lower frequency of dyspareunia one year postpartum compared to primiparae with episiotomies, I° perineal tears, II° perineal tears and OASIS: $p = 0.027$, $p = 0.008$, $p < 0.001$, $p < 0.001$ respectively. The difference between I° perineal tears and episiotomies did not reach significance, $p = 0.559$, whereas the the primiparae with II° perineal tears had a significant higher frequency of dyspareunia compared to primiparae with episiotomies, $p < 0.001$.

INTERPRETATION OF RESULTS
Bed deliveries, others than bed/water deliveries and vacuum assisted deliveries didn't show a significant different frequency of dyspareunia a year postpartum. Water delivery seemed to have a positive effect because it showed a significantly lower frequency of dyspareunia.

With 20.4% the group of OASIS had a high frequency of dyspareunia one year postpartum. Interestingly the II° perineal tear group had the highest frequency of dyspareunia even significantly higher than the episiotomy group. In earlier years episiotomies were found to have more side effects than benefits like increased blood loss, greater postpartum pain and dyspareunia so opinion shifted to a restrictive episiotomy policy. Still there are data which show better psycho-physical health status 12 month postpartum in women who underwent an episiotomy (3).

CONCLUDING MESSAGE
Dyspareunia is an underdiagnosed and -treated pelvic floor disorder. Vacuum assisted deliveries, OASIS and II° perineal tears increase the frequency of postpartum dyspareunia which lasts over a year.

As up to 20 % of primiparae suffer from postpartum dyspareunia we should focus on two things:

1. the anatomically correct repair of perineal lesions; with a careful use of suture material and a meticulous technique. Residents should be taught and supervised.

2. A systematically and reliable long term follow-up by a gynecologist as the urgency for treatment seem obvious.

Further studies are needed to prove if the pelvic floor exercises/physiotherapy, perineal massage and low dose local estrogen might be beneficial.

FIGURE 1

	Total	Dyspareunia		No Dyspareunia	
Birthing method		**N**	**%**	**N**	**%**
Bed delivery	1210	189	15.6	1021	84.4
Water delivery	1148	139	12.1	1009	87.9
Other deliveries	421	55	13.1	366	86.9
Vacuum assisted delivery	519	94	18.1	425	81.9
Perineal lesions		**N**	**%**	**N**	**%**
Intact perineum	765	68	8.9	697	91.1
Episiotomy	797	99	12.4	698	87.6
I° Perineal tear	530	72	13.6	458	86.4
II° Perineal tear	780	165	21.2	615	78.8
OASIS	191	39	20.4	152	79.6

Tab 1: Frequency of dyspareunia 1 year postpartum

FIGURE 2

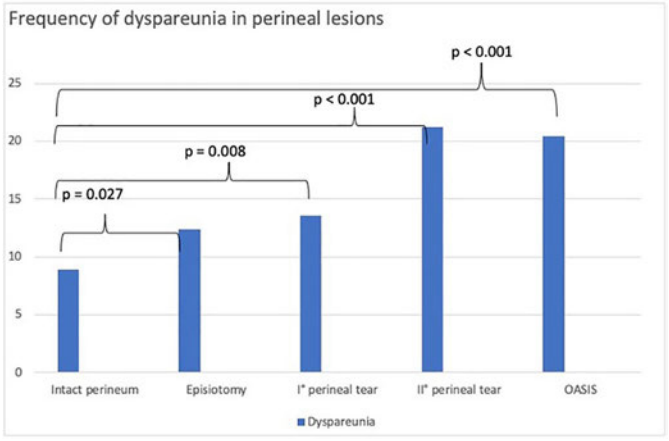

Fig 1: Frequency of dyspareunia in perineal lesions

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OBSTETRIC PERINEAL TEARS, SEXUAL FUNCTION AND DYSPAREUNIA AMONG PRIMIPAROUS WOMEN 12 MONTHS POSTPARTUM: A PROSPECTIVE COHORT STUDY

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HYPOTHESIS / AIMS OF STUDY
Sexuality is an important aspect of human identity and contributes significantly to the quality of life in women as well as in men (1). Sexual function postpartum is affected by the changes in hormonal milieu, anatomy, and family structure following childbirth. Dyspareunia and other sexual problems such as loss of sex drive in the postpartum period is a well-known problem and frequencies of sexual health problems as high as 30-60% three months postpartum and 17-31% six months postpartum have been reported (2). A large cohort study from Sweden found vaginal or perineal tears, regardless of degree, to be associated with a delay in women's resumption of sexual intercourse defined as more than 3 months after giving birth (8), while about 10% of primiparous women had not yet resumed sexual intercourse six months postpartum. The causes of sexual health problems are multifactorial and the mechanisms are still not fully understood. Thus sexual health problems remains an unsolved problem for many women. Among other things, anatomical changes caused by vaginal or perineal tears may contribute to dyspareunia and has important effects on both the timing and quality of the resumption of sexual relations during the initial postpartum months. The association between obstetrical risk factors and postpartum sexual function is not yet well described or understood and thus the aim of this study was to investigate the association between degree of perineal tear, sexual function and dyspareunia 12 months postpartum.

STUDY DESIGN, MATERIALS AND METHODS
The study was a prospective cohort study performed at four Danish hospitals between July 2015 and January 2019.

Women delivering vaginally, at least 18 years old, able to read and speak Danish were eligible. After the delivery, they were informed about the study. Further information was sent by e-mail and the women were invited by phone to participate in a face-to-face interview including baseline question-naires and a clinical examination comprising a perineal inspection at 16 ± 5 days postpartum. Written informed consent was obtained at baseline. At 12 months postpartum, all participants received the same questionnaires electronically and were invited to a gynaecological examination. All examinations took place at the hospital and participants could bring their baby.

Baseline data were obtained 2 weeks postpartum by a questionnaire and a clinical examination. Sexual function was evaluated 12 months postpartum by an electronic questionnaire (PISQ-12) and a clinical examination. Primary outcome measures were the total PISQ-12 score and dyspareunia, while exposure variable was the degree of perineal tear. First-degree tears were defined as injury to perineal skin and/or vaginal mucosa. Second-degree tears were de-fined as injury to perineum involving perineal muscles but not the anal sphincter. Third- and fourth-degree tears were defined as injury to perineum involving the anal sphincter complex. Episiotomies were lateral or mediolateral.

To investigate the association between the degree of perineal tear and dyspareuniaor perineal body length, a relative risk regression by use of a generalized linear model with log-link function and bi-nomial distribution as statistical family was performed with estimates reported as relative risks (RR) with 95% confidence intervals (CI). To investigate the association between the degree of perineal tear and sexual health problems measured as the total PISQ-12 score, a linear regression was performed, and results presented as regression coefficients (β) with 95% CI.

RESULTS
A total of 554 primiparous women participated in the study: 191 with no/labia/first-degree tears, 189 with second-degree tears, and 174 with third-/fourth-degree tears. At 12 months postpartum, more than half of the women who sustained anal sphincter tears had dyspareunia compared to one fourth in women with no/labia/first-degree tears. Women with anal sphincter tears had a higher degree of sexual health problems in general. In addition, we found women with perineal body length $\leq$ 2 cm to be in higher risk of dyspareunia.

Episiotomy was performed in 54 cases and 95 women had an operative vaginal delivery. The proportion of women with dyspareunia was: 25%, 38% and 53% of women with no/labia/first-degree, second-degree or third-/fourth-degree tears, respectively.

Compared to women with no/labia/first-degree tears, women with second degree or third- or fourth-degree tears had higher risk of dyspareunia (aRR 2.05; 95% CI 1.51-2.78 and aRR 2.09; 95% CI 1.55-2.81, respectively). Women with third- or fourth-degree tears had a higher mean PISQ-12 score (12.2) than women with no/labia/first-degree tears (10.4)

INTERPRETATION OF RESULTS
Although sexual problems are common one year after childbirth, especially among women sustaining tears of second-, third- or fourth-degree the proportion of women who ask for help or discuss their problems is low. Thus, it is important to give words to the sexual well-being in the postpartum assessment of women and to put a particular focus on the women in high risk of developing sexual health problems. Further, pregnancy is a time in women's life when they are in contact with the health services. This provides an opportunity to identify and counsel women with dyspareunia as they are at risk of persistent sexual health problems 12 months postpartum.

If dyspareunia seem to be caused by vaginal dryness, local vaginal oestrogen or lubricants should be provided. If tender scar tissue is identified, perineal massage or use of lignocaine gel may be helpfull and thus new mothers should be given these advises.

CONCLUDING MESSAGE
The findings from this cohort study of primiparous women demonstrate that impairment of sexual health is common among primiparous women after vaginal delivery. Women delivering with no tears, tears isolated to the labia or small tears of first-degree reported the best outcomes overall, while more than half of the women with anal sphincter tears were experiencing dyspareunia. It is therefore important to minimize the extent of perineal trauma and to thoroughly counsel women and their partners about sexuality before, during and after pregnancy.

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FUNCTIONALITY OF WOMEN WITH DISPAREUNIA DURING PREGNANCY

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HYPOTHESIS / AIMS OF STUDY

Factors related to women's sexuality are considered a problem by many couples during pregnancy, leading to a significant decrease in the number of sexual intercourses during pregnancy. This decrease in sexual function during pregnancy can be due to a number of factors: religion and sociocultural factors, fear of harming the fetus, discomfort with certain positions, weight of the abdomen, decrease in sexual satisfaction, sexual desire and orgasm, in addition to the emergence of dysfunctions. sexual disorders, such as dyspareunia[1].

Dyspareunia is common in pregnancy and can be associated with other factors such as urinary incontinence and constipation. The intensity and frequency of symptoms increase during pregnancy. Unlike other sexual dysfunctions that tend to decrease after delivery, dyspareunia tends to remain or increase until the third month postpartum[1]. The International Classification of Functioning (ICF) is part of the Classifications developed by the World Health Organization (WHO) and identifies what a person can or cannot do in their daily life, analyzing the functions of the systems and structures of the body, as well as the limitations of activities and social participation in the environment of the person analyzed through functionality [2].

In this sense, it is relevant to study functionality, as it is a concept that integrates a woman-centered approach to examine how a health condition affects her life, but few studies have been carried out from this perspective. Therefore, the aim of the present study is to analyze the functionality of women who had dyspareunia during pregnancy compared to those who did not.

STUDY DESIGN, MATERIALS AND METHODS

This cross-sectional study was approved by the Ethics in Research Committee under registration number CAAE 43945515.5.0000.5568. All participants signed the Free and Informed Consent Term (ICF) to participate in the research. Participants were randomly selected by a sequence of numbers. Women classified as low-risk pregnancies were included, in the second gestational trimester, who were over 18 years of age who underwent prenatal care. The exclusion criteria established were: women who underwent a change in the classification of pregnancy to high risk.

The evaluation form containing sociodemographic aspects and lifestyle habits was created exclusively for this research. The pain complaint was assessed by the woman's self-report. Having the option of answering “yes” or “no” for the presence or absence of pain during the sexual act. To assess functionality, the WHODAS 2.0 questionnaire validated for Portuguese was used. The WHODAS 2.0 has its structure based on the ICF concept and has 36 questions that generate scores for the six domains: cognition, mobility, self-care, interpersonal relationships, life activities and participation in society. The score ranges from 0 to 100, where the higher the score, the worse the functionality of that pregnant woman[2] .

The processing of the collected data was performed using the Statistical Package for the Social Science (SPSS) software, version 20.0 for Windows. The characterization of the sample was performed using measures of central tendency, with their respective values of dispersion, relative and absolute frequencies (for categorical variables). To verify the normality of the data, the Kolmogorov-Smirnov test was performed. Numerical variables are presented as medians and percentiles. Categorical variables were presented as absolute and relative frequencies. The variables resulting from the WHODAS 2.0 were numerical and ranged from 0 to 100, using the Mann-Whitney test. The significance level adopted was 5%, that is, for all tests it was considered significant when $p < 0.05$.

RESULTS

Out of a total of 53 pregnant women accessed for eligibility. The prevalence of dyspareunia was 11.3%. Regarding socio-demographic characteristics and life habits, the majority (71.7%) of the women declared themselves to be non-white. There was a predominance of women who were married (formally or informally), (79,2%), had 11 or more years of schooling (48.1%), did not have paid work (81.1%), had 11 or more years of schooling (48.1%), did not have paid work (81.1%), did not use alcohol (96.2%) did not smoke (98.1%) (Table 1).

When comparing the scores obtained in the WHODAS 2.0, there was a greater disability in those women who had dyspareunia, when compared to those who did not report this condition. Women who had dyspareunia had higher scores in the WHODAS domains: cognition ($P = 0.015$), mobility ($P = 0.003$), self-care ($P = 0.049$), domestic activity ($P = 0.023$), participation (0.016) and in the total score ($P = 0.014$) (Table 2).

INTERPRETATION OF RESULTS

The frequency of 11.3% of dyspareunia was verified in the studied sample, which is lower than what is found in other national studies. Regarding functionality, there was an increase in disability in the total WHODAS scores Also in the cognition domain, which assesses understanding and communication than those who did not have this condition, although this score was relatively low, demonstrating a low impact on functionality in both groups. Concerning the assessment of mobility domains that assess activities such as standing, moving around the house, leaving the house and walking long distances, self-care that assesses hygiene, dressing and eating and being alone. Life activities that assess leisure, work and school household responsibilities. Participation, which assesses participation in community activities and in society, it was verified in the present study that women who had a report of dyspareunia obtained higher scores in all these domains. Corroborating studies that report that gestational adaptations, whether physical, emotional or cognitive, can negatively contribute to the health and functionality of women in the short and long term, and can be intensified if there is any gestational aggravation or discomfort, as well as factors of stress and anxiety, factors that are present in women with dyspareunia [1,2,3]

This study had the limitation of not applying a specific questionnaire for sexual dysfunction, which would result in a better understanding of this symptom. Further studies with longer follow-up and using more adequate instruments are needed to better verify the sexual function and functionality of women during pregnancy and postpartum.

CONCLUDING MESSAGE

The results of this study showed a low prevalence of dyspareunia in the sample studied, however, they suggest that women with dyspareunia during pregnancy, have a greater disability in almost all WHODAS domains, with the exception of interpersonal relationships and school or work activities.

FIGURE 1

Table 1 - Frequency distribution of the demographic variables (n=53).

Variable	n = 53	%
Color / Race		
Black	4	7,5
White	11	20,8
Brown and others	38	71,7
Marital Status		
Single	11	20,8
Married/ Stable Union	42	79,2
Years of study		
Less than 6 years	6	11,5
6 to 10 years	21	40,4
11 years or older	25	48,1
School type		
Public	49	92,5
Private	3	5,7
Did not study	1	1,9
Paid work		
Yes	10	18,9
No	43	81,1
Practice physical exercise		
Yes	2	3,8
No	51	96,2
Alcoholism		
Yes	2	3,8
No	51	96,2
Smoking		
Yes	1	1,9
No	52	98,1

Table 01

FIGURE 2

Table 2 - Comparison of WHODAS 2.0 scores between women with and without dyspareunia during the second trimester of pregnancy.

Outcome variable	Group 1 (n = 6)	Group 2 (n = 47)	p value
Cognition	37,5 (18,7-46,2)	10,0 (0,0-25,0)	0,015
Mobility	62,5 (32,8-75,0)	25,0 (12,5-31,2)	0,003
self care	35,0 (7,5-52,5)	10,0 (0,0-20,0)	0,049
interpersonal relationships	16,6 (0,0-20,83)	8,33 (0,0-16,6)	0,574
domestic activity	80,0 (37,5-92,5)	20,0 (0,0-40,0)	0,023
School or work activities	28,5 (28,5-35,7)	28,5 (28,5-28,5)	0,519
Participation	37,5 (21,8-60,4)	8,33 (0,0-25,0)	0,016
Total	45,65 (25,27-52,99)	13,04 (6,52-23,91)	0,014

Group 1: Dyspareunia. Group 2: No dyspareunia. Values expressed as medians and percentiles (25-75). Mann-Whitney test. Significance of $p<0.05$.

table2

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Funding Federal University of Rio Grande do Norte **Clinical Trial** No **Subjects** Human **Ethics Committee** Comitê de ética em pesquisa (CEP) da Faculdade de Ciências da Saúde do Trairi (FACISA), da Universidade Federal do Rio Grande do Norte (UFRN), que aprovou o projeto sob o número de registro CAAE 43945515.5.0000.5568 **Helsinki** Yes **Informed Consent** Yes

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IS THERE AN ASSOCIATION BETWEEN PELVIC PAIN AND PELVIC FLOOR MUSCLE TONE IN WOMEN WITH PERSISTENT PELVIC PAIN? A SYSTEMATIC REVIEW AND META-ANALYSIS

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HYPOTHESIS / AIMS OF STUDY

Women with persistent pelvic pain may have increased pelvic floor muscle (PFM) tone.[1] Increased PFM tone is closely related to sexual dysfunction and impaired voiding or defecation, which may have a negative impact on women's quality of life.[2, 3] Although the presence of increased PFM tone has been frequently described in women with persistent pelvic pain, the strength or nature of this association is unclear. Therefore, this systematic review aimed to evaluate the association between pelvic pain and increased PFM tone in women with persistent pelvic pain.

STUDY DESIGN, MATERIALS AND METHODS

This was a systematic review with meta-analysis. The review followed PRISMA guidelines and was pre-registered on Prospero.

Six electronic databases (MEDLINE, Embase, Emcare, CINAHL, PsycINFO, and Scopus) were searched from inception to June 2021 using standardised terms. Studies that reported measures of pelvic pain and PFM tone among women over 18 years were included. All study designs were included except for case reports as well as systematic and narrative literature reviews. Studies were excluded if participants were women with neurological conditions or who had received any medications that could affect muscle tone. Studies were entered into Covidence and screened by title, abstract and full paper as necessary. Two reviewers screened titles and abstracts independently and reached agreements on articles that did not meet the inclusion criteria; the two reviewers then also independently reviewed the full text against the selection criteria.

The risk of bias of included studies was assessed using the National Heart, Lung and Blood Institute (NHLBI) Quality Assessment Tools for Observational Cohort and Cross-Sectional Studies by two reviewers. The association between pelvic pain and PFM tone was assessed using Pearson, Spearman's correlation, or odds ratio (OR). Included studies were analysed according to how PFM tone was assessed (i.e., digital palpation, electromyography, dynamometry, manometry, ultrasound imaging, strain elastography, and myotonometry) and data were pooled using a random effects model. Effect sizes calculated from correlation coefficients were classified as: small ($r \geq 0.1$), medium (≥ 0.3), and large (≥ 0.5). Heterogeneity between studies was assessed using the I2 statistic.

RESULTS

The electronic database search identified 1604 potentially relevant articles. Twenty-three studies met the inclusion criteria, from which 16 studies were included in the meta-analysis. The majority of included studies were cross-sectional in design. The mean score from the risk of bias assessment was 8, ranging from 5/10 to 10/10. Pelvic pain was assessed using either patient-reported outcome measures or clinician-reported outcome measures. Pelvic floor muscle tone was assessed using seven different assessment methods.

There was a significant association between the presence of pelvic pain and increased PFM tone assessed by digital palpation (OR 8.72; 95% confidence interval [CI] 2.73, 27.89). Pelvic pain was inversely associated with PFM flexibility when evaluated using dynamometry ($r = -0.29$; 95% CI - 0.42, -0.17). However, there were no significant linear associations between pelvic pain and PFM tone measured by other assessment methods including electromyography, myotonometry, pressure manometry, ultrasound imaging, and strain elastography.

INTERPRETATION OF RESULTS

Pelvic pain and increased PFM tone may coexist in women with persistent pelvic pain but may not necessarily be linearly associated with each other. The association between pelvic pain and increased PFM tone could be mediated by other biopsychosocial factors that we have not necessarily captured in this systematic review and meta-analysis.

CONCLUDING MESSAGE

This review and meta-analysis found some evidence of the association between pelvic pain and PFM tone measured by digital palpation and dynamometry. However, we did not find linear associations between pelvic pain and PFM tone measured by other assessment methods. To better understand the nature of the association between pelvic pain and PFM tone, further research is required using valid and reliable assessment methods to quantify PFM tone while accounting for other factors that could affect the pain experience, such as variations between persistent pelvic pain conditions and the impact of a range of biopsychosocial factors on pelvic pain.

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MINDFULNESS-BASED BODY SCAN TRAINING IN PHYSIOTHERAPY FOR VULVODYNIA – A FEASIBILITY STUDY

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HYPOTHESIS / AIMS OF STUDY
The current study assessed the feasibility and the potential effects of the body scan as a mindfulness-based intervention integrated in physiotherapy for women with vulvodynia. The primary aim of this study is to investigate whether the mindfulness body scan is a safe and feasible tool in pelvic floor physiotherapy for vulvodynia.

The first objective was to determine the feasibility of conducting a randomized clinical trial designed to compare multimodal pelvic floor therapy with and without mindfulness-based body scan training among patients diagnosed with vulvodynia.

The secondary objective was to assess the impact on outcome parameters. For this purpose, a pilot study was conducted and evaluated.

The research question “Do patients diagnosed with vulvodynia benefit more from body scan training in combination with standard multimodal pelvic floor physical therapy than from standard multimodal pelvic floor physical therapy alone in terms of average pain intensity?” was formulated. This study aimed to determine the protocol and the sample size for a follow-up study.

STUDY DESIGN, MATERIALS AND METHODS
In this unblinded randomized controlled trial, participants were women diagnosed with vulvodynia who were prescribed physical therapy. Participating patients were randomized to either multimodal physiotherapy or multimodal physiotherapy plus mindfulness-based body scan training. For the control group as well as for the intervention group, 10 therapy sessions of 60 minutes each of standard multimodal pelvic floor physiotherapy were scheduled over a total period of 10 weeks. The intervention group was instructed to perform the 25-minute body scan 5 times a week in addition to physiotherapy. An audio file for practice and a body scan diary for documentation were handed out. The criteria of feasibility were predefined.

The primary outcome was the average pain intensity assessed with the Numerical Rating Scale (NRS) on the questionnaire "Measuring Pain Intensity". In addition, the following secondary outcomes were collected:

Current, least, most intense pain intensity over the past 7 were conducted using the Measuring Pain Intensity Questionnaire. Sensory and affective pain quality was assessed using the McGill-Melzack Pain Questionnaire (SF-MPQ). Personal distress, related to sexuality, was assessed using the Female Sexual Distress Scale (FSDS). Sexual function was assessed using the Female Sexual Function Index (FSFI). Pain-related self-efficacy was elicited using Pain Self-Efficacy Questionnaire (PSEQ).

The intensity of body awareness was measured using the Awareness Body Chart (ABC). Pain-related Catastrophizing was tested with Pain Catastrophizing Scale (PCS). The impression of change due to therapy was assessed with the Patient Global Impression of Change Scale (PGIC).

To determine trends of a fundamental effect, parallel group comparisons of the mean values of the most important parameters were performed. The evaluation was carried out using non-parametric methods, which enabled a comparison of pain reduction and secondary outcomes between the therapy groups. Based on an intention-to-treat analysis, the values obtained were compared over the course of the 3 survey time points. Assessments were made at baseline, post-treatment and at the 2.5 month follow-up.

RESULTS
Thirty-three women with vulvodynia met the inclusion criteria. The groups consisted of following participants: 17 were randomized to the intervention group receiving multimodal pelvic floor physiotherapy and body scan training, while 16 were assigned to the control group receiving multimodal pelvic floor physiotherapy. Of the participants in the intervention group, a total of 15 women completed the body scan training more than 10 times, at a mean of 27.9 times.

The mean of the average pain intensity showed 2.9 (58 %) sustainable reduction from baseline to follow-up in the intervention group in comparison with no change in the control group.

The following secondary outcomes show distinct differences in comparison of mean values, baseline to follow-up, between the intervention and control group:

present pain intensity (NRS) –3.5 (70 %) (intervention group): ¬–0.3 (10.4 %)

(control group);

least pain intensity (NRS): –2.4 (63.16 %): –0.2 (10.53 %)

worst pain intensity (NRS) –3.8 (51.36 %): –1 (18.18 %)

Female Sexual Distress Scale (FSDS-Revised): –28.2 (51,7 %): –2.8 (8,95 %)

Pain Catastrophizing (PCS): –13,1 (56,22 %): –3.3 (17,18 %)

Pain intensity at internal pelvic floor screening (NRS): –3.4 (61,81%): –0.8 (19,51%)

Sensory pain index (SF-MPQ): –6.6 (50%): –0.9 (7.9%).

Affective pain index (SF-MPQ): –1.9 (59.37 %): –0.3 (11.25 %).

Sexual function (FSFI total score): + 6 (16,66 %): + 4.7 (13,05 %).

Pain-related self-efficacy (PSEQ): + 8.9 (19.14%): + 4.1 (7.9%).

Intensity Body Awareness (ABC): +0.28: +0.27, 0.01 difference.

The change due to therapy, measured by PGIC, shows a clear change only in the intervention group.

The sample size calculation was based on the values of the primary outcome average pain intensity. Recruitment of 99 patients is needed for 0.05 failure probability and variance of 1, drop-out 10 percent in a following trial.

INTERPRETATION OF RESULTS
The criteria to judge the feasibility of the body scan, of the protocol and of conducting a trial were met.

Clear improvements in the group comparison were seen for the outcomes of average pain intensity and sex-related distress.

Comparing the mean values shows clear reduction of pain in all tested pain-parameters. Mindfulness body scan training seems to be a promising pain and stress reduction strategy in physiotherapy for vulvodynia.

Due to the overall small increase in scores, no improvement in sexual function can be measured with the FSFI. Better results for the intervention group were shown on all tests except intensity of body awareness.

CONCLUDING MESSAGE
This was the first randomized controlled unblinded pilot study to examine the use of a mindfulness-based body scan intervention integrated in physiotherapy for vulvodynia. The findings suggest that mindfulness-based body scan training is a safe and feasible tool integrated in multimodal pelvic floor physiotherapy. The intervention studied seems to make physiotherapy for vulvodynia more efficient in terms of pain and stress reduction. A larger double-blind randomized controlled trial should confirm the promising findings of this pilot study.

Funding Non **Clinical Trial** No **Subjects** Human **Ethics Committee** Ethikkommission Wien **Helsinki** Yes **Informed Consent** Yes

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NERVE SPARING RADICAL HYSTERECTOMY: WHY TO DO IT AND HOW?

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1. AIIMS

HYPOTHESIS / AIMS OF STUDY

Nerve Sparing Radical Hysterectomy (NSRH) is desirable in all cases of hysterectomy to avoid bowel, bladder and sexual dysfunction which are as high as 40% in literature. Meticulous anatomical knowledge of pelvic nerves, course of ureters, vessels, vessels plexus, various pelvic spaces and over all the skill of the surgeon are pivotal for this technically challenging surgery.

STUDY DESIGN, MATERIALS AND METHODS

We performed NSRH in our 105 cases of carcinoma cervix (up to stage IIA), endometrial carcinoma and carcinoma ovary (both upfront and interval setting). We adopted our technique in all cases and observed perioperative outcomes in terms of bowel bladder and sexual dysfunctions and quality of life issues by asking questioners on follow-up.

Standard operative steps are followed till the ligation of uterine artery and superficial uterine vein. The next zone of dissection is crucial, and we termed it as 'Red Alert Zone' of pelvis. We were careful in the following area to safeguard the Hypogastric and pelvic Splanchnic nerves during the division of uterosacral and rectovaginal ligament, during the division of deep uterine vein in cardinal ligament, division of Vessels plexus in vesicouterine ligament, vaginal blood vessels in paracolpos area and during bladder mobilization from the anterior wall of the vagina.

RESULTS

We performed 105 cases of NSRH. This includes 45 ca cervix (up to stage IIA), 28 cases of ca endometrium and 32 cases of carcinoma ovary. The mean operative time for NSRH alone was 120 minutes (90 min to 150 minutes). The mean blood loss was 200 ± 50 ml as compared to 450 ± 50 ml with our previous conventional technique. In a multivariate analysis, we found that obese patients (BMI >30), and post chemotherapy desmoplastic changes were associated with longer operative time. We followed ERAS protocol for all patients, underwent NSRH. We removed Ryle's tube in the evening of the day of surgery. In the following day, we removed Foley's catheter. Urinary retention was noted in 4.76% (N = 5). We observed obese and diabetic patients having the tendency for urinary retention more. We used EORTC Ov28 questionnaire to assess sexual dysfunction at around 8 weeks.28.5% (n-30) patients were sexually inactive and 5.7% (n = 6) reported vaginal dryness during sexual activity. There was no post-operative mortality. Intraoperative complications included bladder injury 2.9% (n = 3), ureteric injury 3.8% (n = 4) which occurred in post NACT ovarian cancer patients.

INTERPRETATION OF RESULTS

Nerve Sparing Hysterectomy is essential to sustain quality of life after Radical Hysterectomy, Sexual Dysfunction is usually 13-37% after pelvic surgery. The limited data suggests that NSRH can have some impact in improving female sexual life. Bowel bladder dysfunction reported as 20-40%. Development of new diagnostic test and perfect surgical techniques can spare genital nerves and vaginal and clitoral blood supply to preserve female sexual function and bowel bladder dysfunctions like ours technique. The detailed anatomical knowledge of pelvic nerves helps in meticulous dissection for NSRH and hence improving perioperative quality of life. Defining different pelvic zones, delineating of all anatomical structures, like our technique, need to be implemented in routine practice for expected outcomes.

CONCLUDING MESSAGE

Nerve sparing Hysterectomy should be the standard of care for any patient undergoing radical hysterectomy procedure. It is feasible for selected gynae oncology patients even after chemotherapy .It improves quality of life in terms of bowel ,bladder and sexual dysfunction significantly.

FIGURE 1

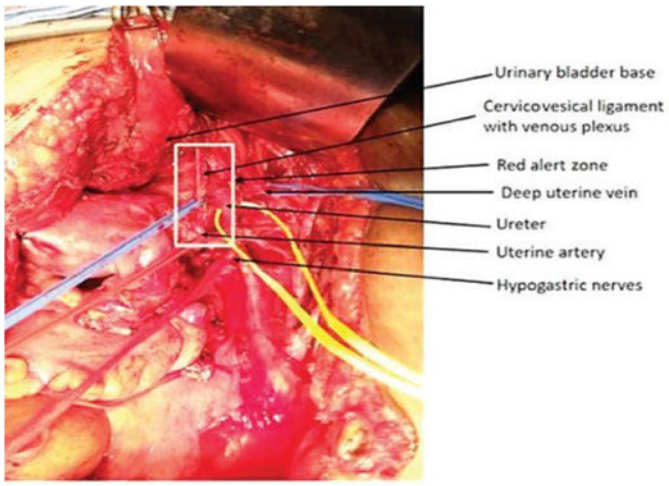

Figure 1: Red Alert Zone showing various important structures

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EFFECTS OF COVID-19 PANDEMICS ON SYMPTOMS AND QUALITY OF LIFE IN PATIENTS AFFECTED BY INTERSTITIAL CYSTITIS/ PAINFUL BLADDER SYNDROME (IC/PBS) AND IRRITABLE BOWEL SYNDROME (IBS)

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HYPOTHESIS / AIMS OF STUDY
Interstitial Cystitis (IC), also known as Painful Bladder Syndrome (BPS), is a chronic painful bladder condition characterized by persistent unpleasant sensations attributable to the bladder, of which the most consistent feature is an increase in discomfort with bladder filling and a relief with voiding. IC/PBS often coexists with other chronic pain syndromes such as irritable bowel syndrome (IBS). IBS is a chronic functional disorder of the gastrointestinal tract characterized by chronic abdominal pain and altered bowel habits. Both IC/BPS and IBS do not have a certain aetiology and are characterized by chronic relapsing course. There is a positive correlation between the incidence of this association and increased healthcare seeking, reduction in quality of life, and higher levels of mood disorders, which suggests a common underlying pathophysiology. Furthermore, exacerbations of IBS and IC/BPS symptoms have been associated to acute stressful life events. Those determine a high prevalence of anxiety, depression and stress, chronic reduction in coping capacity and endurance of pain and fatigue. The COVID-19 pandemic has led to unprecedented disruptions in healthcare. During the first months of the pandemic, mental health was influenced by various vulnerability factors and stressors, led alone in patients affected by chronic diseases such as IC/BPS and IBS. One of the most evident psychological consequences of Coronavirus was the deterioration of quality of life of those patients, as their daily life is dominated by management of sphincter functions and pain. The aim of this study was to observe the changes that the covid19 lockdown brought in terms of symptoms and quality of life.

STUDY DESIGN, MATERIALS AND METHODS
We here present a prospective observational study conducted in our referral center from March 2020 to June 2020. We enrolled patients diagnosed with CI/BPS and IBS, referred to our outpatient clinic in the previous year. Ethical committee approval was obtained, and patients signed an informed consent. All patients had previously undergone a complete urogynecological evaluation and had completed the following questionnaires: Gastrointestinal Symptom Rating Scale (GSRS), Bristol Stool Chart (BSC), Euro - QoL Visual Analogue Scale (EQ-VAS), State-Trait Anxiety Inventory STAI-Y1 and STAI-Y2, Psychological General Well-Being Index (PGWBI), Hospital Anxiety and Depression Scale (HADS), General Self-Efficacy (GSE), Connor-Davidson (CD-RISC), O'Leary-Sant IC Symptom Index (ICSI) and IC Problem Index (ICPI). Enrolled patients completed the same questionnaires between March 2020 and May 2020, during the lockdown. Between June and July 2020, all patients underwent a second urogynecological examination.

Our primary endpoint was to evaluate the extent of exacerbation of symptoms of IC/PBS and IBS caused by the COVID19 pandemic. Our secondary endpoint was to assess the effectiveness of remote management of these patients during those months through the administration of questionnaires. We included patients with clinical and histological diagnosis of PBS / CI and IBS. Exclusion criteria included: age <18 years, patients unable to provide informed consent, malignancies, previous diagnosis of major depressive disorder, chronic use of opioids.

RESULTS
Twenty-eight patients affected by IC/BPS and IBS were included in this study. Patient demographics are shown in table 1. In Table 2, all results regarding the questionnaires and physical examination are reported at T0 (before the covid-19 pandemic), and at T1 (during lockdown). The EQ-VAS values evaluated at T0 and T1 were compared, and no statistical significance was noted. We assessed the presence of GI symptoms by analysing the Bristol Stool Chart (BSC) and the Gastrointestinal Symptom Rating Scale (GSRS). Twelve patients reported having stool type compatible with irritable bowel syndrome (IBS) at T0, whilst at T1 15 patients fit into this category, although the rise did not reach statistical significance. As for GSRS results, average score reported by patients showed that 14 out of 28 patients (42.9%) had a score higher than the cut-off at t0, while 16 patients reached the same scores at T1, without statistical difference. As for the psychometric assessment of patients with PBS / CI, we used six different tests: STAI-Y1, STAI-Y2, PGWBI, HADS, GSE and CD-RISC. We compared the specific scores evaluated at T0, before the COVID-19 pandemic struck, with the results of the same scores at T1 corresponding to the period of full lockdown. No statistical significant difference was noted. On the other hand, the results regarding the O'Leary-Sant IC Symptom Index (ICSI) and IC Problem Index (ICPI) showed higher scoring after the lockdown, reaching statistical significance. In accordance with this result, patients reported an increase in frequency during lockdown, that proved to be statistically significant. Furthermore, the urogynecological physical exam performed after the end of the lockdown showed an increase in pain using the VAS scale evoked by muscle palpation, as well as higher severity of pelvic floor muscles hypertonicity.

INTERPRETATION OF RESULTS
The statistical differences between the psychometric assessment as well as the gastrointestinal symptoms turned out to be non significant, which drove us to the conclusion that psychological profile of PBS/IC patients was not highly influenced by lockdown. On the other hand, a small increase in psychological and GI symptoms was noted, so the small number of patients included might have influenced the results. On the other hand, the results regarding the O'Leary-Sant IC Symptom Index (ICSI) and IC Problem Index (ICPI) indicated a worsening in urinary symptoms and a higher perception of IC as a problem in daily life during lockdown. This was also confirmed by the urogynecological evaluation, that showed a higher pelvic floor muscles contraction and higher pain perception.

CONCLUDING MESSAGE
In conclusion, remote management through questionnaires seems to be an effective tool to show any worsening in symptoms in patients with disabling conditions such as IC/PBS and IBS, to avoid delays in medical care.

In our experience, IC/PBS symptoms seem to have worsened during those months of isolation and forced home stay, even though the small number of patients included might have underestimated its impact on their quality of life.

FIGURE 1

TABLE 1 - DEMOGRAPHICS

Characteristics (n=28)	Mean±SD
Age, years	48,5±11,7
Weight (Kg)	65,6±12,4
Height (cm)	164,2±6,8
BMI (Kg/ m²)	24,2±3,7
Number of comorbidities	2,7±3,0
Number of previous surgeries	2,5±1,6

Table 1

FIGURE 2
TABLE 2 - RESULTS

SCORE	MEAN T0 +- SD	MEAN T1 +- SD	P VALUE
EQ-VAS (normal range >70)	55.2 ± 23.9	56.9 ± 20.1	> 0.05
STAI Y1 (normal range <40)	42.5 ± 7.69	40.3 ± 7.1	> 0.05
STAI Y2 (normal range <40)	44.3 ± 5.3	44.25 ± 5.3	> 0.05
HADS (normal range <11)	18.2 ± 4.8	17.9 ± 4.9	> 0.05
PGWBI (normal range >70)	54.1 ± 20.5	53.7 ± 22.2	> 0.05
CD RISC (normal range >40)	62.1 ± 8.7	61.8 ± 11.2	> 0.05
GSE (normal range >20)	27.3 ± 5.6	27.9 ± 7.2	> 0.05
BSC (% of type 1/2/5/6)	12/28 (42.9%)	15/28 (53.6%)	> 0.05
GSRS (normal range >22.5)	14/28 (50%)	16/28 (57.1%)	> 0.05
ICSI	8.9 ± 4.4	12.3 ± 3.4	**< 0.05**
ICPI	7.7 ± 4.6	11.4 ± 3.0	**< 0.05**
Frequency	8.25 ± 2.47	13.57 ± 2.97	**< 0.05**
VAS at pelvic floor examination	3.46 ± 1.95	5.45 ± 2.27	**< 0.05**
PC TEST	1.54 ± 1.10	1.57 ± 1.4	>0.05

Table 2

Funding The authors declare that they do not have relevant or material financial interests that relate to the research described in this paper **Clinical Trial** No **Subjects** Human **Ethics Committee** Catholic University of Sacred Heart, Rome, Italy **Helsinki** Yes **Informed Consent** Yes

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ASSOCIATIONS BETWEEN UROLOGIC CHRONIC PELVIC PAIN SYMPTOM FLARES AND QUALITY OF LIFE, HEALTH-CARE SEEKING ACTIVITY, AND ILLNESS IMPACT: FINDINGS FROM THE MULTIDISCIPLINARY APPROACH TO THE STUDY OF CHRONIC PELVIC PAIN SYMPTOM PATTERNS STUDY

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HYPOTHESIS / AIMS OF STUDY

Symptoms of urologic chronic pelvic pain syndrome (UCPPS, including interstitial cystitis/bladder pain syndrome and chronic prostatitis/chronic pelvic pain syndrome) are well-known to fluctuate, with symptom exacerbations – periods of time when symptoms are much worse than usual – often referred to as "flares." Previous studies have shown that flares are associated with decreased quality of life (QOL) and greater health-care utilization, with the degree of impact driven by the frequency, pain intensity, duration, and unpredictability of flares.

Despite their negative impact on patients' lives, flares are rarely documented in UCPPS research. Most UCPPS studies monitor changes in participants' condition by assessing changes in their typical or average levels of pain and urinary symptoms or their impression of changes in their condition over time (i.e., global response assessment). Both of these measures have been shown to correlate with QOL and illness impact, supporting their use as outcomes in UCPPS research. Although flares have also been shown to impact QOL, no studies, to our knowledge, have investigated whether flares influence QOL, health-care seeking behavior, and illness impact independently of typical pain intensity, and thus whether they merit consideration as additional outcomes in UCPPS research (i.e., whether reducing flare frequency without reducing mean pain intensity may still be important to patients). Therefore, we used data from the Multidisciplinary Approach to the Study of Chronic Pelvic Pain (MAPP) Symptom Patterns Study to investigate associations between flares and QOL, health-care seeking activity, and illness impact, independent of mean pain levels. We hypothesized that flares would be associated with QOL, health-care seeking activity, and illness impact, independent of typical pain intensity, and that this impact would be greatest for patients with the highest flare frequency.

STUDY DESIGN, MATERIALS AND METHODS

The MAPP Symptom Patterns Study was a three-year longitudinal study of UCPPS patients designed to investigate the "usual-care" natural history of UCPPS and to identify patient sub-groups with possible differing etiology and clinical course. Initial study participation involved attending a "screening" visit (week 0); completing three weekly, online "run-in" assessments (weeks 1, 2, and 3); and then attending a "baseline" study visit at week 4. After the baseline visit, participants were followed by quarterly online assessments and in-person visits at 6, 18, and 36 months of follow-up. Recruitment began in July 2015 and ended in February 2019.

At the screening visit and each run-in assessment, participants were asked to report their frequency of flares and typical pelvic pain levels; as well as to provide information on condition-specific QOL (Genitourinary Pain Index Quality of Life Impact Sub-Scale), condition-specific health-care seeking activity (MAPP-specific item), and general illness impact or disability (World Health Organization Disability Assessment Schedule). Standardized beta coefficients were calculated by generalized estimating equations and used to estimate associations between flare frequency and QOL, health-care seeking activity, and illness impact, independent of typical pelvic pain levels (Figure 1).

RESULTS

Overall, 592 of 620 Symptom Patterns Study participants were eligible for the analysis. In minimally-adjusted models, participants who reported at least 1 flare/week had worse condition-specific QOL, and those who reported at least 2 flares/week had greater health-care seeking activity and general disability than those who reported no flares in the past week. After adjustment for typical pelvic pain intensity, associations attenuated, but remained statistically significant for at least one flare/week with worse condition-specific QOL, at least 2 flares/week with greater health-care seeking activity, and at least 1 flare/day with worse overall disability (Table 1 and Figure 1).

INTERPRETATION OF RESULTS

Our findings suggest that patients who experience flares have worse QOL and greater health-care seeking activity and illness impact than patients who do not experience flares, independent of typical pelvic pain levels. Our findings also suggest greater impact with increasing frequency of flares.

CONCLUDING MESSAGE

Our observation of independent associations between flares and QOL, health-care seeking behavior, and illness impact suggest that patients may benefit from treatment and management strategies that reduce their flare frequency, even if they do not reduce their overall pain intensity. For this reason, we propose that flares are worth considering as additional outcomes in clinical trials and other research studies, as well in clinical practice.

FIGURE 1

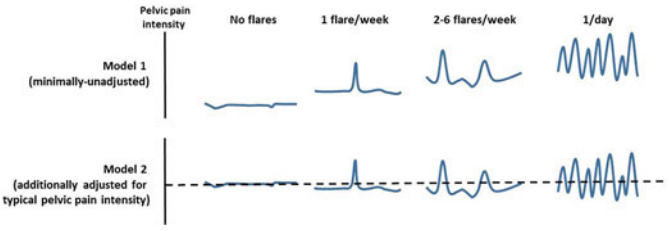

Figure 1: Illustration of adjustment for typical pelvic pain intensity

FIGURE 2

Flare frequency	Model	Condition-specific		General
		Quality of life	Health-care seeking activity	Disability
Reference: 0 flares				
1/week	1	**0.27 (0.17-0.36)**	0.13 (-0.01-0.09)	0.03 (-0.04-0.09)
	2	**0.12 (0.03-0.20)**	0.07 (-0.07-0.22)	-0.02 (-0.09-0.04)
2-6/week	1	**0.54 (0.45-0.62)**	**0.24 (0.11-0.36)**	**0.14 (0.08-0.21)**
	2	**0.28 (0.21-0.36)**	**0.12 (0.00-0.24)**	0.04 (-0.03-0.10)
1/day	1	**0.65 (0.53-0.76)**	**0.55 (0.29-0.80)**	**0.24 (0.14-0.35)**
	2	**0.31 (0.20-0.42)**	**0.40 (0.14-0.66)**	**0.11 (0.00-0.20)**

Estimates with p-values<0.05 are bolded and shaded in grey.
Model 1: Adjusted for typical urinary symptom intensity, typical non-pelvic pain intensity, age, and sex.
Model 2: Additionally adjusted for typical pelvic pain intensity.

Table 1: Associations (standardized beta coefficients) between flare frequency and quality of life, health-care seeking activity, and illness impact (disability) in urologic chronic pelvic pain syndrome participants

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BELIEFS AND EXPERIENCES OF PEOPLE WITH CHRONIC PELVIC PAIN

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HYPOTHESIS / AIMS OF STUDY
This is the first study that aims to profile the beliefs and experiences of females with chronic pelvic pain and their healthcare management based on contemporary clinical management guidelines.

STUDY DESIGN, MATERIALS AND METHODS
A cross-sectional cohort study using an anonymous online questionnaire distributed through social media groups and private practice clinics. Ethics approval was provided, and patients' informed consent was public and accessible to all participants and provided at the start of the questionnaire.

A sample size of 384 was calculated by Qualtrics Precision Sample Size Calculator to give 95% confidence level and a significance level of 0.05.

Methods: Development and implementation of a novel questionnaire informed by recommendations in clinical management guidelines.

Main outcomes and measures: Descriptive data related to demographics including two validated tools (the Brief Pain Inventory and the Brief Illness Perception Questionnaire), beliefs and experiences related to diagnosis, health care practitioner interaction, assessment, and management of chronic pelvic pain.

RESULTS
Of 465 participants, 64.3% experienced their pain before 18 years of age, but only 36.4% first sought help before 18 years of age. In those seen by a health care practitioner 42.9% felt their pain was not validated and 45.6% were not asked what their personal beliefs were for the cause of their pain. Participant's pain profiles included 85.6% experienced pain during and in between menstruation with 59.3% using at least one form of hormonal therapy. Of 428 participants whom consented to answer optional sexual abuse questions, only 25.6% were screened by health care practitioners for a history of sexual abuse.

Of all participants, 90.8% received a physical examination to assist diagnosis, 60.0% felt the examination was thorough and 51.6% found it to be helpful. In addition, 80.4% of participants believed they needed a diagnosis for their chronic pelvic pain, prior to participating in treatment; 68.8% believed they had been given a diagnosis, and 65.6% felt the diagnosis was correct. However, 15.0% were unsure if the diagnosis was correct and 38.5% believed that something 'worse' was happening to them that had not been diagnosed yet.

INTERPRETATION OF RESULTS
Supported in a recent systematic review and European Association of Urology guidelines (1) adolescents should be encouraged to seek support before symptoms become severe. Adolescents can use suboptimal self-management strategies if not seen by a healthcare practitioner. If care is delayed it can lead to sequalae impact of chronic pelvic pain on educational study and extracurricular activity demands (2).

Additionally, those experiencing pelvic pain often experience dyspareunia, this was reflected by almost 80% of participants in our study. All educators need to be familiar with Comprehensive Sexuality Education, to help conceptualise positive sexuality from a young age and once more when to seek help.

The guidelines also strongly recommend that healthcare practitioners provide validation of the patient's pain (1). The results of our study show a disconnect between clinical management guidelines and patient experiences which are reflected in other studies. It is well documented that disclosure of pelvic pain can be difficult; failing of healthcare practitioners to validate a patient's pain experience from the outset flows on to an inability for the patient to discuss their concerns as to the cause of their pain (3). This may lead to missed opportunities for the healthcare practitioner to triage accurate specialist referrals, educate and provide probable diagnosis rationale which serves to allay potential fears and catastrophising beliefs. Education would include the purposes of first line management options in line with clinical management guidelines such as hormonal therapy.

CONCLUDING MESSAGE
The highlighted gaps between the clinical management guidelines and the reality for patients are largely represented by missed opportunity for early intervention, invalidation of patient's pain, insufficient education including benefits of management options like hormonal therapy, and suboptimal screening of sexual abuse.

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INTERSTITIAL CYSTITIS/ BLADDER PAIN SYNDROME AND INFLAMMATORY BOWEL DISEASES. IS THERE ANY CLINICAL CONNECTION?

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HYPOTHESIS / AIMS OF STUDY

A possible correlation of inflammatory bowel diseases (IBDs) with interstitial cystitis/ bladder pain syndrome (IC/BPS) has been studied in animal models, demonstrating a bidirectional neural cross-sensitization between colon and lower urinary tract [1][2]. However, clinical trials have not provided yet adequate evidence for a direct correlation in the era of clinical manifestations. Also, the use of monoclonal antibodies as treatment modalities in IBDs and IC/BPS has aroused the question of potent common strategies in these situations, although evidence is low, especially for the IC/BPS [3]. The aim of our study is to evaluate any possible clinical correlation between IBDs and IC/BPS, as well as to overview any effect of monoclonal treatment for IBDs in the clinical manifestations of IC/BPS.

STUDY DESIGN, MATERIALS AND METHODS

This is a clinical observational study enrolling female patients with inflammatory bowel disease under treatment with monoclonal antibodies from the Gastrointestinal Department of our hospital. All women with an at least three months therapeutic scheme were regarded as eligible for the study. Exclusion criteria were any recent or concurrent treatment for any lower urinary tract disease, previous treatment for IC/BPS, a medical history of recurrent urinary tract infections, bladder cancer, bladder stones, pelvic surgery, radiotherapy, pregnancy and a known gynecological disease. The evaluation of lower urinary tract symptoms (LUTS) has been performed with the Incontinence Quality of Life Questionnaire (I-QoL), International Consultation on Incontinence Questionnaire-Female Lower Urinary Tract Symptoms (ICIQ-FLUTS) and International Consultation on Incontinence Questionnaire Female Sexual Matters Associated with Lower Urinary Tract Symptoms Module (ICIQ-FLUTSsex). Bladder pain measurement has been based on Visual Analogue Scale (VAS). All women underwent a cystoscopy at least three months after the beginning of monoclonal treatment, independent of reporting bladder pain or LUTS.

RESULTS

18 women with a mean age of 42.7 years old have been enrolled and finished the study. 11 (61.1%) of them suffered for Crohn's disease, while 7 (38.9%) of them had Ulcerative Colitis. All patients reported symptoms related to IBDs; 6 (33.3%) mucus or blood in stool, 3 (16.7%) diarrhea, 1 (5.6%) abdominal pain and 8 (44.4%) combination of the above. The vast majority (94.4%) received treatment with infliximab, while the 5.6% received vedolizumab with a mean duration of 95 months. Additionally, all women were complaining about LUTS. However, only 2 (11.1%) of them documented in ICIQ-FULTS that these symptoms were bothersome affecting negatively their quality of life. The mean I-QoL score was 102.1, with only 4 patients (22.2%) under the cut point of 100. The mean I-QoL for the subgroup of those 4 women was equal to 92. 6 women (33.3%) localized pain mainly in the bladder area with a mean VAS score of 6.5. Moreover, the same 6 patients reported pain and limitations during sexual intercourse and all of them had a cystoscopy with diffusible bladder inflammation without Hunner's lesions. Only one patient documented improvement of LUTS or pain during monoclinal treatment for the underlying IBD.

INTERPRETATION OF RESULTS

The clinical investigation for the correlation between IBDs and IC/BPS has a lot do in the way of proving a possible common pathophysiological mechanism. In our study, a co-existence of an already diagnosed IBD with lower urinary tract symptoms and cystoscopic findings has been found, implying a potent relationship between them. On the other hand, a possible therapeutic benefit of the monoclonal antibodies, been used for IBDs, on IC/BPS has been investigated without a positive message. The limitations of our study were the small recruitment, the short-term follow-up and lack of bladder biopsies in order to specify the number of macrophages in patients with IC/BPS.

CONCLUDING MESSAGE

Inflammatory bowel diseases and interstitial cystitis/ bladder pain syndrome may have common pathophysiological pathways and parallel clinical manifestations. Our study suggests that basic research investigation and more clinical trials are needed to definite and highlight this correlation.

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SEXUAL DYSFUNCTION IN WOMEN WITH INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME: DO ONABOTULINUM TOXIN-A INJECTIONS IMPROVE SEXUAL FUNCTION?

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HYPOTHESIS / AIMS OF STUDY

Symptoms of IC/BPS have a negative impact on female sexual function. We aimed to evaluate the effect of intravesical botulinum toxin-A(Btx-A) injection on the improvement of sexual dysfunction and urinary syptoms using the multi domain Female Sexual Function Index(FSFI) questionnaire and interstitial cystitis symptom index (ICSI), and interstitial cystitis problem index(ICPI).

STUDY DESIGN, MATERIALS AND METHODS

The data of the 23 patients who were diagnosed with refractory IC/BPS and received intravesical Btx-A between January 2015 and December 2019 were retrospectively reviewed in this single-center study. The study group was named “Group 1” and evaluated in two groups as follows: Group 1A (pretreatment scores) and Group 1B (posttreatment scores). Subsequently, 23 age-matched healthy sexually active women without any urinary disease were determined as the control group(Group 2). This group was created by patients who received routine gynecological examinations in the outpatient clinic. As per our protocol, 23 patients who failed to respond to first-line treatments, such as conservative therapies, and second-line treatments, including oral analgesic drugs and intravesical injections of chondroitin sulfate, heparin, and hyaluronic acid, were included in the study group. The surgical procedure was performed by a single surgeon. Here, 100 units of Btx-A were diluted to 20 cc 0.9% saline, and 1 cc was then applied submucosally on 20 different points of the bladder wall using a 25-gauge needle (5 U/1 ml per site). A 14 F urethral Foley catheter was placed after the injection. On the second day after the injection, the catheter was removed, and all patients were discharged. At this point, patients were warned of the need for clean intermittent catheterization if deemed necessary. In the third week after the surgery, uroflowmetry was undertaken and the postvoid residual volume was measured to exclude urinary retention. Next, all patients were asked to fill out validated versions of the FSFI and ICSI (range of 0 to 20) as well as the ICPI (range of 0 to 16), visual analog scale (VAS) for pain assessment, and three-day bladder diary (BD) which were used to assess pre- and post-operative functional bladder capacity and daytime and night urinary frequency. Specifically, the FSFI questionnaire consists of 19 questions that investigate the following six domains: desire, arousal, lubrication, orgasm, pain, and satisfaction. Finally, the mean scores of FSFI, ICSI, ICPI, VAS, and BD data of the study and control groups were compared at baseline and three months after the treatment. Here, the primary endpoint was the assessment of improvement in SD, while the secondary endpoints were the changes in urinary symptoms and pain after the Btx-A injection.

RESULTS

The demographic characteristics of the patients in both groups are displayed in Table 1. Both groups were statistically similar in terms of mean age, parity, and percentage of postmenopausal patients. The mean time between the onset of symptoms and Btx-A injection in Group 1 was 32 ± 5.6 (13–40) months. Moreover, significant lower scores in all domains of FSFI except lubrication during the pretreatment period were shown in patients with IC/BPS compared to the control group. Dyspareunia was described by 17 patients (74%) in the study group compared to seven patients (30%) in the control group. In the third month after surgery, 20 patients had increased FSFI scores, whereas three patients had decreased FSFI scores. The baseline mean total FSFI score increased from 21.53 ± 7.02 to 28.14 ± 7.85 in the postoperative period as compared to the preoperative period in the study group, which was statistically significant (Table 2). As can be seen from Table 3, the improvement in all FSFI domains was statistically significant in the follow-up period as compared to the baseline period.Further, the total FSFI and post-treatment scores in the three domains of desire, lubrication, and pain were similar to those in the control group after the treatment.

Meanwhile, 20 of the 23 patients showed an improvement in the ICSI and ICPI scores, whereas no improvement was demonstrated in three patients in the postoperative evaluation. Although ICSI and ICPI scores showed statistically significant improvements in the post-treatment period as compared to baseline scores, the posttreatment scores showed no significant difference as compared to the control group. Moreover, 18 patients had a lower VAS score while one patient had a higher VAS score in the postoperative as compared to the pretreatment period. Here, a review revealed no change in the VAS scores in four patients. The preoperative assessment of the mean VAS score was 8.31 ± 1.45, which decreased to 6.52 ± 1.72 in the third follow-up month. Finally, statistically significant improvements were observed with treatment in parameters such as daytime frequency, nighttime frequency, and mean voided volume, which were evaluated using the voiding diary (Table-4).

INTERPRETATION OF RESULTS

This is the first study in the current literature about the effect of Btx-A injection on SD in patients with IC/BPS, in addition to its proven effect on the improvement of urinary symptoms. Specifically, we investigated the effect of intravesical Btx-A on different domains of sexual function as the primary endpoint of the study.

CONCLUDING MESSAGE

Although bladder pain and lower urinary symptoms are prominent in the diagnosis of IC/BPS, the disease is associated with a remarkably high incidence of SD. Further, pelvic and bladder pain appear to be major contributors to the development of SD in IC/BPS patients, yet several factors contribute to the pathogenesis of SD. In addition to improvements in pain and urinary symptoms, significant improvements in sexual function were observed in this study following the intravesical injection of Btx-A in patients with IC/BPS. Intravesical injection of Btx-A also resulted in statistically significant improvements in all aspects of sexual function, including desire, arousal, lubrication, orgasm, pain, and satisfaction. Patients can achieve a similar level of sexual function as the general population with Btx-A injection.

FIGURE 1

Table-1:

	Group 1 (Study group)	Group 2 (Control Group)	P value
Mean Age	46.8±12.1	45.7±10.2	0.134
Postmenopausal	15 (% 65.2)	16 (% 69.5)	0.246
Mean Parity	2.1±0.8	1.9±0.7	0.234

Table 1: Baseline demographic characteristics of groups

Table 2.

	Group-1A (study group, preoperative scores) (n:23) X±SD	Group-1B (study group, postoperative scores) (n:23) X±SD	Group-1A versus Group-1B (study group) P value	Group-2 (control group) (n:23) X± SD	Group-1A versus Group-2	Group-1B versus Group-2
FSFI	21.53±7.02	28.14±7,85	0.015	29.34±8.45	0.029	0.234
ICSI	15.43±3,06	12.45±3.62	0.023	8.45±2.20	0.013	0.027
ICPI	12.26±2.59	9.74±2.66	0.035	6.54±1.80	0.021	0.044
VAS	8.31±1.45	6.52±1.72	0.011	3.34±2.34	0.015	0.036

Table 2: Change in scores of questionnaires from baseline pretreatment period to postoperative period in study group and in comparison to control group

FSFI: Female sexual function index; ICSI: Interstitial cystitis symptom index; ICPI: Interstitial cystitis problem index; VAS: Visual analog score; SD: Standart deviation

table1-2

FIGURE 2

Table-3.

	Group-1A (study group, preoperative scores) (n:23) X±s.d.	Group-1B (study group, postoperative scores) (n:23) X±s.d.	Group-1A versus Group1B (study group) P value	Group-2 (control group) (n:23) X±s.d.	Group-1A versus Group-2	Group-1B versus Group-2
Desire	3,42 ±0,59	4,97 ±0.67	0,013	5.14±1.02	0.014	0.442
Aurosal	3,91 ±0,82	4,88 ±1,67	0.021	5.23±2.08	0.021	0.029
Lubrication	3,89 ±0,54	4,43 ±1,49	0,043	4.42±1.84	0.456	0.856
Orgasm	3,19 ±0,67	4,24 ±1,62	0,035	5.02±1.66	0.016	0.022
Pain	3,09 ±0,98	4,84 ±1,55	0,022	5.08±1.96	0.018	0.132
Satisfaction	4,03 ±,0,58	4,98 ±1,59	0,031	5.52±1.84	0.035	0.046
Total	21.53±,7.02	28.14± 7,85	0,015	31.51±8.32	0.011	0.028

Table 3: Change in domains of Female Sexual Function Index (FSFI) from baseline pretreatment period to postoperative period in study group and in comparison to control group

FSFI: Female sexual function index; ICSI: Interstitial cystitis symptom index; ICPI: Interstitial cystitis problem index; VAS: Visual analog score; SD: Standart deviation

Table-4.

	Group-1A (study group, preoperative scores) (n:23) X±SD	Group-1B (study group, postoperative scores) (n:23) X±SD	Group-1A versus Group-1B (study group) P value
Daytime frequency	13.6±4.9	9.4±3.5	0.009
Nighttime frequency	2.9±1.5	1.9±1.3	0.038
Mean voided volume (min-max) (ml)	126 (30-250)	159 (45-280)	0.024

Table-4: Changes in and bladder diary components from baseline pretreatment period to postoperative period in study group

SD: Standart deviation

table3-4

Funding there is no funding source **Clinical Trial** No **Subjects** Human **Ethics Committee** Local **Ethics Committee** of Ankara University School of Medicine (No. I01-46-22) **Helsinki** Yes **Informed Consent** Yes

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505 | www.ics.org/2022/abstract/505

EFFECT OF TRANSCUTANEOUS ELECTRICAL NERVE STIMULATION PLUS LOW-INTENSITY SHOCK WAVES THERAPY IN WOMEN WITH CHRONIC PELVIC PAIN

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HYPOTHESIS / AIMS OF STUDY

Chronic pelvic pain is characterized by persistent pain lasting longer than 6 months or recurrent episodes of abdominal/pelvic pain, hypersensitivity or discomfort often associated with elimination changes, and sexual dysfunction often in the absence of organic etiology (1). The prevalence on women is about 14% who experience chronic pelvic pain at least for one time during their life.

The chronic pelvic pain affects the quality of life of the women who suffers it, and the current treatments offer limited effectiveness. Low-intensity shockwave therapy has been used as a clinical treatment modality in many types of urological diseases (2).

• This study is clinical, not surgical and the category is pelvic pain syndromes.

• The hypothesis is: Women with chronic pelvic pain will improve more than 70% after the transcutaneous nerve electrostimulation plus low-intensity shock waves therapy.

• The objective of the study is to determine if in these women with chronic pelvic pain, the use of transcutaneous nerve electrostimulation plus low-intensity shock waves therapy is an effective treatment.

STUDY DESIGN, MATERIALS AND METHODS

An intragroup Clinical trial was launched inside hospital facilities. It included all women who entered the private consultation of Urogynecology who met the selection criteria. The inclusion criteria: Women with chronic pelvic pain history refractory to previous treatment and who agree to participate. Exclusion criteria: Those with neurological disease history, pregnancy, pelvic organ prolapse equal to or greater than stage III, uterine and/or adnexal pathology. Elimination criteria: Incomplete information.

The sample size was estimated with the technique for analytical studies in which the T-test is used to compare the means of continuous variables between groups, attempted to detect an intragroup difference of 60%. In this way, an effect magnitude of 2.64 was calculated; standardized effect size of 1.05; one-sided alpha of 0.025 and beta of 0.20. The required sample size was seventeen women. This project received the approval of the ethics and research committee. Patients have informed consent. No disclosures and funding were received.

All women underwent a complete medical history and urogynecological physical examination. It was evaluated the anatomical points established by the POP-Q system determining the degree of pelvic organ prolapse; ultrasound was performed with multifrequency endovaginal transducer; urodynamics evaluation to investigate the function of the lower urinary tract with Laborie Goby Urodynamics System. All women received pelvic floor rehabilitation program consisting of twelve sessions. One a week of 45 minutes each one with transcutaneous electrical nerve stimulation (TENS) technique applied with perineal patch using Laborie Urostym and Low Intensity Shock Wave Therapy administering the protocol in an abdominal approach, above the pubic bone to receive a total of 1000 shock waves per session. This last protocol consists in four sessions (1 per week); 3 weeks off and four additional sessions using Medispec ED-1000. Pain was evaluated before and after treatment with “Visual analog scale.”

RESULTS

Twenty-three women with a history of chronic pelvic pain syndrome were included. Of these, four were excluded (3 due to gynecological pathology and one due to neurological damage). In the end, nineteen patients were analyzed. The sample was completed. Pelvic pain was assessed using "Visual Analogue Scale" before and after treatment. The demographic characteristics (mean/range) were Age: 47 years (26-77); evolution time: 7 years (1-40); pregnancies: 2 (0-4). The main urodynamic findings were normal studies (26%); Bladder outlet obstruction/Dysfunctional voiding (53%); Idiopathic (primary) detrusor overactivity (16%); Urodynamic stress incontinence (5%).

INTERPRETATION OF RESULTS

Pain was evaluated before and after treatment with “Visual analog scale.” The assessment of pain in women with chronic pelvic pain before and after treatment was analyzed with T-test for paired samples as well as a General Linear Model (SPSS statistical program, license 2021). Before the treatment, the mean of pain was 9.16 points and after the treatment was 1.7 points. This difference, before and after intragroup treatment, is statistically significant.

CONCLUDING MESSAGE

This is the first research in the world where chronic pelvic pain in women is treated with transcutaneous electrical nerve stimulation plus low-intensity shock waves therapy. The treatment in women with chronic pelvic pain is effective. Low-intensity shock waves therapy is a promising treatment in the urogynecological area, understanding that we need more time and studies. In principle, it will be an important treatment in pelvic floor dysfunction.

FIGURE 1

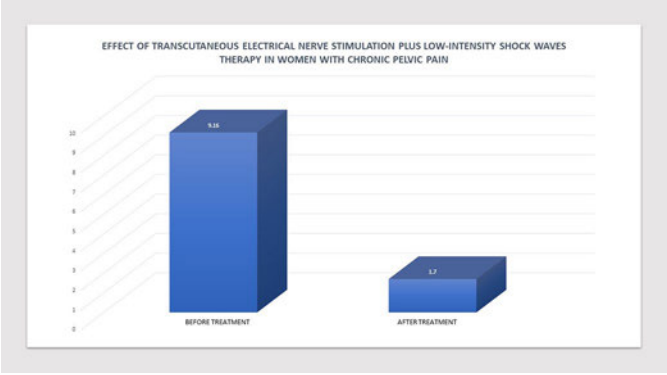
EFFECT OF TRANSCUTANEOUS ELECTRICAL NERVE STIMULATION PLUS LOW-INTENSITY SHOCK WAVES THERAPY IN WOMEN WITH CHRONIC PELVIC PAIN

Chronic pelvic pain (N=19)	Before treatment	After treatment	P value
Visual Analogue Scale	mean	mean	<0.001
	9.16 (1.1)	1.7 (1.5)	

T-test for paired samples

EFFECT OF TRANSCUTANEOUS ELECTRICAL NERVE STIMULATION PLUS LOW-INTENSITY SHOCK WAVES THERAPY IN WOMEN WITH CHRONIC PELVIC PAIN

FIGURE 2



EFFECT OF TRANSCUTANEOUS ELECTRICAL NERVE STIMULATION PLUS LOW-INTENSITY SHOCK WAVES THERAPY IN WOMEN WITH CHRONIC PELVIC PAIN

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Funding None **Clinical Trial** No **Subjects** Human **Ethics Committee** COMITE DE INVESTIGACION DEL HOSPITAL ANGELES ACOXPA **Helsinki** Yes **Informed Consent** Yes

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SESSION 33 - THE BEST OF THE REST IN SCIENCE

Abstracts 506-517
11:30 - 13:00, Hall N
Chair: Prof Karl-Erik Andersson (United States)

506 | www.ics.org/2022/abstract/506

ANDROGEN RECEPTOR LOCALISATION IN BUCCAL MUCOSA: CAN BUCCAL MUCOSA BE USED IN PRIMARY HYPOSPADIAS SURGERY IN PREPUBERTAL BOYS?

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HYPOTHESIS / AIMS OF STUDY
Hypospadias is a common congenital abnormality. In the Netherlands 1:200/300 boys is born with hypospadias. During hypospadias surgery there may be not enough local tissue. Oral mucosa is widely used in adults for urethroplasties and repair after failed hypospadias. Little is known about how oral mucosa reacts on the hormonal effect of puberty. To predict whether oral mucosa can safely be used in prepubertal hypospadias patients, we investigated the androgen receptor (AR) localization in oral mucosa, and tested testosterone sensitivity of cells isolated from oral mucosa.

STUDY DESIGN, MATERIALS AND METHODS
Surgical waste (oral mucosa) from onlay urethroplasty, was collected under local biobank protocol. Part of the tissue was embedded in paraffin and tissue sections were prepared. Tissue sections were used in hemotoxilin and eosin (HE) staining, but also in immunohistochemistry for proliferation marker Ki-67 and AR. We collected tissue from 15 different patients. Human male urethra and oral mucosa as well as urethra from fertile male rats were used as controls for AR staining.

From five of the fifteen patients, we isolated cells. Using keratinocyte and fibroblast markers we optimized the efficiency of keratocytes isolation.

RESULTS
AR staining of rat oral mucosa showed nuclear localization in the basal layer, and cytoplasmic localization in the apical layer. The basal layer was Ki-67 positive, associated with cell proliferation. In oral mucosa from patients a diverse pattern was seen: in hypospadias patients cytoplasmic AR localization was seen throughout all layers of the epithelium, in other patients localization was similar to the rat mucosa: nuclear localization in the basal layer. In all oral mucosa samples the basal layer was Ki-67 positive. The human and rat urethra both showed nuclear localized AR expression, with less cells positive in the human sample. Human oral keratinocytes could be isolated from four of the five patients, from one patients cells stopped dividing after two passages and we were unable to test the cells for androgen sensitivity. One patient cell line exposed to testosterone showed switch from cytoplasmic to nuclear localized AR after 30 minutes, indicating active testosterone signaling. We are currently performing testosterone treatment for the other three patients cell lines.

INTERPRETATION OF RESULTS
In most oral mucosa AR is localized in the nucleus in the basal layer, indicating that the testosterone signaling is active in these cells. Active testosterone signaling overlaps with Ki-67 staining, which is a marker for proliferation. This finding suggests that graft taken from oral mucosa is sensitive to androgens and might grow during puberty like other hormone sensitive tissue. We found that in oral mucosa from hypospadias patients, androgen receptors were localized in the cytoplasm throughout the whole thickness of the epithelium. As we do not know the genetic background of these patients, we can only speculate that these patients have an aberrant testosterone signaling. However, in isolated cells from a hypospadias patient, testosterone treatment induced nuclear translocation of the androgen receptor, indicating active testosterone signaling.

CONCLUDING MESSAGE
Preliminary observations indicate that human oral keratinocytes are sensitive to testosterone, predicting that oral mucosa used for urethral reconstruction will keep up with penile growth during puberty.

Funding None **Clinical Trial** No **Subjects** Human **Ethics Committee** local METC to check the biobank protocol **Helsinki** Yes **Informed Consent** Yes

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507 | www.ics.org/2022/abstract/507

CELLULAR PATHWAYS CONTRIBUTING TO FIBROSIS IN THE BLADDER WALL OF CHILDREN WITH EXSTROPHY

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HYPOTHESIS / AIMS OF STUDY

Bladder exstrophy, as part of the exstrophy-epispadias complex, is characterised by a pathologically open and protruding organ. Despite improvements in surgical repair, many patients continue to have poorly contractile, low-capacity bladders. These pathophysiological features are associated with significant fibrosis and greater biomechanical stiffness of the bladder wall (1). The current investigation was designed to yield insight into changes to Wnt-signalling pathways, important in organ and tissue development, but also in the regulation of connective tissue deposition (2). The study used multiplex immunolabelling of target proteins and single mRNA molecules, followed by imaging and unbiased, quantitative image analysis. Data were obtained from children undergoing exstrophy repair and compared to those from children with functionally normal bladders (controls). We hypothesise that exstrophy bladders show excessive connective tissue deposition associated with altered regulation of Wnt-signalling targets.

STUDY DESIGN, MATERIALS AND METHODS

Anterior bladder wall samples were obtained from N = 9 control patients with normally-functioning bladders (age; 26 [18,48] months; 2 female, 7 male; for ureteric re-implantation) or N = 18 children with exstrophy (age; 62 [63,86] months; 6 female, 12 male; for bladder closure). Samples were immediately placed in 10% formaldehyde at 4°C, dehydrated and fixed in paraffin (FFPE samples). The study design was double-blind, all tissue blocks and antibodies used were blinded to the experimenter; the code was broken only when all analyses were completed. Previous functional data obtained with these tissue samples indicated a sample size of N = 7 was adequate for $p < 0.05$ at 80% power.

Tissue arrays were made from 0.8 mm diameter cores of FFPE samples and sectioned at 6-8 μm with an HM355S automatic microtome (Thermo Scientific). Sections were stained using a Leica Automated Bond System RXTM IHC/ISH for H&E/van Gieson staining (Figure 1A) and also probed with four different primary antibodies against Pygo1, Cx43, FRA1 and TCF7L1(Figure 1B) and single molecule RNAscope detection for CCND2, JUN, SOX-9 and TCF7L2(Figure 1C). These markers were chosen as they are known transcriptional downstream targets for Wnt-signalling pathways. Protein expression and gene transcription were detected by specific fluorophore labels for each antibody and chromogens for RNAscope labelling and were adjusted for variation in total amount of tissue in each core. Data are medians [25,75% interquartiles], differences between data sets were tested by two-way ANOVA with post-hoc non-parametric tests.

RESULTS

Exstrophy tissue had a lower proportion of smooth muscle in tissue cross sections, compared to samples from normally functioning bladders (30.6% [21.7,56.9] vs 65.6% [57.0,75.8]; p = 0.0150: Figure 1A), as measured by van Gieson staining. Protein expression was assessed by measuring the appropriate fluorophore label intensity (pixel counts) for each section and collected from ten regions of interest (RoI; each 60 μm diameter); five from areas dominated by smooth muscle and five from non-muscle areas. Antibody or RNAscope label intensity and total amount of tissue in each core was calculated using modified ImageJ plugins. Data from smooth muscle areas show increased expression in exstrophy sections for Pygo1 (p = 0.044) and Cx43 (p = 0.001) compared to normal tissue, but no differences for FRA1 and TCF7L1: Figure 2A). For non-muscle regions only Cx43 counts were different between exstrophy and normally-functioning bladder (p = 0.006: Figure 2A). Single molecule RNA counts for CCND2 were significantly fewer in exstrophy tissue (p = 0.013) but similar for JUN, SOX-9 probes. Counts for TCF7L2 were on the borderline for significance (p = 0.051: Figure 2B).

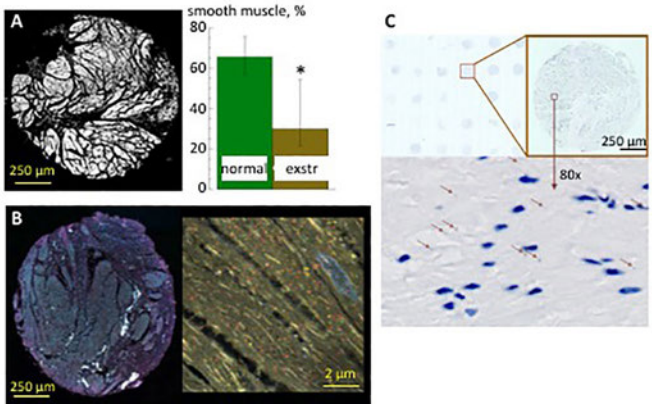
INTERPRETATION OF RESULTS

The data confirm previous findings that the smooth muscle content of exstrophy bladder wall is less than that of normally functioning bladders. However, changes to pathways associated with Wnt-signalling were not uniformly altered. Particular reasons for choosing these targets were: they may have a role in development of the congenital anomaly itself, and they are potentially associated with fibrosis deposition. Pygo1 is an essential transcription factor of beta-catenin canonical Wnt signalling which enhances and upregulates this pathway. In the bladder wall Cx43 expression is found in the interstitial/fibroblast cell population (3) consistent with greater deposition of connective tissue. However, FRA1 another transcription factor, known to be regulated by Wnt signal activation showed no change in expression. Previous work suggests that there was actually a decrease in the key transducer of Wnt signaling, namely, beta-catenin whose expression is reduced in exstrophy (1) and is consistent with unchanged expression of TCF7L1, another protein involved in Wnt signal mediated gene transcription. This is the first study to demonstrate the feasibility of high throughput, single molecule mRNA imaging in formalin-fixed bladder wall specimens. Although counts were low it has been possible to demonstrate dysregulation of transcription of Wnt target genes; in particular CCND2, critical in G1/S transition in the cell cycle.

CONCLUDING MESSAGE

These experiments emphasise the increased deposition of extracellular matrix at the expense of smooth muscle in exstrophy human bladder. Whilst an enhanced activity of Wnt-signalling pathways is associated with such fibrosis the particular sub-pathway requires further investigations and assessment of a larger number of target genes. A further possibility will be that in some bladder diseases downregulation of Wnt signal activity induces fibrosis.

FIGURE 1



A: van Gieson stained normal bladder bit map; muscle, white. Percentage smooth muscle:normal & exstrophy sections; *p < 0.05. B: four-protein label image, exstrophy section & high-power image. C: single molecule mRNA labels (brown arrows); normal bladder

FIGURE 2

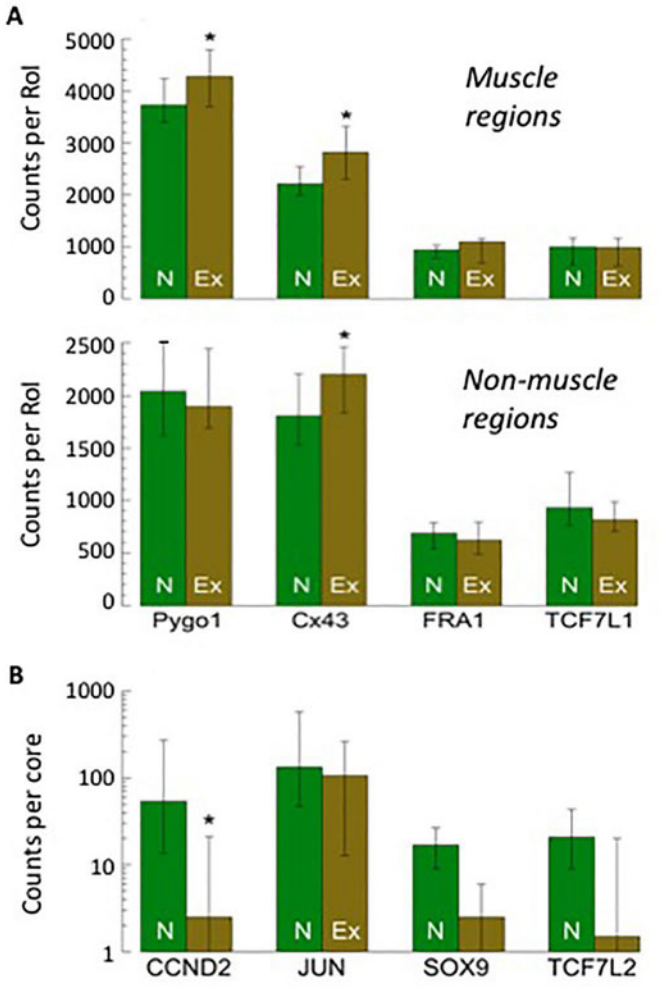


Figure 2. Protein, mRNA counts. A: protein counts in muscle and non-muscle areas in sections from and exstrophy bladder sections. B: single molecule mRNA counts in normal and exstrophy bladder sections. N - normal; Ex - exstrophy *p < 0.05

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Funding NIH; R01 DK098361 **Clinical Trial** No **Subjects** Human **Ethics Committee** Great Ormond St Hospital R&D **Helsinki** Yes **Informed Consent** Yes

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508 | www.ics.org/2022/abstract/508

DOWNREGULATION OF CYTOCHROME B5 REDUCTASE 3 IN THE MOUSE BLADDER INDUCES URINARY FREQUENCY

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HYPOTHESIS / AIMS OF STUDY

Cytochrome B5 reductase type-3 (CYB5R3) is a flavoprotein that regulates redox pathways in the mitochondria, endoplasmic reticulum and nitric oxide signalling by reduction of the soluble guanylate cyclase haem group. Inflammatory conditions can downregulate CYB5R3 activity with detrimental consequences to critical cellular processes [1]. We hypothesized that selective knockdown of CYB5R3 in the urinary bladder could be used to model pathological situations that result in chronic inflammation including exposure to ionising radiation, urinary tract infections or natural aging. To address this hypothesis, we generated a conditional CYB5R3 knockout mouse and performed 4-hydroxytamoxifen (4-OHT, active metabolite of tamoxifen) injections into the urinary bladder wall. The voiding activity of mice was monitored over 6 weeks and bladder contractile function assessed by isometric tension recordings. This study aimed to generate a new model for evaluating the consequences of metabolic/mitochondrial dysfunction and resultant inflammation localized to the urinary bladder.

STUDY DESIGN, MATERIALS AND METHODS

Generation of CYB5R3 conditional knockout mouse. A mouse with loxP sites flanking exon3 of the CYB5R3 gene [2] (CYB5R3flox/flox) was crossed with a mouse expressing the tamoxifen inducible Cre recombinase under the β-actin promoter (CAG-Cre, Jackson laboratories, stock#:004682) to generate the conditional CYB5R3flox/flox + CAG-Cre (CYB5R3 KO) mouse. Both mouse strains were based on a C57Bl/6 background. At 8-12 weeks of age, female CYB5R3 KO and age matched CYB5R3 wildtype (WT) mice were used for 4-OHT bladder wall injections. Mice were anesthetized with isoflurane and a lower midline incision made to expose the urinary bladder using sterile surgical conditions. The bladder wall was injected from the serosal surface at 4 locations with 0.5 mg/ml 4-OHT (10 µl total, dissolved in ethanol/CremophorEL/saline) using a 32-gauge insulin syringe. The incisions were sutured, and mice were given prophylactic ampicillin (100 mg/kg, SQ, 7 days) and ketoprofen (3 mg/kg, IM, 3 days) during the recovery period.

Urine void spot and metabolic cage assessments. Voiding activity was assessed by two-hour urine spot tests starting one week before 4-OHT injections and performed weekly thereafter up to 6 weeks. Filter papers lining the metabolic cages were imaged using a ChemiDocMP (Bio-Rad) and analysed with FIJI ImageJ software. The area of urine spots was measured and analysed as previously described [3] where primary void spots (PVS) were determined as those ≥80 mm2. 24-hour voiding analysis was also performed using metabolic cages (Columbus Instruments Inc.) where the mice were maintained in a climate-controlled cabinet with a 12-hour light/dark cycle (7am-7pm).

Isolated bladder strip contractility. Mice were humanely sacrificed for tissue collection at 6 weeks after surgery. Urinary bladders were dissected into strips in the dome to base orientation and examined by isometric tension recordings. Strips were stimulated by electrical field stimulation and stretched incrementally to determine the baseline tension for optimal alignment of contractile fibres, i.e., optimal length. Responses were measured to purinergic (10 µM α,β-methylene ATP) and muscarinic (0.1-10 µM oxotremorine-M) agonists and direct depolarization (120 mM KCl). Tension was normalised to force per cross-sectional area of tissue (mN/mm2).

Data and statistical analysis. Data are expressed as mean ± standard error of mean. Pairwise comparisons were performed using Student's t-test where the null hypothesis was rejected at $p < 0.05$.

RESULTS

CYB5R3 KO and WT mice exhibited differences in voiding behaviour at 28 days following 4-OHT treatment (Fig 1A-C). The KO mice showed increased number of PVS which were corroborated by metabolic cage studies that indicated smaller voided volumes and increased number of voiding events (Fig 1D and 1E). There was no significant difference in total voided volumes or total water intake (not shown). Gross examination of isolated bladder showed no significant difference in wet weights or obvious signs of irritation in KO or WT mice. Lastly, muscle strip experiments demonstrated no significant differences in responses to agonist stimulation, force generation or tissue elasticity between KO and WT animals (Fig 1F).

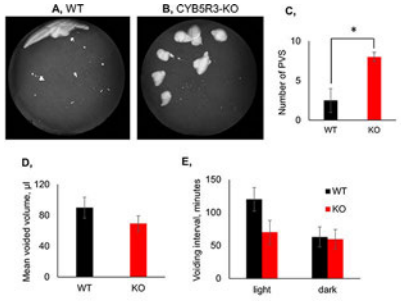
INTERPRETATION OF RESULTS

Decreased CYB5R3 levels in the bladder induced urinary frequency and decreased voided volumes. Altered voiding behaviour was not associated with changes to the contractile or viscoelastic properties of the detrusor. Thus, observed bladder overactivity is likely neurogenic in origin and mediated by changes in cellular metabolism and localised inflammation.

CONCLUDING MESSAGE

CYB5R3 is an important redox regulator in many cellular processes and its dysregulation is associated with multiple inflammatory pathologies. The CYB5R3 KO mouse represents a unique animal model for studying the consequences of metabolic/mitochondrial dysfunction in the urinary bladder.

FIGURE 1



F,

	10 µM Oxo-M (mN/mm²)	Oxo-M EC_{50} (µM)	10 µM ABMA (mN/mm²)	120 mM KCl (mN/mm²)	20 Hz EFS (mN/mm²)	EFS half-max frequency (Hz)	Baseline at optimal length (mN/mm²)
KO	87±6	0.2±0.1	14±4	35±10	55±6	5.2±1.0	21±8
WT	64±16	0.3±0.1	13±4	26±0.1	42±9	8.3±1.8	22±14

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Funding National Institutes of Health (R01DK098361) **Clinical Trial** No **Subjects** Animal **Species** mouse **Ethics Committee** University of Pittsburgh Institutional Animal Care and Use Committee

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509 | www.ics.org/2022/abstract/509

LOW-ENERGY SHOCKWAVE THERAPY AMELIORATES ISCHEMIC-INDUCED OVERACTIVE BLADDER IN A RAT MODEL WITH HIGHER EXPRESSION OF SOLUBLE GUANYLATE CYCLASE AND VASCULAR ENDOTHELIAL GROWTH FACTOR.

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HYPOTHESIS / AIMS OF STUDY

Overactive bladder (OAB) has been treated with medications and invasive treatments. However, there is a strong demand for non-invasive treatment for refractory OAB. In these days, low-energy shockwave therapy (LESW) is known to induce various biological effects such as angiogenesis, anti-inflammation, nerve regeneration, cell proliferation, and alteration of membrane permeability. The aims of this study were to evaluate whether LESW improves ischemic-induced OAB in a rat model (AI model) and to investigate its therapeutic mechanisms.

STUDY DESIGN, MATERIALS AND METHODS

Sixteen-week-old male Sprague-Dawley rats were randomly divided into three groups: the AI, AI-SW and control groups. The AI and AI-SW groups underwent endothelial artery injury and received a high cholesterol diet. In the AI-SW group, LESW was shot onto the abdominal wall once a week from 4 to 7 weeks after AI surgery (20-23 weeks of age). A shockwave generator DUOLITH SD1 was used with an intensity of 0.25 mJ/mm2 (total energy flux density), a frequency of 3 Hz, and 1800 shots. At 24 weeks of age (8 weeks after AI), a conscious cystometry was performed followed by measuring blood flow of the bladder using the laser speckle contrast imaging (n = 8 for each group). Blood flow was normalized by blood pressure simultaneously monitored from left internal carotid artery. The bladder was harvested in the early phase (24 hours after the first LESW: 20 weeks of age) and in the chronic phase (24 weeks of age) for molecular analyses and histological evaluations.

RESULTS

Voiding interval was significantly shorter in the AI group (mean ± SEM: 5.1 ± 0.8 min) than the control group (17.3 ± 3.0 min), while significant improvement was observed in the AI-SW group (14.9 ± 3.3 min). Blood flow of the bladder significantly increased in the AI-SW group than in the AI at three points of saline infusion: 0, 0.5, and 1.0 ml.

Microarray analysis showed higher gene expression of soluble guanylate cyclase (GC) alpha and beta in the AI-SW group than in the AI group in the chronic phase. Polymerase chain reaction (PCR) and Western blotting revealed that gene/protein expression of GC alpha was significantly higher in the AI-SW and control groups than in the AI group. mRNA of vascular endothelial growth factor (VEGF) was highly expressed in the early phase after LESW, followed by increased protein expression (P = 0.069) in the chronic phase. Enzyme-linked immunosorbent assay (ELISA) demonstrated a significant elevation of cyclic guanosine monophosphate (cGMP) in the bladder of the AI-SW group.

Histological examinations showed rich vascularity in the suburothelium with positive stain of VEGF and GC alpha/beta in the AI-SW group, in contrast to poor vascularity in the thinned suburothelium of the AI group.

INTERPRETATION OF RESULTS

LESW is considered to stimulate mechanosensors on cell membranes. Previous In-vitro studies revealed that LESW upregulated VEGF and enhance nitric oxide (NO) production via activation of eNOS in human umbilical vein endothelial cells (HUVECs). In-vivo studies of LESW demonstrated that angiogenesis involving VEGF improved various pathophysiological conditions such as cardiac dysfunction and erectile dysfunction.

Possible mechanisms of therapeutic effect of LESW on OAB:

1. Recovered blood flow due to angiogenesis may decrease oxidative stress and inflammatory cytokines, which can ameliorate OAB in the pathophysiology of chronic pelvic ischemia.

2. GC is known to be degraded under hypoxia. Improved blood flow due to angiogenesis may restore GC in the bladder, resulting in elevation of cGMP. (LESW may also stimulate GC-cGMP pathway via activation of eNOS.) Elevated cGMP relaxes vascular smooth muscle (vasodilation) and sphincter/detrusor smooth muscle and inhibits afferent nerve activities.

As limitations, we do not yet investigate upstream mediators (e.g. NO, eNOS and Akt) and several genes related to anti-inflammation and neurogenesis which were indicated by microarray analysis.

CONCLUDING MESSAGE

Our study demonstrated that LESW improved urinary frequency and blood flow of the bladder along with higher expression of VEGF, GC, and cGMP in the rat model of pelvic ischemia. Recovered blood flow and activation of GC-cGMP may play therapeutic roles in the functional recovery of the bladder. LESW can be a novel therapy for OAB in the future.

FIGURE 1

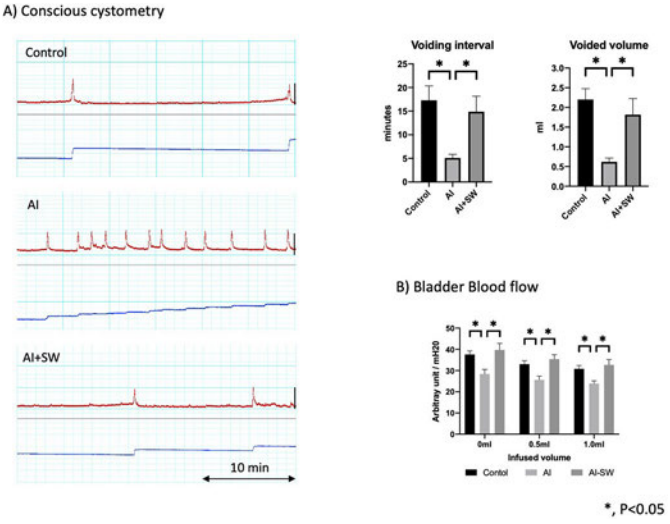
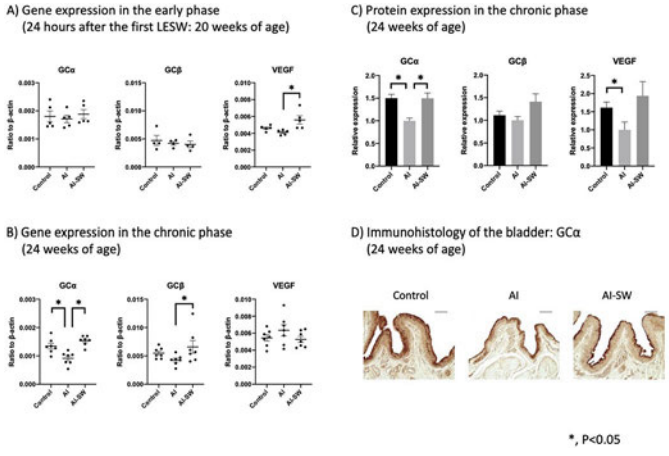


FIGURE 2



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NEURITE OUTGROWTH AGENT TAS3731 PREVENTS URETHRA DENERVATION AND DYSFUNCTION FOLLOWING DIABETES MELLITUS IN RATS

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HYPOTHESIS / AIMS OF STUDY

Underactive bladder syndrome (UAB) is a voiding symptom syndrome involving detrusor underactivity (DU), defined as reduced detrusor muscle power and/or duration. Since UAB can cause complications such as urinary tract infections and renal disorders, it is vital to cure voiding dysfunction. DU is reportedly caused by partial loss of nerves innervating the bladder in patients with diabetes mellitus (DM) and bladder outlet obstruction (BOO) (1). TAC-302, which has a neurotropic factor-like effect, is reportedly effective in some animal models (prevention of patchy denervation in the bladder of BOO model and amelioration of neurological function in the urethra of DM model) (2, 3). A randomized, placebo-controlled, double-blind, parallel-group trial of TAC-302 in DU patients with overactive bladder was conducted (NCT03175029). We found TAS3731 to be a derivative of TAC-302, with an equivalent potential in terms of neurite outgrowth but better pharmacokinetics profile compared with TAC-302. In this study, we examined the effect of TAS3731 on neurite outgrowth in neurons and the ameliorative effect of oral administration of TAS3731 on streptozotocin (STZ)-induced diabetic voiding dysfunction in rats.

STUDY DESIGN, MATERIALS AND METHODS

To evaluate neurite outgrowth, a neuronal cell line was stimulated using TAS3731 for 6 h.

DM was induced by an intravenous injection of STZ (50 mg/kg) in Wistar rats (Crlj:WI, female, 10 weeks old). DM rats were orally administered with either vehicle or TAS3731 daily for 4 weeks. Physiological and pathological studies were conducted as follows:

1. To evaluate voiding functions, cystometry was performed at an saline infusion rate of 12 mL/h under urethane anesthesia (0.8 mg/kg, s.c.) at 4 weeks after inducing DM. Residual urine volume was measured by stopping saline infusion and withdrawing intravesical fluid through the catheter by gravity.

2. To evaluate nerve distribution in the urethra, 4% PFA-fixed tissues were cryoprotected with 20% sucrose and frozen in optimal cutting temperature compound. The frozen sections were stained with anti-PGP9.5 antibody, and the PGP9.5-positive area in the sections was assessed quantitatively.

RESULTS

Treatment of neuronal cell line with TAS3731 for 6 h increased neurite length per cell and percentage of neurite-bearing cells in a concentration-dependent manner.

Compared with sham rats, DM rats showed increased blood glucose concentration and residual urine volume and decreased voiding efficiency, indicating that STZ-induced diabetic rats exhibited UAB-like symptoms. TAS3731 treatment did not affect blood glucose concentration and maximal voiding pressure; however, it significantly suppressed the increase in residual urine volume and decrease in voiding efficiency observed in vehicle-treated DM rats in a dose-dependent manner. Additionally, TAS3731 treatment tended to suppress the decrease in the PGP9.5-positive area ratio in the internal urethral sphincter, as observed in vehicle-treated DM rats. Incidentally, TAS3731 treatment did not affect the weight of the study animals, and it is considered that it did not have toxicity issues.

INTERPRETATION OF RESULTS

Partial denervation of the internal urethral sphincter causes voiding dysfunction in rats with DM. TAS3731 treatment alleviated voiding dysfunction in rats with DM by preventing partial denervation of the urethra.

CONCLUDING MESSAGE

Treatment with TAS3731, a novel compound with neurite outgrowth promoting activity, alleviates lower urinary tract dysfunction in rats with DM. Therefore, TAS3731 could be a novel therapeutic agent in patients with voiding dysfunctions.

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AGE-RELATED CHANGES IN LOWER URINARY TRACT FUNCTION IN RATS WITH ALTERED NITRIC OXIDE MECHANISMS

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HYPOTHESIS / AIMS OF STUDY

Aging patients with bladder dysfunction often have lower urinary tract symptoms, which are related to both overactive and underactive bladder conditions, also known as detrusor hyperreflexia with impaired contractility (1). In recent years, the importance of nitric oxide (NO), a transmitter of non-adrenergic, non-cholinergic nerves, in the control of lower urinary tract function has been documented (2). NO promotes cyclic guanosine monophosphate (cGMP) production intracellularly in smooth muscles, reduces the intracellular calcium concentration, and enhances smooth muscle relaxation (3). However, it is not known whether changes in the expression of NO-related molecules are associated with development of lower urinary tract dysfunction during aging. In this regard, to the best of our knowledge, this is the first report, which investigated the bladder and urethral activity and NO-related molecular changes in aging rats.

STUDY DESIGN, MATERIALS AND METHODS

Female Sprague-Dawley rats (Envigo, Fredrick, MD, USA) were divided to two different age groups: (A) control (12 weeks old, n = 8) and (B) aging rats (15 months old, n = 6). In both groups, a 24 h voiding assay was performed and the urodynamic parameters using awake cystometry (CMG) and urethral perfusion pressure (UPP) recordings were evaluated under urethane anesthesia. The mRNA expression levels of NO-, ischemia-, and inflammation-related markers in urethra and bladder tissues and the levels of cGMP in the urethra were also assessed. In CMG, parameters such as opening pressure (pressure at which the urethra opens and urine flow starts), intercontraction intervals, the number of non-voiding contractions (NVCs) per voiding, postvoid residual (PVR), bladder capacity, bladder compliance, and voiding efficiency (VE) were measured. NVC was defined as an increase in intravesical pressure of more than 8 cm H2O above the baseline. In UPP recordings, parameters such as baseline urethral pressure (UP), UP nadir, UP at which the urethra starts to relax (UPUR), UP reduction (the difference between UPUR and UP nadir), and high-frequency oscillation (HFO; the amplitude of the UP changes during the micturition reflex) were measured. Urethral HFO induced by bursting activity of the striated urethral sphincter muscle is known to be necessary for its pumping function to enhance efficient voiding in rats. Gene expression of NO-related markers such as nitric oxide synthase 1 (NOS1) and protein kinase G (PKG) and ischemia- and inflammation-related markers such as hypoxia-inducible factor 1 alpha (HIF-1α), vascular endothelial growth factor (VEGF), transforming growth factor beta 1 (TGF-β1) were quantified using real-time PCR. Urethral tissues were pulverized and processed for cGMP measurements using an ELISA kit. All values are expressed as mean ± standard deviation. Mann-Whitney U test was used to evaluate statistical differences between the groups. Statistical significance was set at $P < 0.05$.

RESULTS

Body weight was significantly higher in Group B than in Group A (340.5 ± 39.0 vs 286.8 ± 19.5 g, P = 0.0037). There was no significant difference in the 24 h voiding assay results. In CMG, the number of NVC per voiding cycle and PVR were significantly higher in Group B than in Group A (0.2 ± 0.1 vs. 0.1 ± 0.0 number/min, P = 0.0080; 0.1 ± 0.0 vs. 0.0 ± 0.0 mL, P = 0.0007, respectively), and VE was significantly lower in Group B than in Group A (91.4 ± 3.7 vs. 99.4 ± 1.1 %, P = 0.0007) (Fig. 1A, B). In UPP recordings, UP reduction and HFO amplitude were significantly lower in Group B than in Group A (8.6 ± 3.1 vs. 15.5 ± 2.3 cm H2O, P = 0.0079, 1.3 ± 0.3 vs. 4.0 ± 2.0, P = 0.0079, respectively) (Fig. 1C, D). In molecular studies, mRNA expression levels of HIF-1α, VEGF, and TGF-β1 in the bladder were significantly higher in Group B than in Group A (4.0 ± 1.0 vs. 1.0 ± 0.8 fold, P = 0.0003, 3.0 ± 0.4 vs. 1.0 ± 0.2 fold, P = 0.0003, 7.8 ± 2.4 vs. 1.0 ± 0.6 fold, P = 0.0003, respectively) (Fig. 2A). The mRNA expression levels of NOS1 and PKG were significantly lower in Group B than in Group A (0.6 ± 0.2 vs. 1.0 ± 0.4 fold, P = 0.0260; 0.2 ± 0.1 vs. 1.0 ± 0.2 fold, P = 0.0022, respectively) (Fig. 2B). cGMP concentrations in the urethra were significantly lower in Group B than in Group A (0.1 ± 0.0 vs. 0.2 ± 0.0 pmol/mg of tissue, P = 0.0022) (Fig. 2C).

INTERPRETATION OF RESULTS

Animal studies focusing on aging and NO in association with urinary tract dysfunction are scarce. Our results indicate the following: (a) 15-month-old rats exhibited the bladder overactive condition as evidenced by increased NVCs and the bladder underactive condition as evidenced by increased PVR and decreased VE. The urethral dysfunction was also shown by decreases in UP reduction and HFO amplitudes, (b) aging bladder tissues showed increased mRNA expression levels of HIF-1α, VEGF, and TGF-β1, and aging urethral tissues showed decreased mRNA expression levels of NOS1 and PKG, and (c) aging urethral tissues showed decreased levels of cGMP as compared to controls, suggesting that the cGMP level in the urethra is decreased with aging, leading to impaired urethral relaxation mechanisms underlying aging-related voiding and storage dysfunction.

CONCLUDING MESSAGE

In aging rats, reductions in mRNA expression levels of NO-related molecules and the cGMP level in the urethra, which induced functional urethral obstruction during voiding due to impaired urethral relaxation, might play an important role in bladder overactivity, as well as in incomplete emptying and bladder underactivity. Aging rats would be a useful model for studying the natural progression of age-related lower urinary tract dysfunction, especially, in relation to alterations in the NO-mediated transmitter function.

FIGURE 1

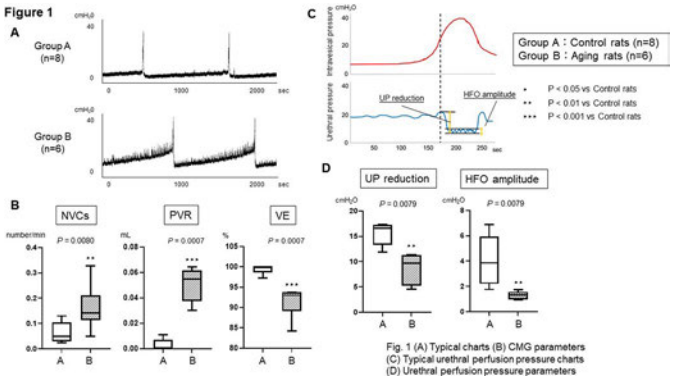

Figure 1

FIGURE 2

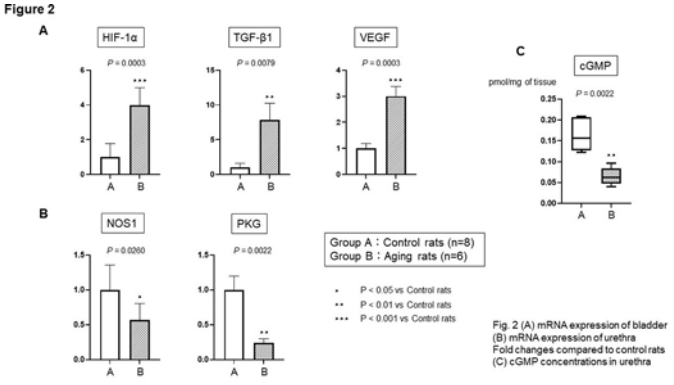

Figure 2

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Funding None **Clinical Trial** No **Subjects** Animal **Species** Rat **Ethics Committee** Institutional Animal Care and Use Committees of the University of Pittsburgh

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AGING RESULTS IN REDUCED SENSORY INNERVATION OF THE BLADDER TRIGONE IN RATS

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HYPOTHESIS / AIMS OF STUDY

The prevalence of lower urinary tract symptoms (LUTS), characterized by problems regarding storage and/or voiding of urine, is known to significantly increase with age [1]. Multiple bladder components may become dysfunctional with age including mucosal, muscular, stromal and neural physiology [2]. Optimal execution of visceroceptive processes is essential for the maintenance of a proper homeostatic balance and is achieved by interactions between the central and peripheral nervous systems at multiple levels. Interestingly, the process of aging decreases visceroceptive awareness. Currently, it is unclear how this interaction is organized, and how the aging process negatively impacts these functions.

The correct execution of communication between the lower urinary tract and the central nervous system is crucial for optimal bladder functioning. Moreover, this system is highly dependent on effective interaction between the bladder urothelium and afferent nerve fibers located in the lamina propria in close proximity to the urothelium. In the current study we quantified aging-related differences in the expression of calcitonin gene-related peptide (CGRP, an established marker for sensory nerve fibers) in the trigonal mucosal layers of young (3 – 4 months) and aged (25 – 30 months) rats. We hypothesized that trigonal mucosa obtained from aged rats shows significantly less CGRP expression compared to young rats.

STUDY DESIGN, MATERIALS AND METHODS

We collected bladders from 3 animals per age group. The bladder was cut open longitudinally and pinned flat with the lumen side upwards. Tissue was post-fixed for 60 minutes in 4% PFA, immersed in 30% sucrose for > 24 hours. The trigonal region between the ureteral orifices and the urethra was isolated, embedded in optimum cutting temperature compound medium (Tissue-Tek OCT, Sakura Finetek, Torrance, CA, USA) and stored at -80˚C until cutting. Tissue was then serially sectioned at 10 µm and mounted on glass slides (Fisher Scientific, Pittsburgh, PA) with 3 sections per slide. Sections were air dried >1hour, washed with PBS, incubated with permeabilizing block solution (5% normal donkey serum, 1% bovine serum [Sigma-Aldrich, USA] and 0.2% Triton X-100) for 1 hour, followed by incubation with primary antibody (anti-CGRP, 1:2000, Sigma) overnight at 4˚C. The following day, slides were washed with PBS and incubated with secondary Cy3 goat anti-rabbit (Alexa Fluor 555, 1:500) in blocking solution for 2 hrs at room temperature. DAPI (1:2500) 15 min at room temperature was then used to counterstain the nuclei. Slides were post fixated with 4% PFA for 10 minutes and washed with PBS. Slides were then cover slipped using mounting medium (Immuni-Mount) and dried >24hours at room temperature in the dark. Control experiments included omission of primary antibody from blocking solution.

Images were taken so that the full length of each section was fully imaged. The images (N = 160) were binarized in ImageJ using the triangle algorithm for optimal thresholding and median filtering was applied to reduce single pixel noise. A region of interest detection threshold was applied to detect a minimum of 10 connected CGRP positive pixels. For each image we computed the total CGRP positive area (µm2) and the median value for each animal was used for further analysis.

RESULTS

Representative images of CGRP expression in young and aged trigonal mucosa are shown in figure 1.A and B. Upon statistical analysis the trigonal mucosa of aged animals shows a significantly lower CGRP positive area compared to young animals (p = 0.0049) (Fig. 1.C). These results indicate that aging has a negative effect on the area of CGRP positive signal in the trigone. The structural and functional integrity of the web of sensory nerves in the trigonum of aged animals is significantly affected, and communication between the bladder urothelium and the central nervous system is highly likely compromised as a result.

INTERPRETATION OF RESULTS

Based on the findings reported here, we argue that damage to the sensory system in the trigonal mucosa may be a likely contributor to the development or exacerbation of LUTS. To our knowledge, the detrimental effects of aging on sensory nerve fibers in the bladder has not been quantified before. These new insights advance our understanding of LUTS in older adults and improve treatment selection strategies and therapeutic developments.

CONCLUDING MESSAGE

The structural and functional integrity of the web of sensory nerves in the trigonal mucosa of aged animals is negatively impacted by the aging process (in part due to increased oxidative stress over time [3]), and communication between the periphery and the CNS is highly likely compromised as a result. These detrimental changes to the sensory system are highly likely associated with the reported decrease in visceroceptive awareness in older adults and may be a contributor to the development or exacerbation of LUTS. Future research should assess potential regional differences within the bladder in aging-related changes in sensory innervation with the potential to identify novel therapeutic targets which might improve the quality of life and self-reliance of many older adults suffering from LUTS.

FIGURE 1

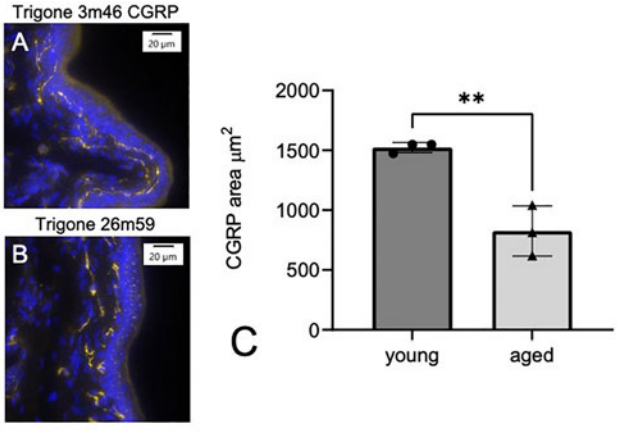

Figure 1: A) Aged animals show a significantly lower CGRP positive area compared to young animals (p = 0.0049) **B)** Representative image of the trigonal mucosa of young rats. CGRP positive areas are yellow and nuclei are blue. **C)** Representative images of the trigonal mucosa of aged rats. Data are represented as individual replicates and by the mean ± SD; **p < 0.01.

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MITOCHONDRIAL-TARGETED FREE RADICAL SCAVENGER, XJB-5-131, PROTECTS THE BLADDER AGAINST RADIATION CYSTITIS WITHOUT AFFECTING TUMOUR SHRINKAGE

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HYPOTHESIS / AIMS OF STUDY

The urinary bladder can develop radiation cystitis when exposed to ionizing radiation during treatment for pelvic malignancies. The severity and timing at which symptoms develop are highly variable [1], thus, it is difficult to predict the susceptibility of radiation induced bladder dysfunction. Furthermore, with increasing rates of cancer survivorship consequences of radiation injury are likely to become more pronounced. We propose that an intravesical radioprotective agent could be used to mitigate collateral damage during treatment of non-bladder tumours. This possibility was examined by subcutaneous implantation of TRAMPC-1 mouse prostate tumour cells in the lower abdomen of male C57Bl/6 mice. Mice were subjected to fractionated X-ray irradiation to the tumour following a single bladder instillation with XJB-5-131, a nitroxide free radical scavenger that is conjugated to a hemi-gramicidin-S moiety [2] allowing enrichment in the mitochondria. The aim was to evaluate if XJB-5-131 could protect the urinary bladder against acute radiation injury without hindering tumour shrinkage.

STUDY DESIGN, MATERIALS AND METHODS

Ectopic tumour implantation and irradiation protocol. TRAMPC-1 mouse tumour cells were obtained from ATCC and cultured as instructed. Male adult C57Bl/6 mice (Envigo, 6 months old) were anesthetized with isoflurane and using sterile surgical methods, subcutaneous injections of TRAMPC-1 cells (1x106 cells in 100 µl) were made 3 to 5 mm bilaterally of the urinary bladder. Two weeks following implantation, mice were anesthetized (300 mg/kg, 2,2,2-tribromoethanol) and subjected to fractionated irradiation [3] to one of the tumours (8 Gy/day/4 days, Fig 1A, red box denotes the irradiated field, black line indicates location of urinary bladder) using collimated X-ray irradiation (X-RAD320, Precision X-ray Inc.). On the first day of treatment, mice had their bladders instilled with 1 µM XJB-5-131 (150 µl in saline) or vehicle just prior to irradiation. There were no further instillations performed during subsequent irradiation events.

Voiding assessments. Voiding activity was analysed by two-hour urine spot tests starting one week prior to implantation of tumour cells and performed weekly after fractionated radiation treatment commenced.

RESULTS

All mice survived the tumour implantation and radiation treatment up to the experimental endpoint of 14 days after irradiation. There was significant shrinkage of irradiated tumours compared to those on the untreated side (Fig 1B). Vehicle instilled mice showed increased urinary frequency and smaller void spots at 14 days after irradiation compared baseline (Fig 1D versus 1C). Instillation of XJB-5-131 prevented development of bladder overactivity/frequent voiding as there was no change from baseline voiding spot profiles (Fig 1E and 1F). The average void spot areas were significantly smaller (Fig 1G) and greater in number (Fig 1H) in vehicle treated irradiated mice compared to XJB-5-131 treated cohort.

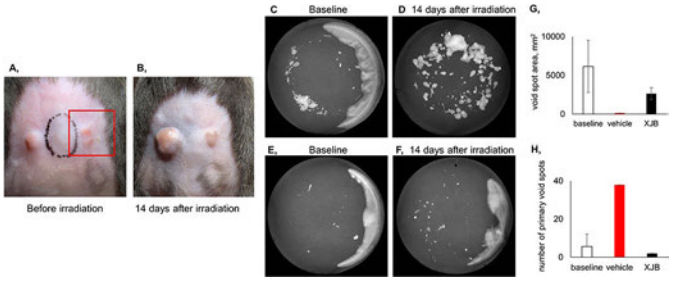
INTERPRETATION OF RESULTS

XJB-5-131 did not hinder radiation induced tumour shrinkage and protected against development of radiation cystitis. The protective effect of XJB-5-131 persisted despite only being administered on the first day of radiation treatment.

CONCLUDING MESSAGE

This study demonstrates that intravesical radioprotectors may be used as a prophylactic agent against radiation cystitis during treatment of pelvic tumours in the vicinity of the urinary bladder. This method may have utility in preventing development of the late-stage condition which in many cases manifest years after radiation exposure.

FIGURE 1



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Funding National Institutes of Health (R01CA251341) **Clinical Trial** No **Subjects** Animal **Species** mouse **Ethics Committee** University of Pittsburgh Institutional Animal Care and Use Committee

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RATIONAL DRUG DESIGN TO IDENTIFY A NEW UREASE INHIBITOR TO TREAT URINARY CATHETER BLOCKAGE.

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HYPOTHESIS / AIMS OF STUDY

Urinary catheter blockage is a frequent problem for long-term catheterized patients, who are often referred to as 'blockers'. Encrustation of the catheter is generally caused by urease-positive microorganisms, such as Proteus mirabilis [1]. Urease metabolizes urea to ammonia, resulting in alkaline urine, causing precipitation of struvite and apatite crystals, and these encrustations then lead to catheter blockage [1]. Long-term catheterized patients often have asymptomatic infections present within the bladder, therefore the prescription of antibiotics is generally discouraged. Here, we examine the use of urease inhibitors as an anti-virulence mechanism to prevent catheter blockage. Acetohydroxamic acid (AHA) is a urease-inhibitor and is prescribed for the treatment of frequent catheter blockage, it is not licensed in the UK or EU and is rarely used owing to its toxic side effect. Urease inhibitors have been well-examined in the literature, often for use in agriculture. However, other than AHA, none have been licensed as a therapeutic for catheter blockage. Our study aims to identify new and improved urease inhibitors which can be prescribed to long-term urinary catheter users who are frequent blockers.

STUDY DESIGN, MATERIALS AND METHODS

Computational modelling docking experiments were used to dock small molecules onto the target-site using the crystal structure of the enzyme, urease from Sporosarcina pasteruii (PDB: 4UBP) (Fig.1). Docking was carried out using Cresset Flare software. Compounds were designed around the structures of known inhibitors: 2-mercaptoacetamide (2-MA), thiourea, and the natural flavonoid, quercetin [2,3]. Analysis of the docking score and the contacts of the compound to the urease crystal structure were used to rank the compounds. Compounds were filtered by Lipinski's rules and the ability to purchase the compounds, the potency of the compound was assessed in vitro using the Berthelot assay against purified Canavalia ensiformis urease and a whole-cell assay of P. mirabilis.

RESULTS

From the virtual screening of high-ranking compounds, A5, A6, and A11, were identified and purchased. The ability of these compounds to inhibit urease was assessed using in vitro urease activity assays, with comparisons to known inhibitors (Fig. 2). Inhibitory concentration 50 (IC50) describes the ability of the compound to reduce the enzyme activity by 50%, IC50 can be used to determine the potency of the compounds.

INTERPRETATION OF RESULTS

Analysis of the IC50 showed that A11 appears to be 500-fold more potent than AHA against purified C. ensiformis urease (Fig. 2A). The whole-cell P. mirabilis assay informs on the ability of compounds to cross the bacterial membrane and access the intracellular urease. Results appear to show A11 to be 50-fold more potent than AHA (Fig. 2B).

CONCLUDING MESSAGE

We have demonstrated the small molecule, A11, as a potential therapeutic to treat recurrent catheter blockages. Future work is required to assess A11's ability to prevent urinary catheter blockage using in vitro models of a catheterized urinary tract.

FIGURE 1

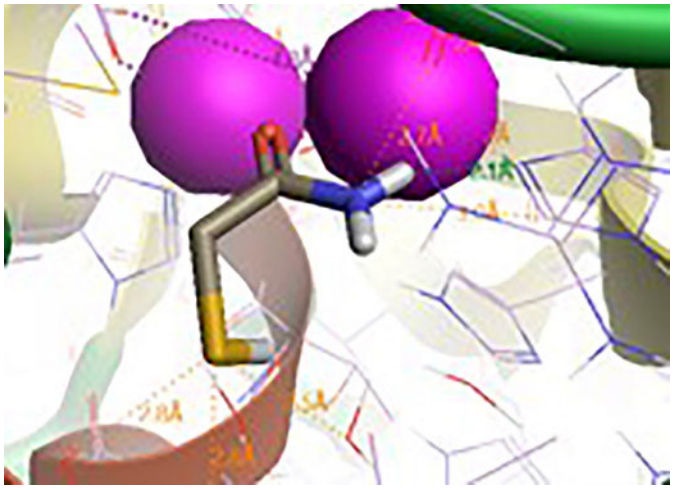
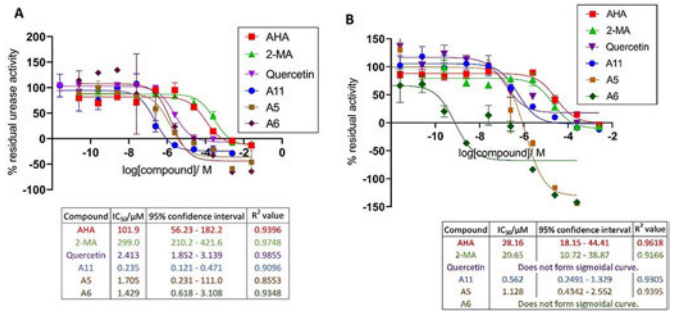


Figure 1: 2-mercaptoacetamide (2-MA) docked into the crystal structure of urease from Sporosarcina pasteruii. 2-MA's chelate the nickel ions in the active site, as well as making additional contacts with amino acids, shown by dotted lines, and measured i

FIGURE 2



Compound	IC_{50}/μM	95% confidence interval	R^2 value
AHA	101.9	56.23 - 182.2	0.9396
2-MA	299.0	210.2 - 421.6	0.9748
Quercetin	2.413	1.852 - 3.139	0.9855
A11	0.235	0.121 - 0.471	0.9096
A5	1.705	0.231 - 111.0	0.8553
A6	1.429	0.618 - 3.108	0.9348

Compound	IC_{50}/μM	95% confidence interval	R^2 value
AHA	28.16	18.15 - 44.41	0.9618
2-MA	20.65	10.72 - 38.87	0.9166
Quercetin	Does not form sigmoidal curve.		
A11	0.562	0.2491 - 1.329	0.9305
A5	1.128	0.4342 - 2.552	0.9395
A6	Does not form sigmoidal curve.		

Figure 2A: Determination of IC50 against purified C. ensiformis urease. B: Determination of IC¬50 against whole-cell P. mirabilis, for the following compounds: AHA, 2-MA, Quercetin, A11, A5 and A6. Three independent biological repeats were carried out, er

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515 | www.ics.org/2022/abstract/515

CELL SHAPE CHARACTERISTICS OF HUMAN SKELETAL MUSCLE CELLS AS A PREDICTOR OF MYOGENIC COMPETENCY: A NEW PARADIGM TOWARDS PRECISION CELL THERAPY FOR INCONTINENCE

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HYPOTHESIS / AIMS OF STUDY
Skeletal muscle derived cells (SMDC) hold tremendous potential for replenishing dysfunctional muscle associated with incontinence. Autologous SMDC-based therapy for faecal incontinence (FI) is reported to be safe, but the level of efficacy reported in previous studies suggests that heterogeneity in the proposed therapy may contribute to inconsistent clinical outcomes.

Improved methods for patient stratification to identify patients who are (un) likely to respond well to regenerative therapies are advocated to ensure the potential benefits of cell-based regenerative medicine can be fully exploited. Predicting the therapeutic potency of SMDC in vitro prior to implantation will facilitate development of successful therapeutics in regenerative medicine and reduce implementation costs.

Here, we report on the development of a novel SMDC profiling tool to examine populations of cells in vitro derived from different donors. The primary aim of the study was to evaluate the applicability of multi-parametric imaging-based phenotypic characterization to distinguish myogenic potency of SMDC. Heterogeneity in the formation of myotubes from different donors was correlated with cell shape descriptors.

STUDY DESIGN, MATERIALS AND METHODS
Commercially available human SMDC (Cook MyoSite) consisting of non-differentiated primary human muscle cells were derived from 14 individual human donors. Image acquisition of SMDC growth was performed using a CytoSMART Lux2 microscope. Images were acquired every 5 minutes over a period of 72 hours. CellProfiler software was used to create an image analysis pipeline for analysis of different cell shape characteristics during 2 hours of tracking at 12- and 24-hours post-culture. The Konstanz Information Miner (KNIME; open-source data analytics) software was used to calculate the mean and SD of the characteristic for all the objects identified in one image. These data were then used for statistical correlation with the fusion index calculated from myotube formation assays established in the same cultures after 5 days of subsequent incubation in differentiation medium. The fusion index was calculated as the ratio of nuclei number in myocytes with 2 or more nuclei divided by the total number of nuclei. Correlation studies used the Spearman test with $r < -0.5$ or $> +0.5$ indicating correlation.

RESULTS
Several early cell shape characteristics were found to negatively correlate with the fusion index. Images collected at 12 hours after initiating culture revealed that 5 cell shape characteristics negatively correlated with the fusion index, including the total area occupied by cells ($r = -0.815$, $p = 0.001$), area shape ($r = -0.631$; $p = 0.028$), bounding box area ($r = -0.576$; $p = 0.049$), minimum ferret diameter ($r = -0.589$; $p = 0.044$) and minor axis length ($r = -0.614$; $p = 0.034$). Images collected at 24 hours after initiating revealed 8 cell shape characteristics that negatively correlated with the fusion index. These included: total area occupied by cells ($r = -0.686$; $p = 0.007$), area shape ($r = -0.709$; $p = 0.005$), bounding box area ($r = -0.563$; $p = 0.036$), compactness ($r = -0.534$; $p = 0.049$), equivalent diameter ($r = -0.576$; $p = 0.031$), minimum ferret diameter ($r = -0.620$; $p = 0.018$), minor axis length ($r = -0.590$; $p = 0.026$) and perimeter ($r = -0.654$; $p = 0.011$). There was a high correlation between all these characteristics at 24 hours of imaging after initiating culture.

INTERPRETATION OF RESULTS
Results indicate that monitoring of cell shape during the early stages of bioprocessing using real-time imaging could be used to predict cellular competency necessary for differentiation and myofibre formation in vivo.

CONCLUDING MESSAGE
Further studies could establish whether selection of either patients or cell populations on this basis have a higher probability of yielding better outcomes in cell-based therapy for incontinence.

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BEST IN CATEGORY PRIZE: NEUROUROLOGY

FUNCTIONAL CONNECTIVITY ANALYSIS IN HEALTHY MEN AND WOMEN UTILIZING 7 TESLA MRI DURING FULL AND EMPTY BLADDER STATES

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HYPOTHESIS / AIMS OF STUDY

Functional magnetic resonance imaging (fMRI) has given way to quantifiable metrics for observing brain activation during specific states, such as functional connectivity (FC). This metric reflects communication networks between multiple regions of the brain that, although not structurally adjacent, collaborate with each other. which demonstrates how multiple regions that may not be structurally connected interact with each other in time. Our objective is to investigate the characteristic resting state FC (rsFC) between both full and empty bladder states, as well as compare rsFC between healthy men and women. In this study, we report observations from our second 7T study evaluating rsFC of the brain during neural control over full and empty bladder states using a noninvasive, passive bladder filling. However, this study differentiates from the previous by the inclusion of males and females, as well as evaluating how rsFC differ at each bladder state.

STUDY DESIGN, MATERIALS AND METHODS

Healthy adult men and women (≥ 18 years) with no history of urinary symptoms or neurological diseases were invited to participate in this study. Uroflow was performed, post-void residual (PVR) volume was measured, and those who failed to meet all inclusion and exclusion criteria were excluded. For data collection, each subject was asked to consume 500mL to 750mL of water and empty their bladder. Next, subjects were placed within the 7T MRI. Anatomical and diffusion tensor imaging (DTI) scans were obtained. An fMRI obtaining brain activation during the empty state was also collected. Participants then remained within the scanner until they felt the urge to void, prompting a functional scan during the full bladder state. rsFC was then obtained from the fMRI scans, different Talairach regions were investigated and areas with a t-value greater than 2.1 were considered statistically significant. Further investigation into gender distinction was performed and FC differences were calculated and reported.

RESULTS

Twenty individuals (10 women and 10 men) participated in the study. One male participant's fMRI did not yield usable rsFC data and was therefore excluded from analysis. The mean age of all participants was 27.21 years (22-55), with an average male age of 22.78 (23-33) and female age of 28.9 (22-55). Ethnicity breakdown showed 6 participants of Asian descent (3M, 3F), 1 female African American subject, 11 white subjects (6M, 5F), and 1 Hispanic female subject. Several areas see increased rsFC during full bladder such as the left lenticular nucleus, left uvula, right ventral posteromedial nucleus of the thalamus, and the right mammillary body, while increased rsFC during empty bladder was seen in the left fusiform gyrus, left putamen, and right ventrolateral nucleus of the thalamus (Figure 1). Eight areas were statistically significant between full and empty bladder states, including the left fusiform gyrus, lenticular nucleus, putamen, uvula, right superior temporal gyrus, ventroposterior medial nucleus of the thalamus, ventrolateral nucleus, and mammary body (Figure 2a). Furthermore, a difference in rsFC between men and women at both bladder states (empty and full) was noted. During the empty bladder state, a statistically significant difference was noted within the right uvula and tubercle with males having a higher rsFC, while during the full bladder state, a significant difference occurred in the right middle temporal gyrus, again depicting males with a higher rsFC value (Figure 2b).

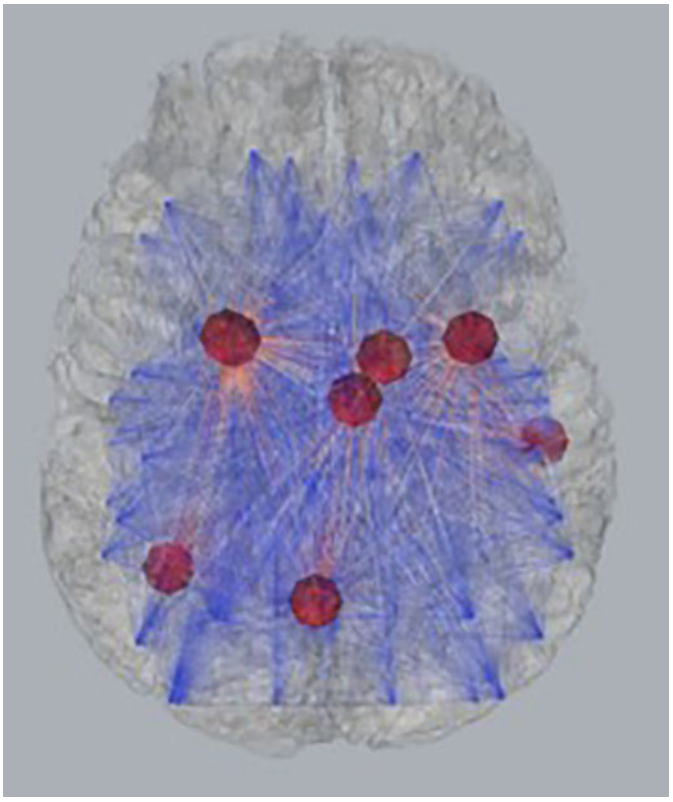
INTERPRETATION OF RESULTS

Functional connectivity has proven to be one of the best indicators of how the brain is communicating when "at rest" in various states. In our study, the two time periods of "rest" correlate with either the full or empty bladder state. Utilization of the 7 Tesla MRI has further increased the resolution and data accuracy of fMRI and thus allowed discovery of functionally connected regions within the brain rather than structurally connected. This information will help us further understand the relationships between the working model of the three brain-bladder circuits . We therefore conclude that the 8 regions that were identified as statistically significant between empty and full bladder states represent regions that play a role in supraspinal control of bladder cycle. Further analysis will be required to discover how involved each region is in maintaining continence, potentially leading to new treatments for lower urinary tract symptoms. When comparing women to men, we see a higher rsFC for men during the empty phase with more involvement of the uvula which aids in motion processing, while men also have higher rsFC during the full bladder state within the middle temporal gyrus, commonly associated with memory processing and visual perception. Further investigation into differences in brain functionality between men and women as it relates to continence and micturition could yield significant results as we believe this is the first time those differences in rsFC have been brought to light.

CONCLUDING MESSAGE

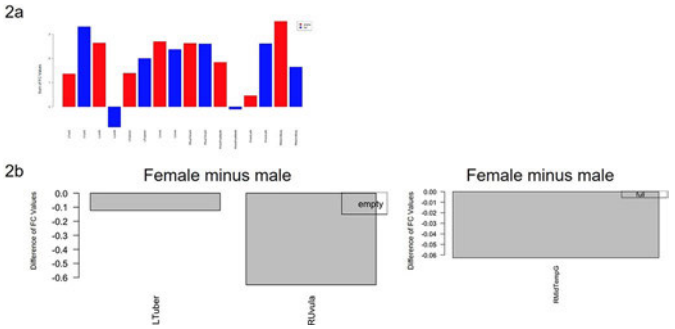
Although these are preliminary results, they hold promise for both better understanding continence and voiding, as well as future trials of pathologic conditions utilizing noninvasive brain-bladder protocol and the 7T MRI scanner to investigate how rsFC in these regions are affected by disease.

FIGURE 1



Graphic depiction of significant rsFC values within the brain

FIGURE 2



2a. Cumulative rsFC values of significantly different regions at full and empty bladder 2b. Regions with a significant difference in rsFC between women and men

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IN VITRO: GENE EXPRESSION OF GAG SYNTHESIZING GENES IN RELATION TO GAG-THERAPY.

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1. Radboudumc, 2. MUMC+

HYPOTHESIS / AIMS OF STUDY

Glycosaminoglycans (GAGs) are molecules that trap water to from a highly impermeable barrier layer on the urothelium. In Interstitial cystitis/Bladder pain syndrome (IC/BPS) this layer is thought to be disrupted. GAG replenishment therapy is used as therapy for IC/BPS, adding exogenous GAGs such as chondroitin sulfate (CS) and hyaluronic acid (HA). The exogenous GAGs are intended to repair the impaired GAG layer. New insights about the functioning of these exogenous GAGs and influence on the urothelial cells are being investigated. [1]

The scope of this study is to examine the effect of GAG therapy on gene expression in damaged urothelial cells for CS and HA synthesizing genes.

STUDY DESIGN, MATERIALS AND METHODS

Cell Culture

Porcine urothelial cells were cultured in complete keratinocyte serum-free medium (cKSFM; containing KSFM, 1% penicillin/streptomycin, 30ng/mL cholera toxin, 50 µg/mL bovine pituitary extract and 5 ng/mL epidermal growth factor). The cells were seeded in 12-wells plates (75.000 cells per well/3.9cm2/1mL). When confluency was reached (7 days) the medium was supplied with 5% fetal calf serum (FCS) and 2mM calcium chloride (Ca2+-Cl) to induce terminal differentiation (7 days). This protocol has previously been applied and controlled on the same primary cell culture with Trans Epithelial Electrical Resistance (TEER) measurements that demonstrated high barrier properties (TEER values of >1000 Ω·cm2).

GAG replenishment therapy

All cells, except for the untreated group, were challenged with protaminesulfate 10mg/mL for 1h with a 1:1 ratio with medium to approximate inflamed urothelial and mimic IC/BPS environment.

Afterwards, all the damaged cells were divided into three treatment groups:

1. CS, 0,2%, Gepan Instill, Pohl-Boskamp GmbH & Co., Hohenlockstedt)
2. CS 2% & HA 1.6%, IALURIL® Prefill, IBSA, Goodlife
3. HA 0,16%, Instylan, BMODESTO, Diaco Biofarmaceutici S.R.L. Triest.

Thereafter, cells treated with the GAG therapy in a 1:1 ratio with fresh medium for one hour. Afterwards, all cells were washed three times with Hank's Balanced Salt Solution (HBSS) and fresh medium was added. Cells were harvested at T3, T5, T7, T12 and T24. In an earlier similar setting undamaged cells were treated with the three GAG therapies and harvest at T3 and T24.

RNA isolation and RT-qPCR

RNA isolation was done using TRIzol reagent (Invitrogen). The RNA was evaluated using a Nanodrop ND-1000 system (ThermoFisher Scientific). RNA was DNase I treated, and cDNA was synthesized with Superscript II reverse transcriptase (Invitrogen). Gene expression was evaluated by SYBR Green qPCR analysis (Roche) on a LightCycler LC480 instrument (Roche). The expression of CS and HA GAG synthesis genes (CSGALNACT1, CSGALNACT2, HAS2 and HAS3) were assayed.

RESULTS

Treating healthy urothelial cells with GAG therapy (HA and/or CS) resulted in a strong (96%) down regulation of HAS2. For HAS3 and CSGALNACT1 approximately 50% reduction was seen compared to controls. CSGALNACT2 was the least affected with a reduction of 20-35%.

HAS2 was upregulated under inflamed conditions, there is a five times higher expression in protamine treated samples in comparison with normal conditions. This response was quick with a peak at T7 hrs and is normalized again at T24hrs. HAS3 expression follows a similar pattern with a 2,5-fold increase in expression compared to controls. The CS synthesizing genes were not evidently influenced by protamine exposure. CSGALNACT1 expression increased at T3hrs for protamine only and with CS treatment afterwards. CSGALNACT2 expression increased after protamine exposure followed by HA treatment. See Figure 1.

The effect of HA+CS treatment (IALURIL®) after protamine exposure resulted in lower HAS2 expression, except for T5hrs. At T24hrs al GAG therapies led to an increased HAS2 expression compared to control and protamine only. CS treatment stimulates at T3hrs the expression of HAS3 strongly and slightly of CSGALNACT1. The CSGALNACT2 expression is slightly increased by HA treatment at T3hrs.

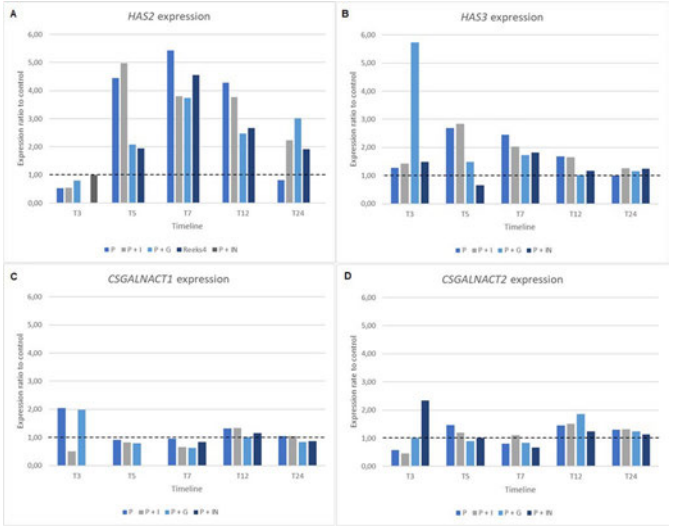
INTERPRETATION OF RESULTS

The downregulation of the GAGs synthesizing genes in healthy urothelial cells after treatment with exogenous GAGs demonstrates that it influences urothelial endogenous GAG synthesis with a negative feedback loop. On the other hand, inflicting damage to the urothelial cells increases the synthesis of hyaluronic acid by increasing HAS2 and HAS3 expression. This is a fast-acting mechanism that normalizes after 24 hrs, with a beneficial effect in expression of adding exogenous GAGS. This is in line with earlier findings, that recovery of the barrier function after protamine treatment is completed after 24h. [2] Interesting CSGALNACT1 and 2 do not increase after inflammation is induced, this is in line with findings by Rooney et al. [1], even though earlier research shows the digestion and/or replenishment of CS does affect barrier function directly.[2, 3] Rooney et al showed a slight tendency of increase of CSGALNACT1 and CSGALNACT2 at T24 after GAG therapy in damaged cells.[1] In our series no evident increase of CSGALNACT1 and 2 was seen. Our data for HAS2 shows that adding exogenous GAGs reduces the need for endogenous HA synthesis. These observations suggest that there is a protective effect of GAG therapy and that it modulates urothelial inflammatory responses. Future prospective could be to debate about the concentration of the given GAG therapy, with the negative feedback loop in mind.

CONCLUDING MESSAGE

GAG therapy influences urothelial GAG synthesis genes during normal conditions and damage. Adding exogenous GAGs (HA and/or CS) to healthy urothelial cells induces a negative feedback loop for the HA GAG synthesizing genes. This process is also seen in inflammatory conditions whereby GAG therapy attenuates activation of GAG synthesizing genes, thereby suggesting that GAG therapy not only works a liquid barrier patch, but also interacts with urothelial (barrier) repair mechanisms.

FIGURE 1



Expression of the GAGs synthesizing genes after protamine exposure and adding exogenous GAGs.

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SESSION 35 - CONSERVATIVE MANAGEMENT

Abstracts 580-591
15:05 - 16:35, Hall K
Chair: Ms Tamara Dickinson (United States)

580 www.ics.org/2022/abstract/580

COVID-19, PELVIC HEALTH, AND WOMEN'S VOICES: A DESCRIPTIVE STUDY

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HYPOTHESIS / AIMS OF STUDY
Healthcare overall was a casualty of the Covid-19 pandemic, as was Postnatal care (1). Women's activities day-to-day changed with increased childcare, home-schooling, and working from home, while weight-gain and altered recreational exercise levels were also reported. As these factors impact pelvic floor health, we aimed to examine how women with pelvic dysfunction were affected by the pandemic.

STUDY DESIGN, MATERIALS AND METHODS
A Survey Monkey™ online questionnaire examined the impact of the pandemic and Covid-19 infection on women's pelvic problems, exercise, and weight. Also, history of Covid-19 infection, and its effect on continence and sexual function was sought using a previously developed tool (2). A free text box captured their comments, which were analysed using qualitative methods.

RESULTS
Results:

647 women took part, 540 (84%) replying through a website for support garments (EVBTM).

Bladder control 265 (41%), prolapse 240 (37%), pelvic pain 40 (6%), sexual dysfunction 27 (4%), faecal incontinence 19 (3%) and other symptoms 56 (9%) were women's main pelvic problems. Symptoms were unchanged for 331 (51%), worse for 243 (38%), and improved for 60 (10%). Weight was gained by 290 (45%), unchanged by 243 (38%), and lost by 114 (17%). Exercise levels were unchanged, worse, or better in 33% each.

Access to medical appointments and date for surgery were difficult for 235 (36.5%) and 38 (6%) women respectively.

Sixty-six (10.3%) women reported covid-19 infection: distribution of pelvic problems, changes through the pandemic, weight and exercise patterns, and difficulty accessing a date for surgery or healthcare were similar to those not contracting infection. Sexual dysfunction was the main new/worsening problem, featuring 13 women (18%).

Seventy women commented- 16 postnatal, 54 with pre-existing pelvic symptoms. Five core themes were identified: mental health impact and physiotherapy services especially affected delivered women, while lifestyle alterations and conservative treatment tools were prominent in women with a pre-existing problem.

INTERPRETATION OF RESULTS
Our study found little difference between women who contracted Covid-19, and those who did not, apart from prominent sexual dysfunction in women recovered from Covid infection: this may be secondary to inflammatory change in pelvic organs and merits further study.

Our respondents tended towards weight-gain: national lockdowns curtailed movement, contributing to increased BMI: this has been linked to adverse changes in mental health. Psychological distress is a feature of the pandemic worldwide through the strong association of Covid-19 with uncertainty and isolation. 'Juggling' was a phrase used by our respondents in relation to their responsibilities during the pandemic. The UK Household Longitudinal Study found that women who spent long hours on housework and childcare reported increased levels of distress. Our respondents had a more mixed experience of being at home: several used the time gained through not commuting as an opportunity for exercise, and the enhanced sense of control translated into better wellbeing. Presumably those with small children who could not attend school or creche were impacted more negatively, and several mothers viewed exercise as a critical outlet.

Loss of face-to-face contact and personal avoidance by healthcare staff with our respondents were experienced as a lack of compassion, and telephone contact was found to be an inadequate substitute for in-person care. Access to Physiotherapy services was poor, especially postnatally, resulting in some attending privately. Several commented on the paucity of specialist physiotherapy services given the frequency of such issues. Those with pre-existing pelvic problems were familiar with a range of conservative measures, including online classes: these- support shorts in particular- were the subject of positive commentary. Many women commented on the beneficial influence of exercise on pelvic floor function. This adds to the mounting evidence suggesting that exercise and physical activity interventions affect physical and mental-health outcomes positively.

The qualitative data captured through the free text box is the main strength of this study. 'Telling your story' gives subjects the freedom to report in their own words what is important to them. The part played by women's voices in delivery of obstetric and gynaecological care has been recognised (3).. Qualitative methods help us to "enter the world of its participants". and are a rich source of data suitable for analysis13.

Because this research was conducted via the internet, there is a bias towards younger, more computer-literate respondents, and the EVBTM website attracts women who exercise and enjoy sport.

CONCLUDING MESSAGE
Our survey captures the suffering of women with pelvic dysfunction resulting from reduced access to healthcare in the pandemic. It underlines the importance women ascribe to exercise for pelvic floor health, its role in stress relief, and how pelvic floor dysfunction through limiting exercise can adversely affect mental health.

Our study adds to previous calls for enhanced care and support for women postnatally and underlines pelvic health as an integral component. The finding of sexual dysfunction as part of recovery from Covid-19 infection merits further exploration.

Finally, the pandemic exposed the fact that female pelvic health services are not readily available to women in need.

Funding None **Clinical Trial** No **Subjects** Human **Ethics not Req'd** As this was an opt-in survey, ethical approval was not required. **Helsinki** Yes **Informed Consent** Yes

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UROLOGICAL SYMPTOMS IN PATIENTS WITH COVID-19: EXPLORING CHANGES IN FREQUENCY BY PANDEMIC WAVES

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HYPOTHESIS / AIMS OF STUDY

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic erupted in December 2019. As the viral infection is driven by increased angiotensin-converting enzyme-2 (ACE2) expression, with the urothelial cells exhibiting a high expression, it is logical to think that there may be an increase in the frequency of lower urinary tract symptoms (LUTS) in patients diagnosed with coronavirus disease 2019 (COVID-19)(1,2). There does not a relationship between the presence of the virus in the urine and the presence of urological symptoms(3–6). The increase in inflammatory cytokines in the urine and bladder inflammation might be responsible for the presence of associated bladder dysfunction(2,7,8). This is a very little studied subject, and the few studies present a low sample size as well as quite disparate results.

This study aims to examine the effects of infection with SARS-CoV-2 on the male and female genitourinary tract, especially if there is a change in the frequency of genitourinary tract symptoms (consistent with urinary incontinence (UI), urinary tract infection (UTI), urinary retention (UR), hematuria, erectile dysfunction (ED) and neurogenic detrusor (ND) and acute kidney failure (AKF) in the different waves of COVID19, as well as a possible oscillation in the symptoms frequency related to comorbidities and demographic variables, using the medical records of patients who have been hospitalized for this infection.

STUDY DESIGN, MATERIALS AND METHODS

A retrospective study took place in our institution of COVID-19 admitted patients. Only patients with RT-PCR or antigen test confirmed SARS-CoV-2 infection were included, and demographic, clinical, and urological symptoms were explored. COVID-19 patients with LUTS were compared with those without LUTS. Statistical comparisons were conducted by parametric or nonparametric tests for quantitative variables, and x2 test for qualitative variables.

RESULTS

There were a total of 4,661 unique patients. Urological symptoms were found to be increased in COVID- 19 patients, reaching 21,1% of them. The largest proportion of patients come from the first wave (1,492; 32.0%), followed by the second wave (1,062; 22.8%), third (903; 19.4%), fourth (391; 8.4%), fifth (246; 5.3%) and sixth wave (567; 12.2%). Of the 4,661 unique patients, 2,483 (53.3%) were men and 2,178 (46.7%) were women. The mean age of the patients was 69.1 (SD 17.2). Only 74 (1.5%) patients were foreigners.

The median age was statistically significant higher for those patients with urological diseases (Table 1). The gender proportion was very close. Additionally, this group presented a higher percentage of comorbidities (78.9% vs 57.5%) being the all comorbidities higher and statistical different for the group with urological diseases (excluding smoker and former smoker comorbidity), and for the urological history (except for urolithiasis).

The frequency of the different urological diagnosis varied between the waves (Table 2). We analyzed the distribution of demographic variables (sex and age), length of stay and comorbidities in each of the waves in order to explain the frequency change of the different urological diagnosis (Table 2). Male gender was higher in all waves except in the 6th wave, however this difference was not significant ($p > 0.05$). For age, we found that the median age was significantly higher for the 6th wave against the rest ($P \leq 0.001$). The median length stay was higher in the 2nd,3rd, 4th waves. For the comorbidities, we found that in the 6th wave the percentage was significantly lower to the other waves, followed to the 1st wave. Between these comorbidities we found that smokers and former smokers were more frequent in the 4thth wave (32.2%) and in the 6th wave the lowest frequency (15.2%). Mortality was higher in the 1st wave, reaching up to 17.4% of COVID-19 cases. The urological history was significantly lower in the 6th than in the other waves.

The AKF diagnosis showed a significant difference among the waves, with a higher presence in the 5th (16.7%) and 3rd wave (13.3%), and lower presence in the 6th (8.5%) and 2nd (9.3%) waves.

UTI also showed a significant difference along the waves, being more frequent in the 3rd (12.8%) and 5th (12.6 %) waves, and lower presence in the 6th (6.4 %) and 1st (7.0 %) waves. Finally, hematuria and ED also showed a varied significantly, being more frequent in the 5th (1.6%) and 3rd wave (0.5%), respectively.

The difference among gender in each wave showed that for males the diagnosis AKF was significantly higher for the 1st (14.2% vs 9.4%) and 2nd waves (11.3% vs 7.1%), and hematuria diagnosis in the 3rd wave (1.7% vs 0.0%). On the other hand, the presence of UI diagnosis and UTI was higher for females, being significantly higher for 1st (urinary incontinence diagnosis: 3.1% vs 1.0%) and 2nd wave (UI diagnosis: 3.0% vs 1.1%; UTI: 16.1% vs 6.3%).

INTERPRETATION OF RESULTS

This is the largest study about symptoms of an urological nature in patients with COVID19 and provides insights into the natural history of the disease in adults with a considerable frequency of urological symptoms during the first to the sixth pandemic wave. It suggests that UTI, UI, UR and an AKF might be related to a SARS- CoV-2 infection, and could predict a worse prognosis. On the other hand, we did not find statistical differences for hematuria, ED and NB diagnosis. The minimum of urological diseases was reached in the 6th wave most probably for the lower frequency of comorbidities recorded in that wave.

CONCLUDING MESSAGE

Clinicians should be aware of these symptoms of the disease, leading to a faster therapeutic procedure and consequently reducing the mortality rate.

FIGURE 1

Table 1. General characteristics of all patients and those with a positive diagnosis for urological diseases.

Parameter	Result (*n* = 4,661)	Urology diseases[1] Yes (*n* = 982)	Urology diseases[1] No (*n* = 3,679)	*P*-value[2]
Median age, yr (range)	71.0 [17-105]	80.0 [20-105]	68.0 [17-104]	**<0.001**
Male, n (%)	2,483 (53.3%)	527 (53.7%)	1,956 (53.2%)	0.808
Female, n (%)	2,178 (46.7%)	455 (46.3%)	1,723 (46.8%)	
Comorbidity, n (%)	2,882 (61.8%)	765 (77.9%)	2,117 (57.5%)	**<0.001**
Obesity	338 (7.3%)	86 (8.8%)	252 (6.9%)	**0.048**
Diabetes	892 (20.4%)	289 (29.4%)	603 (17.8%)	**<0.001**
Hypertension	1,620 (34.8%)	418 (42.6%)	1,202 (32.7%)	**<0.001**
Smoker and former smoker	1,140 (24.5%)	223 (22.7%)	917 (24.9%)	0.163
Heart disease	368 (7.9%)	132 (13.4%)	236 (6.4%)	**<0.001**
Chronic Kidney Disease	413 (8.9%)	207 (21.1%)	206 (5.6%)	**<0.001**
Urological history	446 (9.6%)	155 (15.8%)	291 (7.9%)	**<0.001**
Benign prostatic hyperplasia	346 (7.4%)	109 (11.1%)	237 (6.4%)	**<0.001**
Urogenital implants	30 (0.6%)	23 (2.3%)	7 (0.2%)	**<0.001**
Prostate cancer	135 (2.9%)	46 (4.7%)	89 (2.4%)	**<0.001**
Urothelial cancer	10 (0.2%)	6 (0.6%)	4 (0.1%)	**0.008**
Urolithiasis	39 (0.8%)	8 (0.8%)	31 (0.8%)	1.000
Urinary system abnormalities	41 (0.9%)	17 (1.7%)	24 (0.7%)	**0.002**
Urethral disorder	4 (0.1%)	4 (0.4%)	0 (0.0%)	**0.002**

[1]Patients with positive diagnosis for acute kidney failure, urinary incontinence, urinary tract infection, urinary retention, hematuria, erectile dysfunction, neuromuscular dysfunction of the bladder/ neurogenic bladder.

[2] Significant differences ($p<0.05$) are indicated by bold text.

FIGURE 2

Table 2. Urological diagnosis depending on COVID-19 waves.

	1st wave (*n* = 1,492)	2nd wave (*n* = 1,062)	3rd wave (*n* = 903)	4th wave (*n* = 391)	5th wave (*n* = 246)	6th wave (*n* = 567)
Demographic variables						
Gender						
Male	819 (54.9%)	558 (52.5%)	483 (53.5%)	215 (55.0%)	128 (52.0%)	280 (49.4%)
Female	673 (45.1%)	504 (47.5%)	420 (46.5%)	176 (45.0%)	118 (48.0%)	287 (50.6%)
Age range	70 [19-101]	70 [22-105]	72 [21-104]	71 [19-102]	71 [18-102]	77 [17-101]
Length of stay	7 [0-178]	8 [0-163]	9 [0-341]	8 [1-130]	7 [0-127]	7 [0-79]
Comorbidities	**926 (62.1%)**	**683 (64.3%)**	**625 (69.2%)**	**273 (69.8%)**	**170 (69.1%)**	**205 (36.2%))**
Diabetes	293 (19.6%)	215 (20.2%)	195 (21.6%)	79 (20.2%)	39 (15.9%)	71 (24.8%)
Smoker and former smoker	**370 (24.8%)**	**232 (21.8%)**	**257 (28.5%)**	**126 (32.2%)**	**69 (28.0%)**	**86 (15.2%)**
Death	**259 (17.4%)**	**136 (12.8%)**	**148 (16.4%)**	**41 (10.5%)**	**26 (10.6%)**	**81 (14.3%)**
Urological history	**142 (9.5%)**	**112 (10.5%)**	**91 (10.1%)**	**42 (10.7%)**	**27 (11.0%)**	**32 (5.6%)**
Diagnosis						
Acute kidney failure	**179 (12.0%)**[1]	**99 (9.3%)**	**120 (13.3%)**	**49 (12.5%)**	**41 (16.7%)**	**48 (8.5%)**
Urinary incontinence	29 (1.9%)	21 (2.0%)	14 (1.6%)	11 (2.8%)	7 (2.9%)	10 (1.8%)
Urinary tract infection	**105 (7.0%)**	**116 (10.9%)**	**116 (12.8%)**	**41 (10.5%)**	**31 (12.6%)**	**36 (6.4%)**
Urinary retention	32 (2.1%)	30 (2.82%)	24 (2.7%)	11 (2.8%)	12 (4.9%)	9 (1.6%)
Hematuria	**10 (0.7%)**	**1 (0.1%)**	**8 (0.9%)**	**0 (0.0%)**	**4 (1.6%)**	**2 (0.4%)**
Erectile dysfunction	**0 (0.0%)**	**1 (0.1%)**	**5 (0.5%)**	**0 (0.0%)**	**1 (0.4%)**	**0 (0.0%)**
Neurogenic bladder	1 (0.1%)	1 (0.1%)	0 (0.0%)	1 (0.3%)	1 (0.4%)	0 (0.0%)
Total	296 (19.8%)	215 (20.2%)	227 (25.1%)	87 (22.3%)	73 (29.7%)	84 (14.8%)

[1] Significant differences ($p<0.05$) are indicated by bold text.

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IMPACT OF COVID IN WOMEN WITH PELVIC FLOOR DYSFUNCTION: HOW DOES IT AFFECT THEIR PELVIC FLOOR?

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HYPOTHESIS / AIMS OF STUDY

COVID pandemic had stormy impact in all health care systems over the world. Hong Kong had just gone through the peak of the Omicron wave in February 2022, which recorded the highest hospitalization and mortality rates across the whole pandemic. This COVID surge had led to much physical, emotional and social disturbances to our population, especially in the elderly group. This study aims to evaluate what was the impact of COVID in their daily life, emotion, practice of pelvic floor training and their pelvic floor symptoms.

STUDY DESIGN, MATERIALS AND METHODS

Women who attended the urogynaecological clinic during this COVID surge, starting from 14 March to 31 March were interviewed. Their current occupation and vaccination record were asked. As currently there was no validated questionnaires addressing pelvic floor symptoms with COVID pandemic, we developed a novel questionnaire in Chinese to explore the impact of COVID to their daily life, emotion and the change of their outdoor activity during the last 4 weeks by using a VAS (Visual Analogue Scale) score of 0-10 (score 0 means no effect; score 10 means maximum effect). Any effect on their compliance of pelvic floor training, symptoms of pelvic organ prolapse, urinary frequency and urinary incontinence were included in the questionnaire. Either the attending gynaecologist or a research assistance helped with the patients to fill in the questionnaire.

Chi-square was used for the comparison of categorical variables between the two groups (incontinence versus prolapse group) and Student's t-test for continuous variables. Correlation between the scores were tested by using Pearson correlation coefficient. A p-value < 0.05 was considered statistically significant. The SPSS system (IBM, Armonk, NY, USA, Version 23) was used for the analysis.

RESULTS

Over the study period, total of 103 women were interviewed, with 26 (25.2%) new cases and 77 follow up cases in the clinic. The mean age was 68.7 (SD:11.4) years old. 46 (44.7%) women were retired from work, 28 (27.2%) were housewife, 13 (12.6%) were manual worker and 16 (15.5%) with other occupations. 78 (75.7%) of them regards as fully vaccinated (52 with 2 doses and 26 with booster doses) and 25 (24.3%) with had not yet completely vaccinated (13 did not receive any vaccine while 12 had only one dose). The impact of COVID causing depressive mood, stress or affecting daily life were reported in Table 1. The change of their compliance of pelvic floor exercise and pelvic floor symptoms were reported in Table 2. Vaccination record was not associated with their reported reduction of outdoor activity (score 6.5 in incomplete vaccinated group vs score 6.0 in vaccinated group, $p = 0.50$) nor the effect on their emotion or daily living ($p > 0.05$). The VAS score on their emotion including stress and depressive mood were correlated with their reported reduction of outdoor activity ($p = < 0.01$ for daily activity and feeling stressful; $p = 0.05$ for depressive mood). However, the reported reduction in outdoor activity was not associated with any change of their compliance of pelvic floor training. Neither the vaccination record, emotional impact or outdoor activity was not associated with the change of pelvic floor symptoms during this COVID surge. Only compliance of pelvic floor exercise was associated with the change of symptoms in urinary frequency ($p < 0.01$).

INTERPRETATION OF RESULTS

The vaccination rate in women with pelvic floor dysfunction attended our clinic was comparable with the reported vaccination rate in this age group by government. However, the completion of vaccination was not associated with the impact on their emotion and daily living during the local COVID surge. The negative impact on their emotion was associated with their reported reduction of outdoor activity. Despite majority of them with reported depressed mood and stressful in their daily life, they have similar compliance on pelvic floor exercise Majority of them had similar pelvic floor symptoms including prolapse and urinary symptoms.

CONCLUDING MESSAGE

COVID pandemic had caused serious emotional disturbance to majority of women. They had reported much reduction in outdoor activity. Majority of them maintained with similar practice on pelvic floor exercise and no change pelvic floor symptoms.

FIGURE 1

Table 1. Impact on their socio-emotional aspects and compliance of pelvic floor exercise

VAS	Impact on daily living	Depressed mood	Feeling stressful	Reduced outdoor activity
0	13 (12.6%)	25 (24.3%)	30 (29.1%	9 (8.7%)
1-4	13(12.6%)	18 (17.5%)	18(17.5%)	5 (4.9%)
5-8	46 (44.7%)	28 (27.2%)	26 (25.2%)	22 (21.4%)
8-10	41 (39.8%)	32 (31.1%)	29 (28.2%)	67 (65.0%)

Table 1. Impact on their socio-emotional aspects and compliance of pelvic floor exercise

FIGURE 2

Table 2. Impact on the pelvic floor symptoms

	Compliance on pelvic floor exercise		Symptoms of prolapse	Urinary frequency	Urinary incontinence
No change	70 (70.0%)	No change	87 (84.5%)	58 (56.3%)	67 (65.0%)
Increased	13 (12.6%)	Improved	6 (9.7%)	9 (8.7%)	21 (20.4%)
VAS 1-5	6 (9.7%)	VAS 1-5	5(4.9%)	5(4.9%)	16 (15.5%)
VAS 6-10	7 (6.8%)	VAS 6-10	1 (1%)	4 (3.9%)	5(4.9%)
Decreased	20 (19.4%)	Worsen	10 (9.7%)	36 (35.0%)	15 (15.6%)
VAS 1-5	10 (9.7%)	VAS 1-5	5(4.9%)	28 (27.2%)	11 (10.7%)
VAS 6-10	10 (9.7%)	VAS 6-10	5(4.9%)	8 (7.8%)	4 (3.9%)

Table 2. Impact on the pelvic floor symptoms

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THE ACUTE EFFECT OF PELVIC FLOOR MUSCLE EXERCISE USING LOCAL VIBRATION AND VISUAL FEEDBACK

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HYPOTHESIS / AIMS OF STUDY

Urinary incontinence (UI) makes a decline in the quality of life. A previous study showed that the pelvic floor muscles (PFM) exercise has been validated for the prevention of UI. These exercises, on the other hand, involve problems such as difficulty for the individual to realize the PFM contraction. For these reasons, the exercise is generally conducted with feedback such as visual feedback (FB). In our previous studies, the possibility of a new PFM exercise method using local vibration stimulation (VB) was examined, and it was confirmed that higher effects were obtained with the combined use of vibration stimulation compared to regular exercise. However, the difference in effectiveness between the VB method and the visual feedback (FB) method is unknown. In this study, we examined the effects of VB and FB method, as well as the effects of a combination of the two methods. Our hypothesis was that both exercise with VB and with FB would increase the effect of exercise over only PFM contraction exercise, although no difference between the two exercises. In addition, the combination of the two would produce a higher exercise effect.

STUDY DESIGN, MATERIALS AND METHODS

This study was laboratory based cross sectional study. Ten healthy men participated in this study (Age; 23.7 ± 0.9 y.o., Height; 171.8 ± 5.9 cm, Body weight; 63.1 ± 7.1 kg, Body Mass Index; 21.4 ± 2.0 kg/ m2 [mean ± SD]). Each participant performed four conditions; only exercise (control), exercise with VB (VB), exercise with FB (FB), and exercise with VB and FB (combination). The measurement item was maximum voluntary contraction (MVC) of the PFM, which we measured using surface electromyography under the pre- and post-exercise. The participants performed 6 sets of 10-second contraction of the PFM as an exercise task. The exercises were performed in the sitting position on the original cushion with VB function and FB function using pressure sensor. The MVC was measured three times, and the average values were used for the analysis. Post-exercise PFM activities were normalized to pre-exercise status under each condition. Data analyses were performed using SPSS Statistics for Windows version 27.0 (IBM Japan Co. Ltd., Tokyo, Japan). The collected data was presented as median (min-max). The differences among the condition were analyzed using Kruskal-Wallis test and the Bonferroni post hoc test. In addition, the effect size (r) and power were calculated using G*power 3.1.9.7 software (Heinrich-Heine-University Düsseldorf, version 3.1.9.4, Düsseldorf, Germany). The significant level was set at 0.05. The study protocol complied with the principles laid down in the Declaration of Helsinki and was approved by our University Committee on Ethics in Research (approval number: E-2005).

RESULTS

The ratio of muscle activity (post-exercise / pre-exercise) between four exercise condition were summarized in Figure 1. The value was 0.96 (0.65-1.31) for control, 1.15 (1.00-2.24) for VB, 1.36 (0.75-2.37) for FB, and 1.32 (1.12-2.49) for combination. Statistically significant differences were shown in control and combination, and moderate to large effect sizes were observed for VB, FB and combination compared to the control condition.

INTERPRETATION OF RESULTS

This is the first study to show the difference between the effects of exercise using VB and FB. Moreover, we examined the effects of exercise when VB and FB were combined. The main finding of this study was that both VB and FB might increase the effect of exercise when used in addition to exercise, but there is no significant difference in effect between the two. Further, the use of a combination of these feedbacks could enhance the effect of exercise even more. In fact, all participants in this study showed an increase in muscle activity after exercise when it was exercise with combination condition.

The ability to transfer, or generalize, practiced motor tasks has long been known to be better in individuals who received FB during exercise than in those who did not. In addition, it is known that VB in combination with skeletal muscle contraction enhances the exercise effect through a mechanism named tonic vibration reflex, and we have reported in a previous study that local VB may increase the exercise effect when applied to PFM exercises. The results of this study also suggest that the effects of exercise were found to be supportive of these effects. For clinical application, however, it is necessary to consider that the participants in this study were healthy males.

CONCLUDING MESSAGE

The results of this study show that using VB and FB in regular PFM exercise enhances the effectiveness of the exercise. Although the use of these two types of feedback could be effective on the own, it is possible that a combination of VB and FB could be used to achieve a higher exercise effect.

FIGURE 1

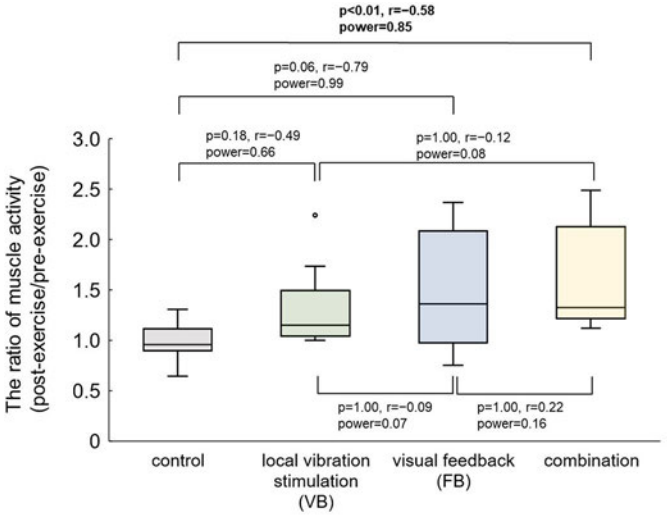

Figure 1. The ratio of muscle activity between four exercise conditions.
r=√ Standardized test statistic/sample number

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BEST IN CATEGORY PRIZE: ETHICS

THE ETHICS OF CONSENT: UNDERSTANDING THE RISKS OF VAGINAL PROLAPSE SURGERY

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HYPOTHESIS / AIMS OF STUDY

Ethical patient care and good medical practice aims to promote patient autonomy, shared decision making and informed consent. Informed consent begins with the giving of information often as a verbal discussion which may be supplemented by additional written information or signposting to the appropriate information source. The discussion should include the risks and benefits of an intervention and what alternatives are available. The process ends with the giving of consent assuming the patient has the capacity to understand the information, retain the information and weigh the information to communicate a decision. For surgical procedures, a signature on a consent form serves as evidence for consent.

Pelvic organ prolapse has a likely prevalence of 25-35% of women with a lifetime risk of surgical intervention at 11-19% [1-3]. The aim of this study was to assess a woman's understanding of surgical risks for vaginal prolapse surgery not utilising mesh.

STUDY DESIGN, MATERIALS AND METHODS

An electronic questionnaire was created using the Qualtrics platform. The questionnaire began with an introduction about vaginal prolapse and its treatment options including no treatment, pelvic floor muscle training, a vaginal pessary or vaginal surgery. This was followed by further information on vaginal prolapse surgery such as operation recovery, operation methods and the short and long term complications.

The information provided to women was taken from validated and peer reviewed publications by the Royal College of Obstetricians and Gynaecologists consent advice as well as the British Society of Urogynaecology patient advice leaflets. Website links to additional information was embedded in the questionnaire for women to review. After reviewing this information, women were asked if they would like to continue to complete an anonymous questionnaire. Ten questions were presented to focus on the woman's understanding of the risks of the surgery.

The questionnaire link was circulated to women aged over 18 years with no professional gynaecology knowledge by email or using instant messaging methods.

RESULTS

89 women had provided consent to complete the questionnaire after reading the surgery information. There were 65 completed questionnaires. Figure 1 shows the age distribution of women completing the questionnaire. The questionnaire took a mean of 8 minutes (range 2-33 minutes) to complete. There was a moderate positive correlation between time to complete the questionnaire and age ($r = 0.416$ $p < 0.001$, Pearson Corr Coeff).

After reading the information about surgical risks 95% (62/65) of the women felt they understood the surgical risks and 98% knew where to find additional information if required. Overall only 20% of women answered all ten questions correctly, 26% had one incorrect answer and 54 % had between 2-7 incorrect answers. There were no significant differences in the ability to answer individual questions as shown in figure 2 correctly between women who felt they understood the risks compared with the women who did not (Chi Squared $p > 0.05$). There was no significant difference in the mean number of correct questions answered between the women who understood the risks of surgery and those who did not ($p = 0.121$ Independent T-Test). There was no correlation between the age category of the responder or the time it took to complete the questionnaire with the number of questions correctly answered.

91% (59/65) of women understood that the surgery was associated with complications that could require further interventions such as further prolapse surgery or treatment of vaginal adhesions at a later date. Of these, 55% (32/59) of responders correctly acknowledged that this could be perceived as a common risk affecting at least 10% or 10 in every 100 women.

74% (48/65) of responders identified that unintended bowel injury could occur and require repair with 85% (41/48) recognising that this was a rare risk. Figure 2 shows the responses to questions that were answered with a yes or a no.

The last question was an open question for additional comments or questions they would wish to ask. This was answered by 41 women with six recurring themes. 12 responders had additional questions about the risks presented. 10 commented on the risks versus the benefits of the procedure, with a further 5 seeking to understand their own personalised risks better taking into account their baseline health. Questions about the recovery were common from 9 responders. Four women (all aged between 18 – 29) asked about the impact of prolapse surgery to fertility. Two commented that the information needed time to understand and processed.

INTERPRETATION OF RESULTS

Most responders reported that they understood the presented surgical risks of vaginal prolapse surgery. However when 'tested' only 19% (12/63) answered all the questions correctly suggesting an incomplete understanding. Conversely those who did not understand the risks answered the questions well, suggesting a lack of confidence in their understanding.

The three questions most commonly answered incorrectly concerned the risk of serious complication with bowel injury, the appearance of the genitalia post-operatively and understanding the realistic success of the operation. Furthermore different age groups may place increased value on different risk elements such as impact to fertility, cosmetic outcome and risk versus the actual benefit.

CONCLUDING MESSAGE

The disparity in our results raises ethical concerns about the understanding of the written presentation of surgical risks for vaginal prolapse surgery. Understanding of the information is likely to be multifactorial. However age of the woman or time taken to complete the questionnaire did not appear to impact our results.

It is the ethical duty of the clinician completing consent to ensure that the procedural information is understood. However how the clinician ensures this is a challenge. We need better methods to improve patient understanding of risks. This could include the way the information is presented as pictorial or as a flow chart, the wording used or the incorporation of techniques such as 'teach-back'.

FIGURE 1

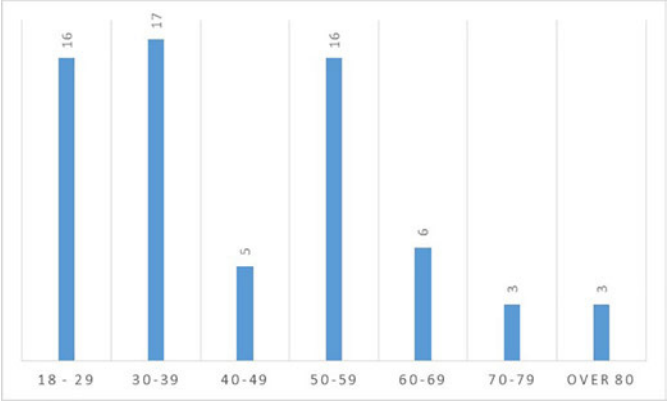

Figure 1: Age distribution of women answering the questionnaire with the numbers reported.

FIGURE 2

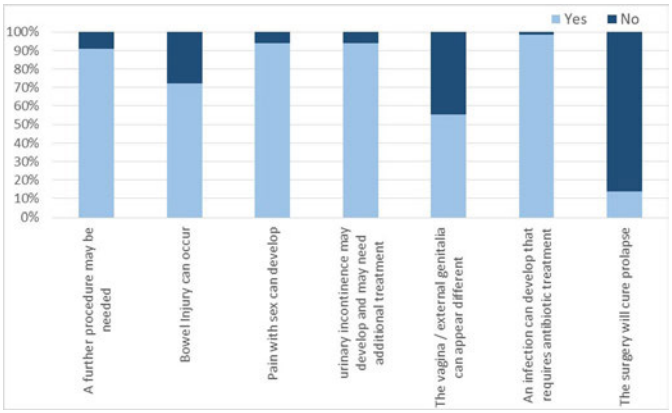

Figure 2: Results of all questions completed with a yes or a no response.

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SERVICE EVALUATION OF A PELVIC HEALTH PHYSIOTHERAPY SERVICE IN A SPINAL CORD INJURY CENTRE

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HYPOTHESIS / AIMS OF STUDY

Pelvic floor muscle training (PFMT) is recommended for people with lower urinary tract (LUT) dysfunction secondary to neurological conditions where they have the potential to voluntarily contract their pelvic floor (1). Yet, the implementation of services providing specialist pelvic health physiotherapy to individuals with neurological conditions is not yet mainstay. In 2017, a Pelvic Health Physiotherapy Clinic was established at a Spinal Cord Injury Centre in the UK. This is a unique clinic, established following the results of a 'proof of principle study' investigating PFMT in incomplete Spinal Cord Injured (SCI) subjects (2). The purpose of this service evaluation was to review the bladder and bowel outcomes of patients who have attended this clinic.

STUDY DESIGN, MATERIALS AND METHODS

This project was categorised as a service evaluation and did not require approval from a Research Ethics Committee. Patients with neurogenic bladder and/or bowel dysfunction, referred to the clinic, completed The International Consultation on Incontinence Questionnaire-Urinary Incontinence Short Form (ICIQ-UI) and Neurogenic Bowel Dysfunction (NBD) at their initial assessment (T0) and subsequent follow-up appointment/s (T1 = 38 +/- 32 weeks (n = 76) (mean +/- SD), T2 = 65 +/- 50 weeks (n = 23)).

Patients received a tailored home exercise programme at their initial assessment, with face to face and telephone follow-up consultations. Treatment included patient education, bladder, bowel, and pelvic floor muscle retraining, manual therapy, and biofeedback, with the aim of improving bladder, bowel, and sexual function.

The scores were expressed as mean +/- SD and compared using paired t-tests. A p-value of < 0.05 was considered statistically significant.

RESULTS

Seventy-six patients attended the clinic between 2017 and 2022, completing questionnaires at a minimum of two time points. A decrease in ICIQ-UI and NBD score indicates an improvement in symptoms. At initial assessment, mean ICIQ-UI score was 11.7 +/- 4.9, decreasing to 9.6 +/- 5.2 at T1 ($p = 0.0002$, 95% confidence interval (CI): 1.0, 3.3). Mean NBD score was 10.0 +/- 7.1, and 8.5 +/- 7.5 ($p = 0.019$, 95% CI: 0.1, 3.0), at initial assessment and T1, respectively.

Patients were categorised by diagnosis, Cauda Equina Syndrome (CES) (n = 52), and upper motor neuron (UMN) SCI (n = 24). Patients with CES improved ICIQ-UI and NBD scores, decreasing by 2.1 +/- 4.5 ($p = 0.002$, 95% CI: 0.8, 3.4) and 2.0 +/- 4.7 ($p = 0.002$, 95% CI: 0.7, 3.4), respectively. Patients with UMN SCI showed trends in improving ICIQ-UI, and NBD score however these were not statistically significant.

Twenty-three patients (CES n = 11, UMN n = 12) completed questionnaires at initial assessment, T1 and T2. Between each time point, there were trends in improving both ICIQ-UI and NBD score, other than ICIQ-UI score between T1 and T2 (mean increase 1.2 +/- 3.8).

INTERPRETATION OF RESULTS

Overall, there were significant improvements in ICIQ-UI and NBD scores after tailored pelvic health physiotherapy for patients with SCIs. Patients with CES demonstrated significant improvements in questionnaire scores, whereas those with UMN SCI did not. There was no additional improvement in questionnaire scores with later follow-up assessments.

CONCLUDING MESSAGE

These findings demonstrate that conservative pelvic health physiotherapy can improve bladder and bowel outcomes in the neurogenic population. Future work will explore the associated changes in patient-perceived improvement and sexual function, alongside bladder and bowel outcomes. Whilst more data is gathered capturing follow-up assessments, it will be interesting to explore the outcomes of both short and long-term pelvic physiotherapy in SCI patients.

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Funding None **Clinical Trial** No **Subjects** Human **Ethics not Req'd** This project was categorised as a service evaluation and did not require approval from a Research **Ethics Committee Helsinki** Yes **Informed Consent** No

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EFFECT OF AN AWARENESS PROGRAM IN IMPROVING ACCESS TO PHYSIOTHERAPY INTERVENTIONS FOR URINARY INCONTINENCE AMONG WOMEN

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HYPOTHESIS / AIMS OF STUDY
Urinary incontinence (UI) is a very debilitating condition, affecting quality of life of millions of women worldwide. International organisations and systematic reviews has recommended pelvic floor muscle training as an effective first-line of conservative management for UI.(1) Studies have revealed multiple possible reasons for women not accessing medical help.(2) Health promotion and awareness programs have helped in reducing the burden and improving access to health care services by improving awareness among women and health care professionals. This study was therefore undertaken with the aim to evaluate if an awareness program among health care professionals will improve the number of women accessing physiotherapy services for management of UI.

STUDY DESIGN, MATERIALS AND METHODS
Pre-post Experimental design was used to conduct the study in which a proposal was planned following ethical approval from the ethics committee of a medical college. A three month awareness program was delivered using a health systems approach. Since the study used health system research and included health care professionals as participants, a-priori sample size estimation was not done. Awareness program in the form of five interactive session was delivered to the faculty, postgraduate students and clinicians in the departments of Obstetrics and Gynaecology and Physiotherapy. The program targeted improving knowledge and awareness about the burden of the health condition and treatment guidelines.

In addition, potential of referral of women with UI for physiotherapy interventions was calculated for three months using hospital new registration data and qualitative analysis was done among key stakeholders as a follow up.

RESULTS
Total 51 participants received five sessions of awareness program. Post intervention the change in the number of women receiving management for UI was calculated from department register and billing codes. There was no difference seen in the trend of referrals and the number of women receiving physiotherapy services for UI pre and post awareness program.

Calculation for estimating potential of referral indicated that during the three-month period, a total of 26546, 5371 and 271 adult women (36 ± 21 years) visited out-patient departments of all departments, high potential departments and physiotherapy department respectively. If there existed a clinical care pathway to screen for UI among all adult women visiting the hospital; even at a conservative estimate of 25% prevalence and screening of 50% women, about 5309, 1074 and 54 women from all departments, high potential departments and physiotherapy department respectively could have been identified with incontinence and referred to physiotherapy department as compared to receiving one per month.

INTERPRETATION OF RESULTS
Awareness program did not improve awareness among key stakeholders as the number of women referred for physiotherapy interventions for UI remain unchanged. Analysis for the estimation of potential of referral and comparison indicated that there is a huge gap between the current referral pattern (one referral / month) and the potential for referrals.

CONCLUDING MESSAGE
There is a huge potential of referrals to physiotherapy services for urinary incontinence among women. Awareness program did not bring the desired result among key stakeholders due to existence of multiple barriers which needs integrated health approach which targets stakeholder and women for reducing burden of a disease and uplifting health care delivery system.

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Funding None **Clinical Trial** No **Subjects** Human **Ethics Committee** M.S Ramaiah Medical College and Hospital Ethics committee **Helsinki** not Req'd this study was not a experiment on patients as it was a awareness program among health professionals

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THE EFFECT OF OVERWEIGHT ON THE PATIENT GLOBAL IMPRESSION OF IMPROVEMENT IN WOMEN WITH STRESS URINARY INCONTINENCE TREATED WITH DULOXETINE AND PELVIC FLOOR MUSCLE TRAINING

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HYPOTHESIS / AIMS OF STUDY
The overweight has a negative impact on pelvic floor muscles. To prevent lower urinary tract dysfunctions, in overweight women, it is important to reduce overweight through regular physical exercise. There are currently few studies on the effects of pelvic floor muscle training and duloxetine in persistently overweight women. The aim of this study was to measure the effect of overweight on the Patient Global Impression of Improvement (PGI-I) in women with stress urinary incontinence (SUI) treated with duloxetine and pelvic floor muscle training.

STUDY DESIGN, MATERIALS AND METHODS
This analysis is a part of the clinical trial realized between February 2019 and 2020. It was a randomized intervention, parallel, multicentre study at urological outpatient clinics for 12 weeks. Women were assigned in a 1:1 ratio to the experimental and control groups, an estimated 63 women were required for each group. The control group received oral duloxetine treatment (40 mg BID), the experimental group received oral duloxetine treatment (40 mg BID) and pelvic floor muscle training with lumbopelvic stabilization (iPFMT). The iPFMT was performed 5 times a week for 20–30 minutes a day, in cooperation with a physiotherapist. Inclusion criteria: woman over 18 years old who provided written informed consent; experienced uncomplicated SUI; experienced symptoms of urinary incontinence for at least three consecutive months immediately prior to the study; scored 14 points or more on ICIQ-UI SF; experienced at least seven urinary incontinence episodes per week (IEF); exhibited a degree of pelvic organ prolapse equal to stage 2 or less; expressed willingness to accept the randomization process and fully participate in tests. Exclusion criteria: a woman who is pregnant, lactating or actively trying to become pregnant; use of any pharmacologic agent to treat symptoms of urinary incontinence in the past 6 months; the history of anti-incontinence surgery in the past 12 months; use of onabotulinumtoxinA for the treatment of urinary incontinence in the past 12 months; the history of pelvic prolapse repair or urethral surgery in the past 12 months; the history of PFMT in the past 12 months; the history of interstitial cystitis or bladder-related pain; the history of chronic severe constipation; the history of clinically significant renal or hepatic impairment; the history of clinically significant heart impairment; non-compliance with limitation of duloxetine treatment for mixed urinary incontinence; current positive urinary tract infection; use of rehabilitation aids; use of antidepressant(s); insufficient understanding of iPFMT and/or omitting iPFMT; participation in any clinical study in the past 6 months. The SUI was analysed during a baseline and a final period according to the International Consultation on Incontinence Questionnaire - Urinary Incontinence - Short Form (ICIQ-UI SF) with the range from 0 (without SUI) to 21 (the most severe SUI). Overweight was assessed by body mass index (BMI) as the ratio of weight to square height of the woman, it was defined as having BMI between 25 and 29.9 kg/m2. The Patient Global Impression of Improvement (PGI-I) score evaluated the status of urinary incontinence at the end of the study compared to the condition before each patient started treatment in the study. It is a seven-point scale instrument of patient reported outcome measures (1 – very much better, 2 – much better, 3 – a little better, 4 – no change, 5 – a little worse, 6 – much worse, 7 – very much worse). The data were presented as mean values and standard deviations (SD), p values were obtained using a t test with ANOVA. The significance level was set at $p < 0.05$.

RESULTS
The number of women who completed clinical study was 129 out of 158 (81.6%). By sub-analysis, women were divided into four groups according to a calculated mean BMI of 27 kg/m2 and a current treatment. The first group was treated with duloxetine and had a BMI below 27 (n = 34), the second group was treated with duloxetine and had a BMI above 27 (n = 35), the third group was treated with duloxetine and iPFMT and had a BMI below 27 (n = 30), the fourth group was treated with duloxetine and iPFMT and had a BMI above 27 (n = 30). There were no significant differences between all groups (ascending order of groups) before the intervention in the ICIQ-UI SF total score of 14.9 (SD 1.1) vs. 15.1 (SD 1.7) vs. 15.5 (SD 2.1) vs. 14.9 (SD 1.1); (ANOVA, p = 0.468) but statistically significant changes following treatment with score of 8.9 (SD 3.5) vs. 8.8 (SD 4.1) vs. 10.6 (SD 4.7) vs. 7.8 (SD 3.4); (p = 0.046). The incontinence episode frequency per week (IEF) were not significantly different before treatment, mean IEF of 23.4 (SD 16.9) vs. 22.0 (SD 13.7) vs. 23.1 (SD 11.2) vs. 21.7 (SD 13.7); (p = 0.277). Relative percentual IEF changes were significant in all groups but most significant in the second and the fourth groups following the current treatment, mean change of -40.5 (SD 41.3) vs. -59.5 (SD 30.3) vs. -38.4 (SD 33.2) vs. -49.9 (SD 36.8); (p = 0.014). Overweight women achieved the best subjective improvement in the PGI-I score, but all groups achieved a statistically significant improvement after the current treatment (mean PGI-I of 3.3 [95% CI: 2.8-3.8] vs. 1.8 [95% CI: 1.6-2.1] vs. 3.3 [95% CI: 2.8-3.8] vs. 1.9 [95% CI: 1.6-2.2]). When comparing the percentage of any improvement in PGI-I compared to the current group of patients, overweight patients had the best subjective improvement (62% vs. 97 % vs. 70 % vs. 93 %).

INTERPRETATION OF RESULTS
The Patient Global Impression of Improvement (PGI-I) score revealed very interesting results because overweight women with a BMI over 27 had better subjective improvement than women with a lower BMI with no difference in current treatment. This group of overweight women achieved the best PGI-I score, as 97% of women with duloxetine and 93% of women with combination treatment subjectively improved.

CONCLUDING MESSAGE
Being overweight with a higher BMI increases the likelihood of a significant subjective improvement in women with stress urinary incontinence treated with duloxetine or duloxetine combination therapy with iPFMT.

Funding None **Clinical Trial** Yes **Registration Number** ClinicalTrials.gov as NCT04140253 **RCT** Yes **Subjects** Human **Ethics Committee** The **Ethics Committee** at University Hospital, Martin, Slovak Republic **Helsinki** Yes **Informed Consent** Yes

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ASSOCIATION BETWEEN COMORBIDITY BURDEN AND DETRUSOR OVERACTIVITY WITH DETRUSOR UNDERACTIVITY IN NEUROLOGIC OLDER WOMEN

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HYPOTHESIS / AIMS OF STUDY

Lower urinary tract symptoms (LUTS) significantly impact older adults and are associated with a substantial deterioration in health-related quality of life in this population. The relationship between LUTS and aging is thought to be due, in large part, to aging of the bladder, as a number of changes in bladder function and structure are known to be very common with advanced age. Two urodynamic abnormalities which may commonly underlie a patient's LUTS, detrusor overactivity (DO) and detrusor underactivity (DU), are both increasingly prevalent with older age. In a subset of patients, DO may coexist in combination with DU (DO-DU). Detrusor overactivity (DO) with detrusor underactivity (DU) (DO-DU) was described as typical of aging (1). Combined DO-DU was first described in older women. This report indicate that non-neurological diseases could cause DO-DU, but other studies show that DO-DU occurred in various neurological diseases (2). The theory of a pathophysiologic progression from DO to DU is supported by growing evidence of common etiological factors between DO-DU, DO, and DU. Nevertheless, the etiology of DO-DU remains poorly understood, and likely involves multiple complex factors.

Older age is separately related to both DO-DU and comorbidity burden, while neurological diseases are related to both DO-DU and comorbidity burden. It remains unclear whether comorbidity burden is associated with this unique form of lower urinary tract dysfunction in patients with neurological diseases. We aimed to explore potential associations between DO-DU and comorbidity burden in neurologic older women.

STUDY DESIGN, MATERIALS AND METHODS

The present study is a single center cross-sectional analysis of consecutive female patients who underwent urodynamic evaluation from 2016 to 2019 in a university hospital-based rehabilitative medicine department specializing in geriatrics.

The participants were community dwelling women who presented for a geriatric assessment and warranted urodynamic evaluation benefited from a same-day urodynamic study, performed by a physiatrist with expertise in functional urology and geriatrics. Inclusion criteria were female gender, age $\geq$65 years, and presence of neurological pathology. Exclusion criteria were an inability to urinate or a bladder voiding efficiency $<$5% (defined as the ratio between voided volume and total bladder capacity) or a bladder outlet obstruction on urodynamic assessment.

Participants were categorized as having DO, DU, combined DO-DU, or a negative study. The clinical assessment consisted of a comprehensive medical history and physical examination, as well as and an assessment of mood, cognition, functional performance, nutrition status, mobility, and urinary symptoms. Demographic and medical data including co-morbidities, as measured by the Cumulative Illness Rating Scale (CIRS), were collected. The CIRS-G has been robustly validated and is known to be predictive of hospitalization and mortality among geriatric patients in multiple settings. The association between DO-DU and comorbidity burden, was assessed in univariate analysis.

RESULTS

A total of 185 women aged $\geq$65 years underwent urodynamic evaluation during the study period, of whom 103 were excluded due to the absence of neurological disease. Correspondingly, sixty-one women met the criteria for inclusion in the analysis (Figure 1). Median participant age was 72 (69-77) years, 57 patients (93%) had a central nervous system disease, and the median CIRS-G score was 7(5-9) (Table 1). The most common neurological pathology was stroke (31%). Among included subjects, the most frequent complaint that led to the urodynamic assessment was urgency urinary incontinence (34%). The most common urodynamic diagnosis was DO (36%), followed by DU (26%), negative urodynamic study (21%), and DO-DU (16%). On univariate analysis, there was no significant association between urodynamic diagnosis, age or comorbidity burden measured by the CIRS-G. Voiding symptoms assessed by urinary symptom profile score were significantly more severe in patients with DU.

INTERPRETATION OF RESULTS

The data do not show any significant differences between this urodynamic diagnosis and comorbidity burden or age. We cannot conclude on the existence of an association between comorbidity burden and DO-DU in our specific population.

The outcome of the study may be explained by a low statistical power, which may be related to a small sample size. The number of patients excluded, for no voiding or uninterpretable voiding, was significant. The main explanation for these exclusions is that the conditions of the urodynamic study were not those of normal voiding. Another explanation could be related to the pathophysiology of DO-DU which could be explain by the impairment of several neurological functions. Indeed, DO-DU could be related to multiple factors rather than a single factor. In the CIRS-G, neurological pathology is a maximum 4-point item. The CIRS may not be the ideal tool to use in these patients with neurological pathologies and perhaps another tool reflecting the patient's disability, such as the frailty index, might be more interesting to use. In addition, data were obtained from a specialized, geriatric-focused practice, such that the observed associations may differ in a primary care or inpatient hospital setting, as well as among younger patient populations. Thus, the comorbidity burden would also be less important in our study population than in another geriatric population. Afterwards, patients referred to our department are often followed by physicians, implying a probable better management of their comorbidities and thus a lower CIRS. One possible explanation is that there is no association between DO-DU and age or comorbidity burden, and the neurological pathology would explain all alone the LUT dysfunction. However, in studies on Parkinson's disease, there is an association between duration of the disease and urodynamic diagnosis, which suggests that age plays a role in the association between DO-DU and neurological diseases (3).

CONCLUDING MESSAGE

We cannot conclude that increased cumulative medical comorbidity burden is predictive of combined DO-DU in the older neurological population. Although DO-DU is more common in older and neurological populations, associations between DO-DU and age or comorbidity burden were not found. Several hypotheses can explain this negative result notably a low statistical power due to the small sample size of the population. The pathogenesis of DO-DU is likely more complex than chronological aging alone and merits further study. This study is part of a desire for a better understanding of DO-DU to improve its treatment.

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Funding No funding source to report **Clinical Trial** Yes **Public Registry** No **RCT** No **Subjects** Human **Ethics not Req'd** Data for the present analysis were ascertained in accordance with the French legislation for retrospective studies (agreement number 2219031-V0) following the principles outlined in the Declaration of **Helsinki Helsinki** Yes **Informed Consent** Yes

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EFFECTS OF REMOTE AND SYNCHRONOUS WOMEN´S GYMNASTIC METHOD APPLIED IN GROUPS AND INDIVIDUALLY ON URINARY SYMPTOMS AND QUALITY OF LIFE OF OLDER WOMEN: A PILOT, CONTROLLED AND RANDOMIZED STUDY.

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HYPOTHESIS / AIMS OF STUDY

The hypothesis is that after practicing Women's gymnastics, a method of body exercises that works on posture, breathing, and body awareness along with training pelvic floor muscles, women will show an improvement in their knowledge of the pelvic region and the action of the pelvic floor muscles, what would decrease urine loss during physical activities, besides improving their quality of life, compared to those in control group. The aim of study is to verify the best approach applied remotely and synchronously to promote quality of life and improvement of urinary incontinence in women over 60 years of age: Women's gymnastics performed in groups or women's gymnastics performed individually, compared to a control group.

STUDY DESIGN, MATERIALS AND METHODS

A pilot, experimental, randomized and controlled study. Sample calculation was performed with the GPower program, finding a number of 21 women per group. The volunteers who agreed to participate, signed the consent form and answered a sociodemographic data questionnaire, the ICIQ-sf and Kings Health Questionnaire (KHQ). They were randomized into three groups: Group women's gymnastics (GG), individual women's gymnastics (IG) and control group (CG). They participated in five remote meetings, lasting one hour, once a week, for five weeks. In each meeting they perform exercises of the Women's Gymnastics, a exercise method that focus on pelvic floor muscle exercises and their integration with breathing, posture and whole body movements. After five weeks, women answered the ICIQ-sf and KHQ questionnaires, in order to compare with the first evaluation.

RESULTS

A total of 52 women agreed to participate in the research and were randomized into the three groups. At the end of the five weeks of training, 32 women finished the study and answered the questionnaires (n = 11 in GG; n = 12 in IG and n = 9 in CG). In terms of treatment adhering, there was a loss of 36.46% of the total sample at the end of five weeks and the analysis of the results was made only with those who finished the research. Mean age was 66 years, mean BMI 26.9 kg/m^2 (overweight) and 91% of the sample have already gested. Women from individual Women's Gymnastics group showed a decrease in the mean of ICIQ-sf score from 6 at baseline to 4.25 after five weeks, the best result. There was no significant difference in the domains of the KHQ that addressed quality of life and UI.

INTERPRETATION OF RESULTS

A synchronous remote exercise program, focusing on body awareness and pelvic floor muscle training was able to promote health for women over 60 years of age, with its benefits demonstrated by decreasing the means of the ICIQ-sf score.

CONCLUDING MESSAGE

The remote modality showed difficulty in participants adherence and the individual modality promoted better results

FIGURE 1

Table 1 – Baseline Characteristics of the Study Population.

		Total sample (n=32)	Control Group (n=9)	Individual women's gymnastics (n=12)	Group women's gymnastics (n=11)
Mean Age (y)		66	68	67	65
BMI, mean as kg/m2		26.9	27.7	26.7	26.4
Parity	None	3 (9.4%)	0 (0%)	2 (17%)	1 (9.1%)
	1	5 (16%)	1 (11%)	1 (8.3%)	3 (27%)
	2	9 (28%)	1 (11%)	3 (25%)	5 (45%)
	3 or more	15 (47%)	7 (78%)	6 (50%)	2 (18%)
Type of Delivery	Vaginal delivery	6 (21%)	3 (33%)	0 (0%)	3 (30%)
	Cesarean section	16 (55%)	3 (33%)	6 (60%)	7 (70%)
	Both delivery routes	7 (24%)	3 (33%)	4 (40%)	0 (0%)
Episiotomy	No	29 (91%)	8 (89%)	11 (92%)	10 (91%)
	Yes	3 (9.4%)	1 (11%)	1 (8.3%)	1 (9.1%)
Hormone replacement therapy	No	30 (94%)	9 (100%)	11 (92%)	11 (92%)
	Yes	2 (6.2%)	0 (0%)	1 (8.3%)	1 (9.1%)

BMI = body mass index

Table 1 – Baseline Characteristics of the Study Population.

FIGURE 2

Table 2 - Primary outcomes of the intervention at baseline and after 5 weeks

	Group women's gymnastics (n=11)		Individual women's gymnastics (n=12)		Control group (n=9)	
ICIQ-sf	Baseline (mean; SD)	Post-intervention	Baseline	Post-intervention	Baseline	Post Intervention
Frequency or urinary incontinence	1.45 ± 1.51	1.27 ± 1.19	1.17 ± 1.47	0.92 ± 1.44	1.22 ± 1.86	1.22 ± 1.72
Amount of leakage	1.45 ± 1.29	1.64 ± 1.50	2.17 ± 2.48	1.33 ± 1.48	0.89 ± 1.45	1.11 ± 1.76
Overall impact of urinary incontinence	2.36 ± 3.23	2.55 ± 3.08	2.67 ± 3.94	2 ± 3.38	1.78 ± 2.39	1.11 ± 1.96
Score	5.26 ± 4.88	5.45 ± 4.78	6 ± 7.56	4.25 ± 5.43	3.89 ± 5.18	3.44 ± 5.1
KHQ						
General health perception	0.182 ± 0.162	0.227 ± 0.07	0.125 ± 0.131	0.208 ± 0.209	0.278 ± 0.195	0.222 ± 0.5
Impact of UI	0.12 ± 0.222	0.18 ± 0.229	0.083 ± 0.149	0.139 ± 0.223	0.221 ± 0.372	0.111 ± 0.167
Role limitation/ daily activities	0.06 ± 0.133	0.106 ± 0.171	0.055 ± 0.108	0.069 ± 0.241	0.222 ± 0.363	0.111 ± 0.167
Physical limitation	0.075 ± 0.135	0.106 ± 0.171	0.041 ± 0.103	0.042 ±0.104	0.092 ± 0222	0.093 ± 0.147
Social limitation	0.02 ± 0. 067	0.01 ± 0.03	0.028 ± 0.096	0.019 ±0.064	0.099±0.2 96	0.02 ± 0.074
Personal relationship	0.091 ± 0.302	0 ±0	0 ±0	0.028 ± 0.096	0.111 ± 0.33	0.74 ± 0.147
Emotions	0.04 ± 0.09	0.404 ± 0.09	0.074 ± 0.119	0.407 ± 0.159	0.148 ± 0.278	0.333± 0
Sleep and energy	0.167 ± 0.149	0.227 ± 0.187	0.139 ± 0.096	0.236 ± 0.241	0.315 ± 0.327	0.241 ± 0.252
Severity measure	0.242 ± 0.205	0.121 ± 0.178	0.217 ± 0.176	0.161 ± 0.194	0.2 ± 0.273	0.111 ± 0.111

*p value <0.005

Table 2 - Primary outcomes of the intervention at baseline and after 5 weeks

Funding None **Clinical Trial** Yes **Public Registry** No **RCT** Yes **Subjects** Human **Ethics Committee** Plataforma Brasil **Helsinki** Yes **Informed Consent** Yes

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EFFECTS OF A GROUP PELVIC FLOOR MUSCLE TRAINING (PFMT) METHOD IN ELDERLY WOMEN OF DIFFERENT SOCIOECONOMIC LEVELS

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HYPOTHESIS / AIMS OF STUDY

To evaluate the effects of a pelvic floor muscles training program on urinary symptoms, sexuality and body awareness in groups of elderly women of different socioeconomic levels.

STUDY DESIGN, MATERIALS AND METHODS

This is a time series study. 57 elderly women were evaluated and divided into two groups: high (A) and low (B) socioeconomic level, according to the human development index of the region where they lived. They participated in a five weekly pelvic floor muscles training group program and answered structured questionnaires before and after each meetings. Participants conversation in each meeting were recorded and transcribed in order to carry out a qualitative evaluation, through discursive analysis. All meetings had specific pelvic floor exercises and each week difficulties were added, including breathing, postural and stability exercises. For statistical evaluation, a descriptive analysis of data was performed with a significance level of 5% ($p < 0.05$). Variables were compared between the two groups (A and B).

RESULTS

The average age of the women was 65.25 years old. 50.87% of them referred urinary incontinence (UI) and 33.33% intestinal constipation. Regarding body mass index, obese women are more likely to have UI when compared to eutrophic women, respectively $p = 0.045$ and $p = 0.041$. Group B had a higher percentage of non-white women (30.4% versus 5.9%; $p = 0.023$), with more pain (82.6%; versus 52.9%; $p = 0.021$), urinary incontinence (30.4%; versus 2.9%; $p = 0.005$), and lack of libido than those in group A (75% versus 46.9%; $p = 0.046$). In relation of the pelvic floor (PF) knowledge before intervention, 70,6% of group B and 32.4% of group A ($p = 0.012$), reported no knowledge about what PF meant and its localization in their bodies. Some evaluated variables showed positive results for both groups after intervention: 61.8% of group A and 81.5% of group B were able to better perceive and control their breathing; 94.1% of the women in group A and 100% in group B reported improved posture; 100% of both groups reported that they learned the correct localization and function of PF in the body and in incontinent women, 32.4% of group A and 64.7% of group B believed that their symptoms improved. The discursive analysis showed that pelvic floor and sexuality were the themes more often discussed in the group meetings.

INTERPRETATION OF RESULTS

Both groups, regardless of socioeconomic level, reported improvement in urinary leakage and body awareness. Discursive analysis of conversations held during the meetings also showed improvement in their knowledge about pelvic floor and an awakening of sexuality.

CONCLUDING MESSAGE

Group meetings with pelvic floor muscles training and body education, constitute an efficient strategy for health promotion for women in process of aging, encouraging them to think about their sexuality, prevent and even treat urinary incontinence. This can also be considered as a practice that promotes positive aging. The group promotes socialization, exchange of experiences and increases the knowledge of those who participate, important factors for improving self-esteem and search for new life purposes.

FIGURE 1

Meeting/week	Content
1	• Explanation about the research and signature of consent form • Introductory conversation and questionnaires answers • Introduction to the method with theoretical explanations about anatomy and pathophysiology of pelvic floor muscles, urinary incontinence and aging • Basic posture and breathing exercises
2	• Body/postural awareness exercises (like meeting 1) • Breathing exercises and global body mobilization • Initial pelvic floor exercises • Relaxation
3	• Body awareness/posture, breathing and mobilization (like meeting 2) • Pelvic floor progression exercises • Stabilization, resistance and strength exercises (bridge) • Relaxation
4	• All exercises from meeting 3 • Pelvic and spine mobility exercises associated with pelvic floor exercises • Conversation about sexuality • Relaxation
5	• All exercises from week 4 • Functional training (how to apply the method exercises in activities of daily living?) • Relaxation • Final conversation and questionnaires answers

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Funding Research support from the Pontifical Catholic University of São Paulo **Clinical Trial** No **Subjects** Human **Ethics Committee** Comité de Ética da Pontifícia Universidade Católica de São Paulo **Helsinki** Yes **Informed Consent** Yes

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SYMPTOMS OF URINARY INCONTINENCE PREDICT DEPRESSION WITH MACHINE LEARNING

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HYPOTHESIS / AIMS OF STUDY

Using data from the publicly available National Health and Nutrition Examination Survey (NHANES) dataset, the aim of the study was to develop a machine learning model to predict Patient Health Questionnaire (PHQ-9) scores, a clinical tool to screen depression, using urinary incontinence (UI) features. We hypothesized that PHQ-9 score can be predicted using the demographic and subjective UI features, especially those reflecting the impact on social dynamics and daily activities. This is the first study to leverage advanced machine learning algorithms to identify an important condition associated with UI.

STUDY DESIGN, MATERIALS AND METHODS

The dataset was procured from nationally representative NHANES responses between 2008 to 2018. Inclusion criteria were any individual older than 20 years with demonstrated incontinence and complete responses to the urology questionnaire (KIQ) and depression screener (DLQ). The feature included both UI and non-UI features. Non-UI features included demographics (DEMO), medical conditions including hypertension and diabetes (MCQ, BPQ, and DIQ), healthcare utilization and access cases (HUQ), disability questionnaire (DIQ), and smoking status (SMQ). Numerical responses to the depression screener (DPQ) were summed to determine the overall PHQ-9 score. A total of 47 UI and non-UI features were included in the machine learning model. Selected urology variables were logically recoded, and an incontinence severity index (ISI) was calculated. Two feature sets were evaluated with the machine learning model: UI and non-UI features versus UI-only features.

We utilized a boosted decision tree-based architecture known as a Light Gradient Boosting Machine (LightGBM). The algorithm was chosen due to its high interpretability and efficiency. Categorical and ordinal (likert-scale) variables were one-hot encoded and continuous variables were transformed using the Yeo-Johnson method. Similarly, PHQ-9 scores were transformed with a Box-Cox method. After omitting the outcome variable, K-Nearest Neighbor imputation was utilized for partially missing data pertaining to 10 non-UI features representing 8% of the total data. This was done to maximize the available data for UI and PHQ-9 scores and enhance model performance and generalizability. For the UI-only model, no imputation was necessary. Feature reduction was conducted using collinearity with a threshold of $R2 > 0.9$. For hyperparameter optimization and model performance evaluation, nested k-fold cross-validation was utilized with ten inner and five outer folds in tandem with a randomized grid search. Scoring was evaluated with mean absolute error (MAE). MAE denotes the mean difference between the predicted continuous PHQ-9 score and the known value from the dataset. Individual feature impacts were interpreted using the Shapley Explanations Framework which determines the numerical effect of each feature on the model PHQ-9 prediction. Python (Version 3.8.1, with packages LightGBM, Scikit-learn, and NumPy) was used for model fitting, prediction, and evaluation.

RESULTS

From a study cohort of 5,717 patients with incontinence, 74% were female and the mean age (std) was 56.0 (16.5) years. The mean (std) PHQ-9 score of the cohort was 10.7 (6.6). Bothersome and effect on daily activities reflected the subjective aspects of UI while nocturia frequency and ISI are objective characteristics. Four variables were most impactful among the ten most influential features to predict PHQ-9 score: bothersome (KIQ052), effect on daily activities (KIQ050), nocturia (KIQ480), and ISI (Figure 1). Higher severity in each aspect of UI produced an increased PHQ-9 score (Figure 2). However, there tended to be a severity threshold in which the effect on PHQ-9 changed from positive to negative.

The model containing UI-only features resulted in an MAE (std) of 3.71 (0.11) for outer loop performance on the held-out test set. When UI features were incorporated with variables known to be associated with depression, the resulting MAE (std) decreased to 3.24 (0.09). Other features including decreased age, diagnosis of diabetes, and lower-income were most influential in predicting a higher PHQ-9 score. Furthermore, the same aspects of UI shown such as bothersome, effect on daily activities, nocturia, and ISI demonstrated a similar high impact in prediction in the UI-only model. Interestingly, the effect on daily activities and nocturia were among the ten most influential features and even exceeded overall health, marriage, and smoking status. The effect of UI on daily activities produced an impact in the top five of all demographic and UI features.

INTERPRETATION OF RESULTS

PHQ-9 scores are most predicted by subjective UI features than objective features. This supports the hypothesis that the individual experience of UI tends to have a more significant impact on depressive symptoms in comparison to frequency or volume-based characteristics. Subjective UI features, as well as nocturia and ISI, appear to be better predictors than other non-UI features known to be associated with depression in patients with UI.

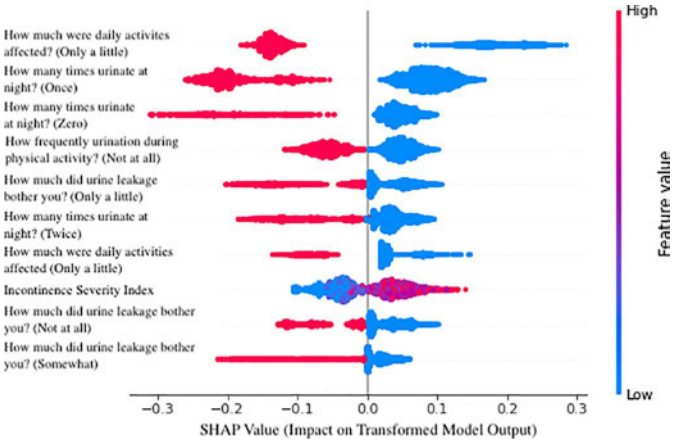
Depression amongst UI patients is correlated to worse quality of living and other medical comorbidities. The findings demonstrate that we may be able to predict and provide early intervention to those at-risk for depressive symptoms in primary care and/or urologic clinical care settings. Additionally, high-performing machine learning models provide highly accurate predictions that allow us to potentially prioritize patient care and value in UI cohort.

There remain limitations to this study. NHANES involves cross-sectional responses, hence, no conclusions can be drawn regarding causation. Additionally, PHQ-9 scores when classified according to no depression, mild, moderate, and severe depression are inherently imbalanced. For patients with lower PHQ-9 scores, the model may perform better than those with higher scores. In the future, class imbalance may be addressed with random oversampling to better predict the PHQ-9 scores in patients with moderate-severe to severe depression.

CONCLUDING MESSAGE

Machine learning models incorporating UI features can accurately predict PHQ-9 scores, a marker of depression and worse quality of life. Subjective UI features may be most influential in the relationship with depression severity, hence, social dynamics, patient well-being, and coping strategies should be emphasized during UI diagnosis and treatment.

FIGURE 1



Shapley Explanations Framework model impact summary for UI-only variables

FIGURE 2

Rank	Feature	Definition	Response Level	Direction of Effect on PHQ-9 Score
1	KIQ052	During the past 12 months, how much did your leakage of urine affect your day-to-day activities?	Only a little	↓
2	KIQ480	During the past 30 days, how many times per night did you most typically get up to urinate, from the time you went to bed at night until the time you got up in the morning. Would you say …	One time	↓
3	KIQ480	During the past 30 days, how many times per night did you most typically get up to urinate, from the time you went to bed at night until the time you got up in the morning. Would you say …	Zero times	↓
4	KIQ430	How frequently does [leaking urine during physical activities] occur? Would you say this occurs . . .	Not at all	↓
5	KIQ050	During the past 12 months, how much did your leakage of urine bother you? Please select one of the following choices:	Only a little	↓
6	KIQ480	During the past 30 days, how many times per night did you most typically get up to urinate, from the time you went to bed at night until the time you got up in the morning. Would you say …	Two times	↓
7	KIQ052	During the past 12 months, how much did your leakage of urine affect your day-to-day activities?	Only a little	↓
8	ISI	Incontinence Severity Index (non-NHANES variable) ISI = KIQ005 x KIQ010	Continuous	↑
9	KIQ050	During the past 12 months, how much did your leakage of urine bother you? Please select one of the following choices:	Not at all	↓
10	KIQ050	During the past 12 months, how much did your leakage of urine bother you? Please select one of the following choices:	Somewhat	↑

Ten most influential features for UI-only variables

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SESSION 36 - ROBOTIC BLADDER NECK, ARTIFICIAL URINARY SPHINCTER, RECONSTRUCTIVE, PEDIATRIC AND TAPES

Abstracts 592-601
15:05 - 16:35, Hall G
Chair: Mr Rizwan Hamid (United Kingdom)

592 | www.ics.org/2022/abstract/592

ROBOT-ASSISTED TRANS-VESICAL ANTERIOR INLAY OF BUCCAL MUCOSAL GRAFT FOR RECURRENT BLADDER NECK CONTRACTURE

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INTRODUCTION
There is no clear consensus regarding the management of recurrent bladder neck contracture (BNC) after endoscopic treatment. The purpose of this video was to describe a robotic transvesical buccal mucosal graft urethroplasty technique for recurrent BNC after a first robotic YV plasty.

DESIGN
The technique is described in the video. This is a 73-year-old man who had benign prostatic hypertrophy treated with monopolar transurethral resection of the prostate (TURP) in 2007 and then had 3 endoscopic treatments (monopolar RTUP, monopolar transurethral incision of BNC, and holmium laser urethrotomy) combined with self-dilations in 2019. He had a robotic YV plasty in March 2020 for a BNC recurrence. He had an urinary tract infection in the post-operative course and had worsening of symptoms 9 months after surgery with mixed symptoms and recurrence of post-void residual at 180cc. The fibroscopy showed a anterior recurrence.

RESULTS
The operation was performed under general anesthesia in 23° Trendelenburg position. The Xi robot is docked and 5 ports are placed. A transperitoneal approach is used and the bladder is wide opened longitudinally. The edges are fixed to the abdominal wall. The contracture is incised anteriorly and the fibrosis is removed. A buccal mucosa graft is then fixed in a running fashion. The graft is fixed with fast-absorbing suture. The bladder is closed and a methylene blue test is performed. The patient was discharged at post-operative day 1. The urethral catheter was removed at day 14. There were no postoperative complications. At 12 months, there was no recurrence of stricture and the patient had 25cc PVR.

CONCLUSION
Robotic trans-vesical buccal mucosa graft for recurrent cervical sclerosis is a feasible technique that seems provide satisfactory results as a revision procedure in patients with recurrent contracture after endoscopic treatment and YV plasty. Long-term follow-up will be necessary to evaluate functional results.

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YV PLASTY FOR VESICO-URETHRAL ANASTOMOSIS STENOSIS BY COMBINED ROBOTIC AND PERINEAL APPROACH AND CONCOMITANT ARTIFICIAL URINARY SPHINCTER IMPLANTATION

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INTRODUCTION

There is no clear consensus regarding the management of recurrent post-prostatectomy vesicourethral anastomosis stenosis (VUAS) after failure of endoscopic treatments. Robotic YV plasty has been reported in that setting but in case of long stricture extending to the bulbar urethra, a purely robotic abdominal approach does not allow to treat the whole stricture. The purpose of this video was to describe a technique of YV urethroplasty by combined robotic and perineal approach for VUAS with concomitant artificial urinary sphincter (AUS) implantation.

DESIGN

We present the case of a 76-year-old man who had prostate cancer treated with radiation therapy in 2008 and then salvage prostatectomy in 2014. He then developed vesico-urethral anastomosis stenosis treated with endoscopic dilation and then intermittent self-dilatations. He had major stress urinary incontinence treated with a penis clamp with significant leakage (3-4 pads per day) upon clamp removal. He had no post-void residual. The urodynamic assessment showed an uninhibited detrusor contractions at 190mL and the cystoscopy confirmed the anastomotic stenosis.

RESULTS

The procedure is performed under general anesthesia in Trendelenburg position. We use the Xi robot with 5 ports and a transperitoneal approach. The Retzius space is opened and dissected down to the bladder neck. A bulbo-membranous dissection by perineal approach is performed by the second operator. The dissections from the perineal and robotic abdominal approach meet below the pubic bone to free anterior part of the anastomosis. The stenosis is opened longitudinally. A bladder V-flap is moved down on the urethral opening using a barbed suture with the needle being passed below the pubic bone from the robotic to the perineal surgeon who performs the distal sutures of the anastomosis. The upper sutures of the anastomosis on each side of the bladder V-flap are then performed by the robotic surgeon. As the bulbar urethra has been dissected extensively, the AUS is implanted concomitantly. The patient was dicharged on day 3. The bladder catheter was removed on day 7 and of suprapubic tube at week 3. There were no postoperative complications. At 9 months there is no recurrence of stenosis and the patient is completely dry.

CONCLUSION

Combined robotic and perineal YV plasty for long VUAS involving the bulbar urethra is a feasible technique that can provide satisfactory results . A concomitant AUS implantation may be of interest although the possible increased risk of AUS erosion/infection compared to a staged approach should be further evaluated.

Funding No **Clinical Trial** No **Subjects** None

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ROBOTIC ARTIFICIAL URINARY SPHINCTER EXPLANTATION AND CONCOMITANT FASCIAL SING INSERTION IN CASE OF BLADDER NECK CUFF EXTRUSION FOR FEMALE PATIENTS

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INTRODUCTION
Female stress urinary incontinence (SUI) is highly prevalent. Artificial urinary sphincter is an option for severe or complex female SUI cases. In case of bladder neck cuff extrusion, AUS explantation is required and further SUI treatment (AUS reimplantation or others) can be challenging. In the present video, we report and describe a new surgical technique aiming both to treat AUS bladder neck extrusion and to prevent recurrence of SUI.

DESIGN
We present the case of a 43-year-old female patient with a history of urethrovaginal fistula after the excision of a paraurethral leiomyoma. After urethrovaginal fistula repair with a Martius flap interposition she reported severe SUI. After failure of two TVT slings, she still reported SUI with 350 g on 24h pad weigh test, massive leakage on cough stress test with a fixed urethra. She underwent robotic AUS implantation with complete resolution of SUI postoperatively. Six months after the implantation, she presented a recurrence of the SUI and urethral pain. Bladder neck extrusion of the AUS cuff was diagnosed on flexible cystoscopy. A robotic AUS explantation was planned. We offered to place a fascial sling at the bladder neck during the explantation to minimize the risk of SUI and urethrovaginal fistula recurrence

RESULTS
Five ports are placed. The Da Vinci Xi robot is docked on the left side of the patient (side docking). The bladder is dropped down from the abdominal wall. The AUS pressure regulating balloon is found, dissected and explanted. Opening the fibrotic tissue surrounding the bladder neck, the cuff is found, dissected and opened.

The anterior aspect of the bladder is opened longitudinally to repair the bladder neck defect transvesically. The edges of the bladder incision are sutured on each side to the abdominal wall to improve the transvesical bladder neck exposure. The inflammatory/necrotic tissues surrounding the extrusion orifice are excised. The orifice is then closed transversally (to avoid bladderneck stenosis) in two layers (detrusor and mucosa individually) using interrupted 4/0 Vicryl sutures

To harvest rectus fascia sling, a 7 cm suprapubic incision is made and carried down to the rectus fascia. A 10x1.5 cm rectus fascial sling is harvested. The fascia is then closed using two running sutures. The fascial sling is inserted through the 12 mm assistant port and placed around the bladder neck in the dissected space of the explanted AUS cuff.

The sling is pulled towards the rectus fascia using two permanent 2/0 monofilament stitches inserted into the abdomen with a Reverdun needle and placed at each end of the sling. We tightened the sling above the rectus fascia moderately on the assistant finger

The bladder and all the cutaneous incision are closed.

The operative time was 280 minutes with minimal blood loss. There was no postoperative complications. The patient was discharged on postoperative day 2. The urethral catheter was removed at day 15 and the patient resumed spontaneous voiding with post-void residual of 70 ml. At 1 month, she is socially continent, wearing 1 pad per day.

CONCLUSION
Robotic artificial urinary sphincter explantation and concomitant fascial sing insertion in case of bladder neck cuff extrusion appears feasible and may be an interesting salvage option to prevent SUI recurrence and avoid further anti-incontinence surgical procedures likely to be highly challenging.

Funding None **Clinical Trial** No **Subjects** Human **Ethics not Req'd** Retrospective **Helsinki** Yes **Informed Consent** No

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ROBOTIC-ASSISTED APPENDICOVESICOSTOMY AND FASCIA LATA PUBOVAGINAL SLING PLACEMENT TO TREAT NEUROGENIC BLADDER AND REFRACTORY STRESS URINARY INCONTINENCE

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INTRODUCTION

Robotic-assisted appendicovesicostomy is a frequently performed procedure in pediatric patients with congenital urinary tract abnormalities but has not been well described in adult patients for benign indications. This video demonstrates a stepwise approach to robotic-assisted appendicovesicostomy in a female with neurogenic bladder and bothersome stress urinary incontinence.

DESIGN

We describe a case of a 48-year-old G0 female with neurogenic bladder and urinary incontinence following spinal cord injury in 1991 requiring chronic intermittent catheterization. Patient had significant high volume stress urinary incontinence (SUI) and previously failed a rectus fascial autologous pubovaginal sling placement. Urodynamics demonstrated atonic bladder with good capacity. Options were discussed with the patient, and she elected for a robotic-assisted appendicovesicostomy and fascia lata pubovaginal sling placement, with the possibility of bladder neck closure in the future, if SUI was persistent.

RESULTS

The patient tolerated the procedure well, had an uncomplicated hospital course, and was discharged on post-operative day #3. At three weeks following the procedure, the patient was taught to catheterize her umbilical stoma. The patient was able to catheterize without issue and had resolution of her stress urinary incontinence six weeks after the procedure.

CONCLUSION

This video abstract demonstrates successful robotic-assisted laparoscopic placement of an appendicovesicostomy with fascia lata pubovaginal sling placement in a patient with neurogenic bladder and stress urinary incontinence requiring chronic intermittent catheterization.

Funding None **Clinical Trial** No **Subjects** Human **Ethics not Req'd** Surgical video **Helsinki** Yes **Informed Consent** Yes

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CONTINENT CYSTOSTOMY (MITROFANOFF APPENDICOVESICOSTOMY) USING THE ROBOTIC APPROACH

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INTRODUCTION
Continent urinary diversions are sometimes necessary for neurological bladder in patients unable to perform self-catheterization by the urethra.

The objective of this video was to present a technique of Mitrofanoff continent cystostomy by laparoscopic robot-assisted approach.

DESIGN
We present the case of 27 years old female. She present a C6 spinal cord injury since 2019. She has a neurological bladder with an overactive bladder treated by intradetrusor botulinum toxin injections and anticholinergics, and a detrusor-sphincter dyssynergia with chronic urinary retention.

She is unable to do urethral self-catheterizations and she refused a non continent urinary diversion by ileal conduit.

After discussion in a neurourology multidisciplinary team meeting, a continent Mitrofanoff cystostomy by the robotic approach is proposed.

RESULTS
We start by placing the trocars: one trocar above the umbilicus for the optic, one in the right pararectal line, one in the left pararectal line and one in the left iliac fossa for the robot arms and a 12 mm assist trocar in the right iliac fossa. The Da Vinci Xi robot is docked on the left side of the patient (side docking).

The appendix is located. It appears to be of good size and caliber. It is disconnected from the caecum at its basis while preserving the meso appendix, then catheterized with a 12-F catheter.

The bladder is then completely removed from the abdominal wall. The bladder dome appears mobilizable up to the umbilicus. We do a longitudinal opening of the detrusor muscle at the top of the bladder until reaching the bladder mucosa. The bladder mucosa is opened and the distal part of the appendix is anastomosed to the mucosa by two running sutures of 5/0 PDS.

An antirefluxing tunnel is made by closing the detrusor above the appendix with separate stitches of 3/0 Polysorb. It is about 4 cm long.

The bladder is attached to the abdominal wall about 3 cm below the umbilicus and 3 cm on either side of the midline using a Reverdun needle. The appendix is externalized in the lower part of the umbilicus. It is hooked up to the fascia and then anastomosed to the skin. We finish by closing the trocar holes.

The operative time was 210 minutes with minimal blood loss. There was no postoperative complications. The patient was discharged on postoperative day 5. The cystostomy catheter was removed at 3 weeks and the patient was able to begin her self-catheterization by the conduit without difficulties.

CONCLUSION
The need for a urinary diversion by continent cystostomy remains a rare situation. The robot-assisted approach appears feasible. Studies are needed to determine if it could reduce perioperative morbidity compared to the open approach.

Funding None **Clinical Trial** No **Subjects** Human **Ethics not Req'd** Retrospective **Helsinki** Yes **Informed Consent** No

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ROBOT-ASSISTED INTRACORPOREAL MONTI CATHETERIZABLE CHANNEL

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1. CHU de Rennes

INTRODUCTION

Continent cutaneous urinary diversions are sometimes necessary in neurogenic bladder patients unable to perform urethral self-catheterization. The Mitrofanoff appendicovesictomy is usually favored because it spares the need to use ileum which increases both the operative time and the risk of postoperative complications. However, ileal “Monti” catheterizable channel creation is a viable alternative when the appendix cannot be used. A few authors have reported robotic Monti catheterizable channel creation but with extracorporeal bowel harvesting and channel creation. The objective of this video was to present a technique of robotic intracorporeal Monti catheterizable channel

DESIGN

We present the case of a 52 years old female patient with a C7 spinal cord injury. Urodynamics showed neurogenic detrusor overactivity which was effectively treated by anticholinergics. She also has detrusor-sphincter dyssynergia with chronic urinary retention and is unable to do urethral self-catheterizations due to upper limb neurological impairment. She has a past medical history of appendicectomy. After discussion in a neurourology multidisciplinary team meeting, a robotic intracorporeal Monti catheterizable channel is planned.

RESULTS

We start by placing the five ports. The Da Vinci Xi robot is docked on the left side of the patient (side docking). Intravenous indocyanine green and Firefly are used to identify blood vessels while dividing the mesentery, ensuring proper vascularization of the bowel segment isolated and of the bowel anastomosis. The bowel segment is isolated using a 45-mm endo-GIA stapler and the enteric anastomosis is done using a 60 mm endo-GIA stapler. The isolated bowel segment is 5 cm long to allow the creation of two Monti catheterizable channel. The bowel segment is split into two equal parts ensuring proper blood supply of each using IV indocyanine green and Firefly. The 2.5 cm bowel segment is opened transversally and the catheterizable channel is created using two longitudinal 5/0 pds running sutures over a 12-Fr catheter. 3/0 Vicryl is used to stuture the catheter to the Monti channel.

The bladder is then widely dissected and completely freed from the abdominal wall and peritoneum to mobilize it as much as possible towards the umbilicus. Here, the bladder dome can be mobilized up to the umbilicus. A longitudinal incision of the detrusor muscle is made at the top of the anterior aspect of the bladder until the bladder mucosa is reached. A 2 cm caudal incision of the bladder mucosa is done and anastomosed to the tip of the Monti channel using two running sutures of 5/0 PDS.

An antirefluxing mechanism is created by closing the detrusor above the bowel with interrupted sutures on a 4 cm distance.

The bladder is attached to the abdominal wall about 3 cm below the umbilicus and 3 cm on either side of the midline using a Reverdun needle. The Monti channel is externalized. The proximal aspect of the Monti catheterizable channel is hooked up to the fascia and then anastomosed to the skin. Ports’ incisions are closed.

The operative time was 270 minutes with minimal blood loss. There was no postoperative complication. The patient was discharged on postoperative day 5. The cystostomy catheter was removed at 3 weeks and the patient started clean intermittent stomal catheterization with no issues. After 3 months, there was no additional complication, especially no stomal incontinence nor issues with catheterization

CONCLUSION

Robot-assisted intracorporeal Monti catheterizable channel appears feasible and may be useful in selected neurourological patients when appendix cannot be used. Studies are needed to determine whether the robotic intracorporeal approach may offer clinically significant benefits over the other surgical approaches

Funding None **Clinical Trial** No **Subjects** Human **Ethics not Req'd** Retrospective video **Helsinki** Yes **Informed Consent** No

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ROBOT-ASSISTED ARTIFICIAL URINARY SPHINCTER IMPLANTATION IN NEUROLOGICAL FEMALE PATIENTS WITH AN HISTORY OF AUGMENTATION CYSTOPLASTY AND APPENDICOVESICOSTOMY

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INTRODUCTION
Over the past 5 years, robot-assisted artificial urinary sphincter (AUS) has been used increasingly. However, the feasibility of this procedure remains to be demonstrated in complex cases which could remain indications for open implantation. The objective of this video was to present a case of robot-assisted AMS 800 AUS implantation in a neurological patient with an history of augmentation cystoplasty ad appendicovesicostomy

DESIGN
We present the case of a 32-year-old female patient with myelomeningocele and an history of augmentation cystoplasty + Mitrofanoff catheterizable channel creation at the age of 9. She presents with stress urinary incontinence due to intrinsic sphincter deficiency with a 24h pad weigh test of 350 g, no detrusor overactivity and normal bladder compliance on filling cystometry. She was leaking during cough stress test with no urethral hypermobility. She was offered three surgical options: pubovaginal sling, bladder neck closure, or robotic bladder AUS implantation. She opted for the later option

RESULTS
The standard robotic AUS “anterior” implantation technique was used. The procedure was done transperitoneally. The bladder is filled with saline right from the beginning to identify clearly its boundaries. A catheter is placed in the catheterizable channel to identify its location so that it would not be injured. The Retzius space is dissected carefully until the endoplevic fascia is reached on both sides of the bladder neck. The lateral aspects of the bladder are widely dissected. A passage is created lateral to the catheterizable channel allowing a prograsp forceps to access the right vaginal fornix which is dissected to find the vesicovaginal “bold” plane as previously described. The same step is performed on the left side. The bladder neck is dissected under direct vision from one side to another, sized with the measuring tape and the cuff is inserted. The operative time was 230 minutes and the patient was discharged on postoperative day 2 after removal of the catheter. There was no perioperative complicaitonsThe sphicnter was activated after 6 weeks and the patient has been completely dry since then after a follow up of 1 year.

CONCLUSION
Robot assisted AUS implantation in female patients appears safe effective and feasible even in complex cases including neurological patients with history of augmentation cystoplasty and appendicovesicostomy.

Funding None **Clinical Trial** No **Subjects** Human **Ethics Committee** CNIL **Helsinki** Yes **Informed Consent** Yes

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ROBOTIC ARTIFICIAL URINARY SPHINCTER IMPLANTATION IN FEMALE PATIENTS UNDER CONSTANT DIRECT VISION

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INTRODUCTION

One of the potential advantages of the robot-assisted approach for artificial urinary sphincter (AUS) implantation in female patients would be to allow direct vision throughout the dissection of the bladder neck. However, this was not the case in the technique initially described (Fournier, Urology 2014) in which the posterior aspect of the bladder neck was dissected blindly. The objective of this video was to describe a change modified robotic anterior AUS implantation in female patients with constant direct vision during bladder neck dissection.

DESIGN

We present the case of a 57-year-old female patient with a history of TOT in 2017 referred recurrence of stress urinary incontinence. She was wearing 4 pads per day, with a 24h pad weight test of 350g. The cystoscopy did not show any sling extrusion. On physical examination, she had a positive cough stress test with a fixed urethra, no pelvic organ prolaps. On preoperative urodynamics, the maximum urethral closure pressure was 16 cmH2O, there was no detrusor overactivity but a poor bladder contractility (PdetQmax = 14 cm H2O, Q max = 13 ml/s), post-void residual = 10 ml. She was offered four therapeutic options: pubovaginal sling, Bulkamid periurethral injections, Adjustable Continence therapy periurethral balloons or robotic AUS implantation and elected this later option.

RESULTS

The patient is placed in 23° Tredelenburg at 23° position with side-docking of the Da Vinci Xi Robot . A transperitoneal approach is used. After bladder filling, the Retzius space is dissected to reach the endopelvic fascia on bothside of the bladder neck. The lateral aspects of the bladder are dissected extensively on both sides. Dissection of the vaginal fornix helped by the assistant finger placed in the vagina is more extensive than in the initial technique, aiming to free the fingertip widely. This will allow a large mobilization of the bladder neck during the dissection granting a direct vision during the dissection of the posterior aspect of the bladder neck using the medial prograsp as a retractor to move the bladder neck medially and upwards.

CONCLUSION

We describe here a modified anterior technique of robotic AUS implantation in female patients that allows continuous direct vision during the bladder neck dissection and may reduce the risk of intraoperative bladder neck and vaginal injury

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ROBOT-ASSISTED BLADDER NECK ARTIFICIAL URINARY SPHINCTER IMPLANTATION IN MALE PATIENT WITH NEUROGENIC STRESS URINARY INCONTINENCE

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INTRODUCTION

In men with urinary incontinence due to spinal cord injruy, it is recommended to place the artificial urinary sphincter (AUS) cuff around the bladder neck to spare antegrade ejaculation, to avoid the risk of pressure ulcers at the perineal incision site and to limit the risk of cuff erosion due to clean-intermittent-self-catheterization (CISC). The objective of this study was to describe a surgical technique of bladder neck AUS implantation in neurogenic male patients.

DESIGN

The technique of bladder neck AUS implantation in men is described in this video. We present the case of a 43 year-old male with a past medical history of urinary incontinence due to spinal cord injury. The patient performed 5 to 6 CISC per day The maximum urethral closure pressure was 25 cm H2O and no detrusor overactivity evidence on urodynamics. Stress urinary incontinence persisted after ACT periurethral ballons implantation.

RESULTS

The procedure is performed under general anesthesia. The patient is placed in a 23° Trendelenburg position. A robotic transperitoneal approach is performed and five ports are placed in total, including three ports for the robotic arms and one 12 mm-port for the assistant surgeon to allow the insertion of the AUS cuff. First, the peritoneum is opened just above the seminal vesicles. The space between the posterior part of the prostate and the seminal vesicles is dissected. The bladder is then released down and the Retzius space is dissected. The lateral sides of the prostate are dissected and the endopelvic fascia is opened on both sides. A Prograsp forceps is used to open the angle between seminal vesicles and bladder on both sides from inside to outside. A measurement tape is then passed around the bladder neck and the AUS cuff is inserted through the 12-mm port. The balloon is implanted in the Retzius space through a 3 cm suprapubic incision and the pump is placed in the scrotum by a subcutaneous passage made from the suprapubic incision.

CONCLUSION

This video report the feasibility of robot-assisted bladder neck AUS implantation in male patient with spinal cord traumatism incontinence. The benefits of positionning the AUS cuff around the bladder neck (vs. bulbar urethra) and of the robot-assisted approach to perform this bladder neck implantation (vs. open or laparoscopic approaches) remain to be proven by clinical research studies.

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TIPS AND TRICKS FOR REMOVAL OF TOT – TRANS-OBTURATOR TAPE

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INTRODUCTION
Urinary incontinence (UI) effects up to 40% of women, while SUI (Stress Urinary Incontinence) is prevalent in at least half of them. Polypropylene tension-free vaginal tapes are highly successful and commonly used to treat that problem. Tension-free vaginal tapes can be placed retropubicly or throw the obturator membrane. Trans-obturator sling (TOT) is inserted through the obturator membrane and placed under the urethra in the mid-urethral portion to provide support for the weak endopelvic fascia to prevent leakage of urine associated with physical activities, sneezing, or coughing.

The complications are voiding dysfunction, urinary retention, and urethral obstruction after sling placement, affecting 3% of women. DeNovo urgency incontinence may affect 6% of women, and mesh erosion (as delayed complications) in 2-4% of women. The sling can be obstructive due to ingrowth, scarring, and inflammation.

In this video, we present the technics for removal of TOT.

DESIGN
To maximize visualization and exact placement of the sling, we place a localization needle in the sling under ultrasound guidance. A urethral manipulator or a Kelly is used to finding the area of urethral obstruction

RESULTS
For maximal visualization, a reverse U incision was made. Once the sling has been located, it is undermined to isolate it from the urethra. Since the sling can retract once cut, a double clamp with heavy clamps such as Heaney on each side is recommended. Afterward, the sling is cut in the middle. Sharp and blunt dissection is used to isolate the sling. For removal of the arms or the anchors, we employ several methods:

1. The hole at the tip of a small Babcock clamp can be used to bluntly clear the tissue as the sling is followed to the obturator membrane

2. A nasal speculum can be used to visualize the sling insertion into the obturator membrane

Since the initial sling placement is due to SUI, we use Kelly plication stitches that can be placed in the bilateral Pubourethal ligaments using two 2.0 PDS sutures for urethral support minimizing the risk of occult urinary incontinence. In the cases of combined intrinsic sphincter deficiency and mesh complications, we advocate concurrent placement of an autologous pubourethral sling rather than a repeat mesh sling.

CONCLUSION
Removal or revision of a sling tape/mesh requires experience and specific methodologic steps. We recommend doing so with the help of a transurethral instrument and ultrasound. For easier dissection of the sling from surrounding deep endopelvic tissue, we recommend using a Babcock clamp or a nasal speculum.

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