W7: Underactive bladder and Voiding Dysfunction: New Insights
Workshop Chair: Gommert van Koeveringe, Netherlands
12 September 2017 09:00 - 10:30

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<thead>
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<th>Start</th>
<th>End</th>
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<th>Speakers</th>
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<tr>
<td>09:00</td>
<td>09:15</td>
<td>Detrusor underactivity, when should we consider this condition in patients with LUTS?</td>
<td>Christopher Chapple</td>
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<td>09:15</td>
<td>09:30</td>
<td>What is new concerning detection of detrusor underactivity in LUTS patients?</td>
<td>Kevin Rademakers</td>
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<td>09:30</td>
<td>09:45</td>
<td>What is new concerning diagnosis of detrusor underactivity in male patients with LUTS?</td>
<td>Matthias Oelke</td>
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<td>09:45</td>
<td>10:00</td>
<td>When do we have to consider, and what do we need to diagnose detrusor underactivity in Female patients?</td>
<td>Gommert van Koeveringe</td>
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<td>10:00</td>
<td>10:15</td>
<td>Discussion</td>
<td>All</td>
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<tr>
<td>10:15</td>
<td>10:30</td>
<td>What future steps are necessary to detect and confirm the condition, develop therapies, and follow-up after treatment?</td>
<td>Christopher Chapple, Matthias Oelke, Kevin Rademakers, Gommert van Koeveringe</td>
</tr>
</tbody>
</table>

**Speaker Powerpoint Slides**
Please note that where authorised by the speaker all PowerPoint slides presented at the workshop will be made available after the meeting via the ICS website [www.ics.org/2017/programme](http://www.ics.org/2017/programme) Please do not film or photograph the slides during the workshop as this is distracting for the speakers.

**Aims of Workshop**
The clinical entity of underactive bladder (UAB) and its urodynamic equivalent Detrusor underactivity (DU) has gained increasing scientific and clinical interest lately as it became obvious that a substantial number of female or male patients suffer from this bladder condition. However, no consensus on the diagnosis or evaluation approach has been reached. The key speakers of this workshop are intensively involved in new research initiatives within this unexplored field. They will present and discuss the latest information and key facts concerning UAB/DU. How do we define the patients with UAB/DU and what are the differences in assessment of male and female patients? Which invasive or non-invasive tools to assess contractility are currently available?

**Learning Objectives**
1. The pathophysiological background of detrusor underactivity
2. The assessment of detrusor contractility amongst other voiding dysfunctions (dysfunctional voiding and bladder outlet obstruction). Tools to detect and diagnose detrusor underactivity
   o Invasive and non-invasive tools
   o Differences in assessing male and female patients
3. Current and future treatment options

**Learning Outcomes**
The delegate will after the workshop:
- Be able to understand some basics of the pathophysiology of voiding dysfunction due to an underactive bladder.
- Be able to identify what is important in differentiating the different causes of voiding dysfunction in a diagnostic workshop.
- Be able to identify current treatment options.
- Be able to identify future needs for diagnostic and treatment tools for voiding dysfunction due to an detrusor underactivity

**Target Audience**
Urologists, Gynaecologists, researchers, epidemiologists, colleagues interested in urodynamics

**Advanced/Basic**
Advanced

**Suggested Learning before Workshop Attendance**
Read some of the literature mentioned below.

**Suggested Reading**
Detrusor underactivity (DU) is an increasingly recognised cause of lower urinary tract symptoms in both men and women. There are an increasing number of research initiatives, that study this entity. Detrusor underactivity is defined by the ICS as: a contraction of reduced strength and/or duration, resulting in prolonged bladder emptying and/or failure to achieve complete bladder emptying within a normal time span. The latter is therefore a urodynamic diagnosis, but still rather vague. For example, what are criteria for normal strength and duration. The underactive bladder as a symptom complex has recently been characterized by the following working definition: The underactive bladder is a symptom complex usually characterised by prolonged urination time, with or without a sensation of incomplete bladder emptying, usually with hesitancy, reduced sensation on filling and a slow stream suggestive of detrusor underactivity. However, to differentiate lower urinary tract symptoms suggestive of detrusor underactivity, from symptoms of, for example, obstruction remains a major challenge.

Speaker 1: Prof Christopher Chapple

In order to detect detrusor underactivity in a larger population, non-invasive tools should be developed and assessed with regard to their specificity to detect the condition. However, to be able to do this, Detrusor underactivity should be diagnosed properly. Symptomatology with a possible relation to detrusor underactivity is assessed. The large dilemma of differentiation of underactive bladder symptoms and obstructive symptoms is addressed. Non-invasive parameters such as voiding efficiency, post void residual urine and bladder volume alone, detrusor wall thickness and other imaging parameters are discussed and compared to the urodynamic diagnosis.

Speaker 2: Kevin Rademakers, MD

For the diagnosis of Detrusor underactivity, several urodynamic parameters have been developed mainly for male patients. Cutoff values have been rather vague and these values have recently been shown to be dependent on the grade of obstruction. Therefore, a nomogram was developed by plotting a contractility parameter to an obstruction parameter. The position in this nomogram is related to clinical symptomatology of the patients. This is an example of a new approach that sheds new light on the problem of, in this case, male LUTS and more specifically detrusor underactivity.

Speaker 3: Prof Matthias Oelke

In female patients with LUTS, it is even more difficult to diagnose detrusor underactivity. As female subjects are able to void, sometimes even without any urodynamically noticeable detrusor pressure increase, the contractility of the detrusor is impossible to assess. If a surgical procedure is necessary, that might compromise the bladder outlet such as anti-incontinence surgery, it is useful to determine the capacity of the detrusor to increase the pressure if necessary (contractile reserve).

Another phenomenon that is quite common in females is a combination of detrusor overactivity and detrusor underactivity: Detrusor hyperactivity, Impaired contractility (DHIC). This phenomenon is interesting from a pathophysiological point of view but can be a complicating factor when initiating treatments that increase the contractility of the detrusor. Detrusor underactivity is also thought to be a contributing factor to the development of larger post void residuals and recurrent urinary tract infections. Recurrent urinary tract infections are a major health problem especially in the institutionalized elderly. It is here, where the health problem is even complicated further by antibiotic resistance. Therefore, if detrusor underactivity can be treated more effectively, we may come closer to a solution for these major health challenges of our time.
Detrusor underactivity, when should we consider this condition in patients with LUTS?

Christopher Chapple
Sheffield Teaching Hospitals
NHS Foundation Trust
UK

Workshop 7
- underactive Bladder and Voiding Dysfunction

Christopher Chapple
Affiliations to disclose†:
- Allergan: Scientific Study/Trial (Researcher/Author), Meeting Participant/Lecturer, Consultant/Advisor
- Astellas: Grant, Scientific Study/Trial (Researcher/Author), Meeting Participant/Lecturer, Consultant/Advisor
- Pfizer: Lecturer

Funding for speaker to attend:
- Self-funded
- Institution (non-industry) funded
- Sponsored by:

The Standardisation of Terminology of Lower Urinary Tract Function: Report from the Standardisation Sub-committee of the International Continence Society

Paul Abrams, Linda Cadmus, Shigaro Fall, Derek Griffiths, Peter Kneifel, Ulf Ulmsten, Philip van Kerrebroeck, Anne Victoria, and Max West

Need to consider:
- Symptoms as reported by the patient
- Signs as observed by the clinician
- Urodynamic findings as observed during urodynamic studies
- Conditions—urodynamics +symptoms/signs
- Treatment based on the above

“The Bladder is an Unreliable Witness”

- The bladder
  - Symptoms are not disease-specific
- The patient
  - Difficulties in reporting symptoms
  - Embarrassment
  - Underestimate seriousness: “normal part of aging”
  - Lack of knowledge or low expectation of treatment
- The clinician
  - Clinical skills: failure to elicit specific history
  - Bias, variations in practice and knowledge

† Turner Warwick 1979 Urol Clin N America
Disturbances or defects could occur at multiple sites: CNS control, sensory nerves, motor nerves and smooth muscle activity.

Fowler, de Groat and Griffith, 2008
Detrusor underactivity: A sensory problem?

Myoglobinuria, bladder outlet obstruction, and neuropathic bladder.

There is no single ideal animal model for DUA/UAB

Animal models for DUA/UAB

Phenotyping women with detrusor underactivity by presumed etiology: Is it feasible?

Phenotyping women with detrusor underactivity by presumed etiology: Is it feasible?
Terminology

“When I use a word… It means just what I choose it to mean—neither more nor less”

- Detrusor areflexia
- Atonic bladder
- Desensate bladder
- Detrusor or bladder failure
- Underactive bladder/detrusor
- Chronic retention
- Detrusor underactivity (DUA) (ICS 2002)

Detrusor Underactivity (DU) and Underactive Bladder (UAB)

- DU is diagnosed urodynamically and has an ICS definition
  - Based on pressure-flow
  - Characterized by low pressure, and/or poorly sustained detrusor contraction in combination with low urinary flow
- UAB has no ICS definition
  - “The clinical syndrome that accompanies DU”

Need for a UAB definition?

UAB could be to DU, as OAB is to DO?

If drug treatment becomes available, patients will need to be identified without pressure-flow diagnosis.

Is UAB synonymous with DUA?

Symptoms associated with DUA

![UAB vs. DUA symptoms comparison chart](image-url)
The patient experience of underactive bladder

**Background**

- **Symptom complex** - suggests a lack of bladder emptying may reflect a spectrum of lower urinary tract dysfunction, which may be associated with neurogenic disorders or be idiopathic.
- **Evolution of the definition** - a new clinical concept for underactive bladder (UAB) is currently proposed as...

**Methods**

- **Qualitative interview study** - conducted in 132 men and 15 women, mean age 68 years.
- **In-depth, semi-structured interviews**
- **Analysis of the transcripts**

**Results**

- More than 30 symptoms, signs or impacts were reported.
- **Proposed Definition**

- Underactive bladder is characterized by a slow urinary stream, hesitancy and straining to void, with or without a feeling of incomplete bladder emptying and dribbling, often with storage symptoms.

**Refining the definition**

- **Qualitative research** to look for characteristic symptoms
- **Quantitative research** in urodynamically defined DU patients
Normal Detrusor Function
ICS Definition 2002

- Normal voiding is achieved by a voluntarily initiated continuous detrusor contraction that leads to complete bladder emptying within a normal time span, and in the absence of obstruction
- For a given detrusor contraction, the magnitude of the recorded pressure rise will depend on the degree of outlet resistance

DU - ICS Definition (2002)

"A contraction of reduced strength and/or duration, resulting in prolonged bladder emptying and/or failure to achieve complete bladder emptying within a normal time span"

Acontractile detrusor (AcD) – ICS (2002)

"(a detrusor) that cannot be demonstrated to contract during urodynamic studies"

Urodynamic assessment of bladder voiding function: Key points

- Most measures of detrusor voiding function assess only strength of contraction rather than sustainability or speed of contraction
- 2 parameters used to estimate strength: Qmax and Pdet@Qmax
- Urodynamic estimation of isometric contraction strength based on Bladder outlet relation (BOR) (Griffiths 1972)

The Bladder Outflow Obstruction Index (BOOI)

Most authors use ranges for Pdet@Qmax (e.g. <40) and Qmax (e.g. <15)

BOOI (Abrams Griffiths Number)

Pdet@Qmax -2xQmax

Unobstructed: < = 20 cmH₂O
Equivocal: 20-40 cmH₂O
Obstructed: > = 40 cmH₂O
Projected isovolumetric pressure (PIP) and its derivations detrusor coefficient (DECO) and bladder contractility index (BCI)

Simplified method of estimating isometric contraction strength by drawing the BOR (simplified to straight line) on pressure flow nomogram (Schäfer)

Assessing bladder voiding function: Strength

Projected isovolumetric pressure (PIP) and its derivations detrusor coefficient (DECO) and bladder contractility index (BCI)

Schäfer's simplified method of estimating isometric contraction strength based on drawing the BOR on (Schäfer's) pressure flow nomogram

Advantages:
- Simple to use
- Measurement easy to obtain
- Estimation of isovolumetric contraction

Limitations:
- May not be applicable to other groups (e.g., men with PPI)
- Poorer test-retest reliability than stop tests

Materials and Methods: Evaluated 1420 in dynamic pressure-flow studies from 1222 men (ages 25-80 years) with lower urinary tract symptoms (LUTS). Excluded were patients with congenital anomalies of the urethra or with renal failure. BCI was estimated by the following formula:

BCI = \frac{P_{\text{det}} - P_{\text{intra}}} {Q_{\text{max}}}

where:
- \( P_{\text{det}} \) is the detrusor pressure
- \( P_{\text{intra}} \) is the intra-vesical pressure
- \( Q_{\text{max}} \) is the maximum voiding flow rate

Results: The correlation showed a high correlation coefficient.

Interventions for DUA/UAB

- Prostatectomy, prostatotomy
- Bladder neck incision or resection
- Urethral stricture repair or dilation
- Intraurethral stent
- Balloon dilatation
- Pharmacologic therapy
- Transurethral resection or incision
- Y-plasty

Behavioural therapy ± biofeedback

Interventional therapy ± biofeedback
- Computed tomography
- Magnetic resonance imaging
- Ultrasound
- Urethral stricture dilation
- Retropubic urethral suspension
- Surgical sphincterotomy
- Pudendal nerve interruption
Conservative management

1) Behavioral interventions
   - Scheduled voiding
   - Double voiding
   - Straining

2) Pelvic floor physiotherapy and Biofeedback

3) Catheterisation
   - Intermittent self-catheterisation
   - Indwelling (suprapubic) catheter

Monitoring

Thomas et al. 30-year urodynamic follow-up of men diagnosed with DU (Qmax < 15 ml/s, Pdet@Qmax < 40 cmH2O) initially managed with watchful waiting (no catheterisation).

- Only eleven patients failed the initial watchful waiting approach and underwent TURP, 8 (72.7%) due to worsening LUTS and 3 (27.3%) due to acute retention.

Monitoring

- Check:
  - Residuals
  - Biochemistry / Urine Cultures
  - Upper Tracts
  - Bladder Wall Thickness

Results: The study population consisted of 143 consecutive men with median of 62 years, IPSS 16, and prostate volume 35 ml. In total, 33 patients (23.1%) had DU. CART analysis showed that all men with DWT ≤ 1.23 mm plus bladder capacity >445 ml had DU. This multivariate model has a sensitivity of 42%, specificity of 100%, positive predictive value of 100%, and negative predictive value of 65%.

Epidemiology

- The contribution of DU to LUTS on a population basis is unknown.
- Possible outcome measures

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Definition</th>
<th>Prevalence</th>
<th>Positive Predictive Value</th>
<th>Negative Predictive Value</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
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<tbody>
<tr>
<td>Urinary Frequency</td>
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<tr>
<td>Urinary Urgency</td>
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<td>Daytime Urinary Incontinence</td>
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<td>Nighttime Urinary Incontinence</td>
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<td>Post-void Residual</td>
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<tr>
<td>Other Lower Urinary Symptoms</td>
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<td>( Q_{max} )</td>
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<tr>
<td>( P_{det} @ Q_{max} )</td>
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<tr>
<td>( A_{max} )</td>
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<tr>
<td>( Q_{mean} )</td>
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<tr>
<td>( Q_{urethra} )</td>
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<tr>
<td>( Q_{voiding} )</td>
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<tr>
<td>Bladder Wall Thickness</td>
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<tr>
<td>Prostate Volume</td>
<td></td>
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</tbody>
</table>
**Prevalence of DUA in clinical studies**

<table>
<thead>
<tr>
<th>Study</th>
<th>Population</th>
<th>Age Range (yrs)</th>
<th>Prevalence of DUA + (% of acontractile detrusors)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fusco et al 2001</td>
<td>541</td>
<td>26 - 89</td>
<td>10%</td>
</tr>
<tr>
<td>Kuo et al 2007</td>
<td>Male</td>
<td>46 - 96</td>
<td>10.6%</td>
</tr>
<tr>
<td>Nitti et al 2002</td>
<td>Male</td>
<td>18 - 45</td>
<td>9%</td>
</tr>
<tr>
<td>Wang et al 2003</td>
<td>Male</td>
<td>18 - 50</td>
<td>10%</td>
</tr>
<tr>
<td>Kaplan et al 1996</td>
<td>Male</td>
<td>18 - 50</td>
<td>23% (5%)*</td>
</tr>
<tr>
<td>Karami et al 2011</td>
<td>Male</td>
<td>18 - 40</td>
<td>12.9% (10.5%)*</td>
</tr>
<tr>
<td>Arbabanel et al 2007</td>
<td>Male, Female</td>
<td>&gt;70, &gt;70</td>
<td>48% in men, 12% in women</td>
</tr>
<tr>
<td>Jeong et al 2012</td>
<td>Male, Female</td>
<td>&gt;65, &gt;65</td>
<td>40.2% in men, 13.3% in women</td>
</tr>
<tr>
<td>Resnick et al 1989</td>
<td>Male</td>
<td>87, +30</td>
<td>23%*</td>
</tr>
<tr>
<td>Resnick et al 1996</td>
<td>Female</td>
<td>87, +45</td>
<td>45%*</td>
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<tr>
<td>Groutz et al 1999</td>
<td>Female</td>
<td>62.6 ± 15.8 yrs</td>
<td>19%</td>
</tr>
<tr>
<td>Valentini et al 2011</td>
<td>Female</td>
<td>&gt;55</td>
<td>13.8%</td>
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</tbody>
</table>

*DUA affects 9-28% of men under the age of 50 years; 48% in those over 70 years undergoing urodynamics.*

**How common are UAB symptoms?**

Survey 633 subjects (54% men, 46% women)

Age range 33 to 92 years old, 97% > 60, mean of 74.3 years

23% of respondents reported difficulty emptying his/her bladder.

**Patho-physiology of LUTS**

- **B.O.O.**

- **Detrusor Overactivity**

- **Reduced contractility**

**Definition of Benign Prostatic Hyperplasia**

- **Prostate Histology (BPH)**
  - Anatomy of the prostate
  - Age-related prevalence
  - ‘Common in men over 50 years of age, histological criteria for BPH are present in 88% of men over 80 yrs’

- **Prostate Size (BPE)**
  - ‘Poor correlation between prostate size, urinary flow rate & symptoms’

- **Urodynamics**
  - Frequency volume charts
  - Flow rate
    - ‘Uroflowmetry in general and Qmax in particular, lack specificity for a reliable urodynamic diagnosis of the cause of decreased voiding’

- **Definition of Benign Prostatic Hyperplasia**

- **Urodynamics**
  - Frequency
  - Flow rate

- **Frequency**
  - Qmax <10ml/sec: 90% B.O.O
  - Qmax 10-14ml/sec: 67% B.O.O
  - Qmax >15ml/sec: 30% B.O.O

- **Flow rate**
  - Abrams' criteria

- **Abrams P et al 2001 Int Cons BPH p236**
Definition of Benign Prostatic Hyperplasia

- Residual Urine
  - "Elevated residual urine is associated with BOO – the relationship is not strong. Approximately 30% of unobstructed elderly men have elevated RU and 50% of obstructed men have none."

What is a significant post voiding residual?

The concept of Bladder Voiding Efficiency

>40% of the Functional Bladder Capacity (volume voided + residual)

Residual 200ml, FBC 200ml - 100%
Residual 200ml, FBC 400ml - 50%

Definition of Benign Prostatic Hyperplasia

- Pressure Flow Studies (BOO)
  - Weak correlation between symptoms (especially voiding symptoms) and BOO

  ‘No clinical or investigative features correlate well with bladder outlet obstruction proven by pressure flow studies’

Abrams P et al 2001 5th Int Cons BPH p261
Clean intermittent self-catheterisation:

- Most prevalent method of bladder management in patients with UAB
- Complications rare compared with indwelling/suprapubic catheters
- UI, urethral trauma, urethritis, epididymo-orchitis and urethral bleeding
- However, many patients find the technique difficult

Pharmacological agents to facilitate bladder emptying

No effective pharmacotherapy for UAB exists

- Parasympathetic agents (bethanechol, distigmine)
- Prostaglandins
- Blockers of inhibition
- Opioid receptor antagonists
  - Increasing intravesical pressure/bladder contractility
  - α-adrenergic receptor antagonists (phenoxybenzamine, prazosin, terazosin/doxazosin, alfuzosin/tamsulosin, silodosin)
- Benzodiazipines
- Baclofen
- Dantrolene
- Botulinum toxin
  - [anti-androgens for reducing prostatic size, e.g. finasteride]
  - Decreasing outlet resistance

Available studies do not support the use of parasympathomimetics

- Specifically when compared with combination provided alpha-receptor antagonists
- Combination therapy with a cholinergic drug and an alpha-blocker appears to be more useful than monotherapy?
Intravesical Electrical Stimulation (IVES)

- Establishes conscious control of the initiation and completion of a micturition reflex
- Activates specific mechanoreceptors in the bladder wall
- Lower the micturition threshold and enhance reflex amplitude
- Randomized placebo-controlled trials lacking
- Achieved long-term normalization of voiding in 20/24 (83%) children with idiopathic, and 8/20 (40%) with neurogenic underactive detrusor


- 10 daily 60 min session (5 b.i.d. 20 min sessions in 22 pts) followed by home treatment (2–3 times weekly) until bladder function normalised/no further improvement
- In responsive children (at 6 months):
  - Median residual volume decreased (75 mL (range 6–419) to 22 mL (range 0–338); p<0.0001)
  - Median voided volume increased (80 mL (range 0–625) to 220 mL (range 30–636); p<0.0001)
- Effects stable for 2 years
- Catheterisation discontinued in 11/15 cases

Electrical stimulation

- Brindley device
  - Ventral root stimulation +/- dorsal root section / sacral deafferentiation
  - Requires intact neural pathway and a bladder capable of contracting (generally used for SCI patients)
  - Post-stimulus voiding:
    - Relaxation time of striated sphincter is shorter than the relaxation time of the detrusor smooth muscle
  - Limitations: Voiding may occur in spurts at above-normal bladder pressures

Sacral nerve modulation

- In patients with retention (n=31), achieved decrease in:
  - Mean volume per catheterisation (379.9 ± 183.8 to 109.2 ± 184.3 mL)
  - Mean number of catheterisations (5.3 ± 2.8 to 1.9 ± 2.8)


Prediction of Sacral Neuromodulation Treatment Success in Men With Impaired Bladder Emptying—Time For a New Diagnostic Approach

Kerin L. Redelmeier,1,2,3 Kerri M. Engrav,4,5 Philip L. V. Young,3,4 Matthias A. Stief,6,* Department of Urology, University of Toronto, Toronto, Ontario, Canada \nDepartment of Urology, Academic Medical Centre, Amsterdam, The Netherlands

Methods and Evidence: The aim of this study was to assess whether the use of the new 10–20 montage–Mindframe TM neuromonitoring can identify and predict SNM non-responders. Our results are consistent with prior research, but also identify a significant correlation between subjective and objective measures of bladder emptying. Conclusions: This pilot study showed that SNM treatment success in male patients with impaired bladder emptying can be predicted with the 10–20 montage–Mindframe TM neuro-monitoring. Men below the 30th percentile can likely be treatment non-responders, whereas the majority above the 30th percentile are responders. Niermeed. 2016. © 2016 Wiley Periodicals, Inc.
Surgical options

- Trans-urethral resection of prostate
- Intrasphincteric Botulinum Toxin
- Reduction cystoplasty
- ? Stem cells/ Tissue engineering
- Neural Reconstruction
- Detrusor Myoplasty—bladder wrap

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Causes for bladder acontractility (n=24)

<table>
<thead>
<tr>
<th>Etiology</th>
<th>Number of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Traumatic spine fracture (Th12 or L1)</td>
<td>3</td>
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<tr>
<td>Tethered-cord syndrome</td>
<td>4</td>
</tr>
<tr>
<td>Lumbar hernia of nuclear pulposis</td>
<td>3</td>
</tr>
<tr>
<td>Megacystis and benign outlet obstruction</td>
<td>2</td>
</tr>
<tr>
<td>Voiding dysfunction post hysterectomy</td>
<td>1</td>
</tr>
<tr>
<td>Neural myelomeningocele</td>
<td>1</td>
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<tr>
<td>diaplectic</td>
<td>4</td>
</tr>
</tbody>
</table>

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Functional Detrusor Myoplasty in Bladder Acontractility: Long-Term Results

- Georges Gakis,* Milomir Ninkovic, Gommert A. van Koevoring, T Shilpa Raja, Gustavo Sturz, Karl-Dietrich Siweth and Arminn Stend

- Reconstruction of the lower urinary tract using autologous muscle transfer and cell seeding: current status and future perspectives

---

Voiding under urodynamic assessment

Pre vs. postoperatively
**Complications**

<table>
<thead>
<tr>
<th></th>
<th>No.</th>
<th>Grade</th>
<th>Complete</th>
<th>Partial</th>
<th>None</th>
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<tbody>
<tr>
<td>Urinary tract infections</td>
<td>6</td>
<td>6</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Lower tract infections</td>
<td>7</td>
<td></td>
<td>1</td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Endocrine disorders</td>
<td>1</td>
<td></td>
<td>3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Associated renal infection</td>
<td>3</td>
<td></td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urinary tract obstruction</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bladder neck obstruction</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Disorder of genitourinary tract</td>
<td>2</td>
<td></td>
<td>1</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 6: Major intraoperative complications (by voiding result)

**Conclusions**

Complete (17/24) or partial spontaneous voiding (3/24), CR+PR 20/24 patients (83%)

91% (21/23 patients) without recurrent UTIs postoperatively

No deterioration of the upper urinary tract during F/U time period of up to 7.5 years

---

**Take Home Messages**

- DUA is a common problem.
- There is little published clinical or scientific research.
- Defining a symptom complex of UAB has not been possible due to the overlap with other LUT dysfunctions.
- Multifactorial aetio-pathogenesis.
- There is a lack of any simple and effective treatments.

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**The Question is - to what extent can we trust the Current Evidence?**
What is new concerning detection of detrusor underactivity in LUTS patients?

Kevin Rademakers
Resident in Training
Department of Urology
Maastricht University Medical Center
The Netherlands

Detection vs. diagnosis

- To “detect” a problem is to objectively observe symptoms caused by the problem or to hear a subjective but credible complaint from the patient about a symptom that is not visible
- To “diagnose” a problem is to ascertain the specific medical condition that is causing the problem

What is the importance of detection

- Upper UT complications?
- Mortality?
- Morbidity (UTI, ......?)

- Complaints
  - Bothersome (voiding) LUTS
  - Recurrent UTIs
  - Urinary retention
- Quality of Life
- Health-Care Related costs

Literature overview 2017: the numbers

- Pubmed 2017: Detrusor underactivity
  - 52 articles
    - 17 clinical studies
      - Mostly focused on desobstruction outcome comparison
Introduction

Physiological measurement

Non-catheter detection methods:
1. The use of symptoms

Symptoms

*Gammie et al. Eur Urol 2016*

*Uren et al. Eur Urol 2017*
Non-catheter detection methods:
2. The utility of post-void residual

EAU Guidelines on PVR in men

<table>
<thead>
<tr>
<th>Study</th>
<th>Patient group</th>
<th>PVR cut-off (ml)</th>
<th>N</th>
<th>Percentage</th>
<th>Risk estimate (OR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Klarskov</td>
<td>AUR patients</td>
<td>&gt;500</td>
<td>228</td>
<td>&gt;500</td>
<td>3.6x</td>
</tr>
<tr>
<td>Thomas</td>
<td>LUTS/BPO</td>
<td>&gt;45</td>
<td>4%</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>Crawford</td>
<td>MTOPS</td>
<td>&gt;50</td>
<td>39</td>
<td>737</td>
<td>0.6%</td>
</tr>
<tr>
<td>Roehrborn</td>
<td>ALTESS LUTS/BPO</td>
<td>&gt;55</td>
<td>350</td>
<td>Placebo (757)</td>
<td>1.8%</td>
</tr>
<tr>
<td>Mochtar</td>
<td>BPH patients</td>
<td>&gt;50</td>
<td>300</td>
<td>914</td>
<td>1.5%</td>
</tr>
<tr>
<td>Roehrborn</td>
<td>CombAT LUTS/BPO</td>
<td>&gt;50</td>
<td>Tamsulosin (1611)</td>
<td>6.8%</td>
<td>2.7%</td>
</tr>
<tr>
<td>Cahn</td>
<td>BPH patients</td>
<td>45–71</td>
<td>100</td>
<td>44</td>
<td>9.1%</td>
</tr>
</tbody>
</table>

PVR and risk of AUR
EAU guidelines on PVR in women (UI)

### Summary of evidence (LE)

<table>
<thead>
<tr>
<th>Evidence</th>
<th>LE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lower urinary tract symptoms correlating with UI are associated with a higher rate of PVR compared to asymptomatic subjects.</td>
<td>2</td>
</tr>
</tbody>
</table>

**Recommendations**

- If No measuring post void residual urine volume, use of catheter.
- Measure post-voiding residual in patients with urinary incontinence who have voiding symptoms.
- Measure post-voiding residual when assessing patients with complicated urinary incontinence.
- Post-voiding residual should be measured in patients receiving treatment that may impact on voiding function, including surgery for severe urinary incontinence.

*Recommendations based on expert opinion.

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### A Plea For Using Voiding Efficiency to Assess Bladder Emptying Capacity?

TA vs TV vs catheterisation!

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### Sensation Related Bladder Diaries (SR-BDs)

Non-catheter detection methods:

3. Bladder filling sensation

---

### Maastricht UMC+
Physiological measurement

Take Home Messages

- Symptoms have not yet been proved beneficial in the detection of DU patients
- Voiding efficiency [(voided volume / bladder capacity) × 100] is a better surrogate parameter to estimate bladder emptying function
- Do not strictly follow the number, look at your patient
  - Can the complaints be related to incomplete bladder emptying?
- Times are changing: Time for real-time data capture instead of artificial measurement techniques?

Detecting Detrusor Underactivity

<table>
<thead>
<tr>
<th>Obvious</th>
<th>Less obvious (grey area)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bladder capacity</td>
<td>Bladder capacity</td>
</tr>
<tr>
<td>Volume filling sensation (SRBDs)</td>
<td>“Normal” filling sensation</td>
</tr>
<tr>
<td>Voiding efficiency</td>
<td>Voiding efficiency</td>
</tr>
<tr>
<td>[rec UTIs with response to CIC]</td>
<td>Irritative and/or voiding LUTS</td>
</tr>
</tbody>
</table>

Thank you for your attention!
What is new concerning the diagnosis of detrusor underactivity in male patients with LUTS?

Matthias Oelke; MD, PhD, FEBU
Department of Urology

Workshop 7: Underactive Bladder and Voiding Dysfunction
International Continence Society; Florence, 12th September 2017

Objectives of the Lecture

• to learn about the definition of DU
• to distinguish between DU and BOO in men
• to know the potential invasive and non-invasive tests to diagnose DU in men
• to become aware of the clinical value of DU

Reasons for Impaired Bladder Emptying
(increased PVR, decreased VE, decreased urinary flow)

Definition of Detrusor Underactivity

• contraction of reduced strength and/or duration, resulting in prolonged bladder emptying and/or failure to achieve complete bladder emptying with a normal time span
• urodynamic diagnosis characterized by decreased detrusor pressure and decreased urinary flow rate

Conflict of Interest

Parts of the presented work have been accomplished with money provided by the Astellas European Foundation Grant 2012
Travel to the ICS in Florence was partially self- and partially institution-funded
Voiding in Men

- Normal voiding with complete bladder emptying within a normal time span when men have an adequate balance between bladder outlet resistance and detrusor contractility.
- Abnormal voiding occurs when men have increased bladder outlet resistance (BOO/BPO) and/or decreased bladder contractility (detrusor underactivity).
- One component may compensate for the other component.

Parameters for Judgment of Voiding

- Existing parameters
- Non-invasive
- Invasive (P/Q, urodynamics)

Measurement of Contractility in Men

Invasive Indicators of DU


Schäfer Nomogram

Problem with Defining Men with Detrusor Underactivity

- Proposed threshold values: BCI < 100 or $W_{max} < 7 \text{ W/m}^2$
- These do not seem to be correct for all men
- No single threshold value for the characterization of men with detrusor underactivity for the entire range of men with different bladder outlet resistance

Solution for Defining Men with Detrusor Underactivity

- Defining threshold values for the entire range of outlet resistance
- Analysis of a urodynamic database of treatment naive men aged ≥40 years (n=822)
- Exclusion criteria: suspicion of prostate or bladder cancer, radiotherapy, pelvic surgery, neurological disorder, UTI, prostatitis, bladder stones, bladder diverticula
- Plotting of BOOI-$W_{max}$ values in a diagram, calculation of percentiles (10th, 25th, 50th, 75th, 90th) and analyzing differences between the percentiles

Defining Threshold Values

<table>
<thead>
<tr>
<th>Variable</th>
<th>10th percentile</th>
<th>25th percentile</th>
<th>50th percentile</th>
<th>75th percentile</th>
<th>90th percentile</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>53.0 (47–63)</td>
<td>58.0 (52–66)</td>
<td>61.0 (55–70)</td>
<td>64.0 (58–76)</td>
<td>70.0 (62–82)</td>
<td></td>
</tr>
<tr>
<td>Height (cm)</td>
<td>178.0 (174–186)</td>
<td>179.0 (173–185)</td>
<td>180.0 (173–185)</td>
<td>181.0 (175–189)</td>
<td>182.0 (175–189)</td>
<td></td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>79.0 (68–100)</td>
<td>80.0 (69–99)</td>
<td>81.0 (72–104)</td>
<td>82.0 (75–107)</td>
<td>82.0 (76–106)</td>
<td></td>
</tr>
<tr>
<td>PSA (ng/ml)</td>
<td>2.1 (1.0–4.0)</td>
<td>3.1 (1.0–5.0)</td>
<td>4.1 (2.0–7.0)</td>
<td>5.1 (3.0–10.0)</td>
<td>6.1 (3.0–10.0)</td>
<td></td>
</tr>
<tr>
<td>Anticholinergic medication (mg)</td>
<td>17 (7–56)</td>
<td>22 (10–100)</td>
<td>28 (15–150)</td>
<td>34 (18–200)</td>
<td>46 (20–300)</td>
<td></td>
</tr>
<tr>
<td>Pharmacological treatment (duration, months)</td>
<td>6 (1–24)</td>
<td>9 (3–36)</td>
<td>12 (6–56)</td>
<td>18 (6–96)</td>
<td>24 (6–108)</td>
<td></td>
</tr>
<tr>
<td>Anticholinergic - number of medications</td>
<td>1 (0–3)</td>
<td>2 (0–5)</td>
<td>3 (0–7)</td>
<td>4 (1–9)</td>
<td>6 (1–12)</td>
<td></td>
</tr>
</tbody>
</table>

Patient Data pre-post TURP

Vlaaasticht-Hannover Nomogram

Contractility-Obstruction Nomogram

- Sacral neuromodulation data

Non-Invasive Indicators of DU

Men with impaired bladder emptying (PVR) and need for CIC

Sacral neuromodulation

Treatment success 86% vs treatment success 20%
**Non-invasive indicators**

- Evaluation of symptoms – patient history?
- Uroflow, PVR and other parameters?
- Urinary biomarkers (uNGF, uBDNF, PGE2)
- Measurement of isovolumetric bladder pressure with penile cuff test?
- Ultrasound measurement of detrusor wall thickness (DWT)
- ..........?

---

**Detrusor Wall Thickness measurement**

- generally acknowledged for diagnosis of BOO in men, DWT reflects the workload of the bladder
  - DWT ≥ 2.0 mm (in a bladder filled ≥250 ml) is highly predictive for BOO on pressure-flow study
  - the use of DWT in men with DU has recently been determined

---

**Ultrasound DWT Measurement for DU Diagnosis**

**Study aim:**

- Evaluation of DU/UAB based on non-invasive (clinical) indicators

**Methods:**

- Cross-sectional study; men with uncomplicated LUTS
- IPSS, free flow parameters (Q\text{max} and Q\text{ave}), PVR, bladder capacity, detrusor wall thickness measurement (DWT)
- DU clinically defined based on PVR + exclusion of BOO / dysfunctional voiding after pressure-flow analysis
- Classification And Regression Tree analysis (CART)

---

**Urinary Biomarkers**

- 37 patients with chronic urinary retention and urodynamically proven DU
- Control groups: 20 urodynamically normal, 34 DO and 15 detrusor hyperactivity and inadequate contractility (DHIC) patients
- Urinary NGF levels were significantly higher in DU vs normals (9.2 ± 20.3 vs 1.85 ± 2.9 pg/ml, p = 0.037)
- Urinary BDNF level was only significantly higher in patients with DU vs normals (153 ± 199 vs 77.4 ± 47.7 pg/ml, p = 0.033) but not in patients with DHIC or DO.
- Compared with the control group, urinary BDNF level was significantly higher in DU patients with bladder function recovery (190 ± 239 pg/ml, p = 0.033)
- The PGE2 level was significantly higher than the control group in DU patients with bladder function recovery (1290 ± 836 pg/ml, p < 0.0001) but not in patients without recovery (383 ± 237 pg/ml, p = 0.130).

---

**Take-Home Messages**

- The balance between bladder outlet resistance and contractile function of the bladder is responsible for sufficient voiding
- Detrusor underactivity is a urodynamically diagnosis but threshold values have to be separately defined for different BOO-grades
- The new (Maastricht-Hannover) nomogram defines threshold values for all obstruction grades; BOOI-\text{W}_{\text{max}} datapoints below the 25\textsuperscript{th} percentile indicate detrusor underactivity
- The nomogram can predict the outcome of treatment in men
- Non-invasive parameters are potentially able to replace computer-urodynamic evaluation in clinical practice; until now, only DWT in combination with bladder capacity has been evaluated
A young lady of 24 years presented to my outpatient clinic:

Performs CISC since one year. Cannot void since a urinary retention due to a urinary tract infection.

Evaluation elsewhere:
- Accontractile bladder on conventional urodynamic investigation.
- Extended patient history:
  - Voided only twice a day since childhood. Voided far less than her friends. Never participated in collective bathroom visits. Ambitious. Voiding was a waste of time. Retention during UTI 1.5 litres, Bad management GP providing delay.
  - CISC afterwards.

Patients question: What are my options?

Female patients with voiding difficulty

- Obstruction has to be differentiated from BU in women.
  - Obstruction (4%) can be:
    - Primary Bladderneck obstruction
    - Dysfunctional voiding
    - Urethral Meatal stricture
  - Females may not have any urethral resistance at all
    - In that case some obstruction is necessary to test contractile capacity of the bladder
    - The flow is not necessarily indicative of contractile capacity. How do we know the bladder is maximally stimulated during voiding. It is not necessary, there is no obstruction present
    - Overactive bladder symptom complex in fact may coincide with an underactive detrusor. (DHIC)

Female patients with voiding difficulty

- Voiding dysfunction in Women due to obstruction
  - Assessment difficult and controversial.
    - Normative age matched data necessary
    - New nomograms to be developed for use in females
    - Pressure and flow are not enough.
    - Voluntary muscular constriction hinders measurements

Studies in female patients

- Study US database: association with Neurological disease, UTI, POP. Cohn et al Neurocrol urodyn 2017
  - Our pelvic care database counts > 6000 patients
    - General questionnaire: Abstract # 7, ICS Tokyo, Moosdorf et al.
    - Specific urological questionnaires:
      - Pilot within a subset of patients (n=259): Conventional Urodynamic Assessment, and
      - Filled in questions regarding voiding symptoms
      - Preliminary scoring system in which each patient can score 0 – 35 points
      - Selection of 10 high and 10 low scoring patients
      - Goal: To evaluate the discriminative ability of the selected combination of questions
Study on general Pelvic floor complaints

- Our pelvic care database counts > 6000 patients
- 2660 women with LUTS
  - 59.5% with self reported voiding complaints!
  - A significant association with the other general Pelvic floor complaints: Incontinence, Constipation, Fecal incontinence
  - No correlation with POP
- Significant correlations also with specific symptoms like: feeling of incomplete emptying, weak stream, intermittency, straining.
- This advocates a multidisciplinary approach to voiding complaints in women.

Specific voiding questions

- Feeling of incomplete bladder emptying after micturition
  - Frequency of the problem?
- Hesitancy during micturition
  - Frequency of the problem?
- Weak stream?
  - Frequency of the problem?
- Need of using abdominal pressure to empty the bladder?
  - Frequency of the problem?
- Does it take a lot of effort to start and maintain micturition
  - Frequency of the problem?
- UTI's during the last 6 months?

- As a pilot 10 patients with the highest and 10 patients with the lowest symptom score were analysed

Study females with voiding dysfunction.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Post-void residual</th>
<th>W max</th>
<th>Voiding Efficiency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median (IQR)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Voiding effectiveness</td>
<td>93% vs. 16%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Charlton 2013
Feeling of incomplete bladder emptying: 0.363 < 0.001 n.s.
Intermittency on bladder emptying: 0.215, 0.042 - 0.241 n.s.
Weak stream: n.s.
Applying abdominal pressure during voiding: n.s.

Can we differentiate between different causes of voiding dysfunction by symptoms alone?

- Maybe:
  - Gammie et al. Eur Urol. 2015
- No:

Possible precipitating factors

Ageing ? + ?
1. Diabetes?
2. Neurogenic disorders?
3. Hyperdistension chronic >> acute
4. UTI's?
5. Obstruction?
6. Psychogenic, sociogenic constitution.
Aging and lower urinary tract function precipitating factors

Precipitating factors?

Therapeutic margins

What are the options for my young patient

1. First ambulatory urodynamics will be done.
2. Tined lead temporary neuromodulation test stimulation
3. Options:
   - sacral neuremodulation
   - Targeted physiotherapy
   - Latissimus dorsi detrusor myoplasty
   - Continue CICS

   - How can we prevent this condition to develop in our children:
     - Stimulate frequent toileting
     - Allow children to go to clean bathrooms at school

New therapies should aim at either increasing:
- contractile reserve and/or increasing:
- the subvesical relaxation capacity.

• Diagnostic tools need to be developed to determine the contractile reserve or the subvesical relaxation capacity. A stress test
Maastricht Urology Team