ICI Chapter 14

Surgery for Urinary Incontinence in Women

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Colposuspension: *Hikaru Tomoe, Japan*
Retropubic Sling: *Ariana L. Smith , USA*
Trans Obturator Tape: *Maurizio Serati , Italy*
Urethral Bulking Agents: *Alex Gomelsky, USA*
Artificial Sphincters/ Buccal mucosal grafts: *Benoit Peyronnet , France*
Stem Cell Technologies: *Zhuoran Chen , Australia*
Sacral Neuromodulation / Augmentation Cystoplasty: *Cris Gomes, Brazil*
Implantable PTNS: *Kate H Moore, Australia*
Urethral Diverticulum Surgery: *Eric Rovner, USA*
Clinical Trial Outcomes: *Chris Harding, United Kingdom*

ICI 7

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Historical Perspective

Previous ICI Chapters presented procedures that are no longer considered in this chapter (even as comparators):

- Bladder neck buttresse/ Kelly Plication
- Aldridge Sling
- Marshall Marchetti Kranz
- Stamey/Raz/Gittes/ Peyeyra needle suspensions
- Goretex/ Lyodura/ Teflon slings
- TVT Secur/ MiniArc
- Bovine Collagen/ Zuidex

'History has moved on'

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New Addition to Chapter, in keeping with Chapter 13 (Surgical Treatment of Incontinence in Men)

- **Recommendation for pre-operative Assessment of Patient**
  - Systematic History; relevant conditions - e.g.connective tissue disorders, nocturnal polyuria, postmenopausal atrophy, hand coordination for CISC, etc.
  - Systematic examination; e.g. increasing awareness of obesity importance, measure prolapse, measure pelvic floor muscle (PFM) strength
  - Ensure women are offered conservative PFM training before surgery for stress incontinence
- **Document baseline severity of incontinence: choices**
  - 24 hour or 1 hour pad test,
  - cough stress test must be at standard volume eg > 300 ml,
  - 3 day bladder diary, recording leakage

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Autologous Pubovaginal Sling

No new studies since last ICI

- Current data indicate that autologous PVS is "gold standard" for correction of incontinence, requires large abdominal incision, vaginal dissection
- Is more effective than open colposuspension in several studies (Cochrane: PVS vs Colposuspensn better ,RR 1.35 medium term, RR 1.19 long term)
- Operation was originally designed for women with previous failed continence surgery
- Because studies show it has higher risk for voiding dysfunction/ CISC/ UTI and de novo OAB,
- Autologous PVS suitable for a primary procedure in the hands of an experienced subspecialist working in a high volume centre who is well versed in providing relevant information about morbidity leading to informed consent, and procedure is likely to have increased benefit for patients with intrinsic sphincteric deficiency

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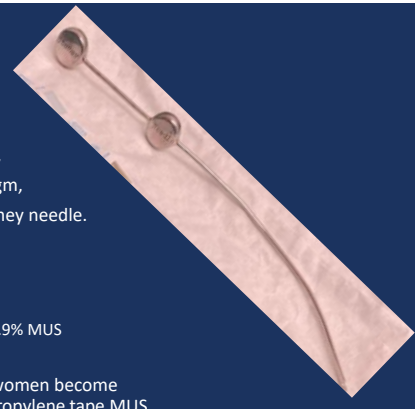
"Sling on a String"



Smaller abdominal incision, 6-8 cm autologous graft,
no need for full dissection of the urogenital diaphragm,
Sutures on the graft brought up to abdomen by Stamey needle.

Mock et al 2015 non randomised cohort study

- Short sling versus Top Down MUS
- At 14 months, objective cure = short sling 75.8% vs 80.9% MUS

This procedure likely to become more attractive as women become concerned about risks of mesh extrusion with polypropylene tape MUS.

Needs more long term studies, RCTs with objective long term data.

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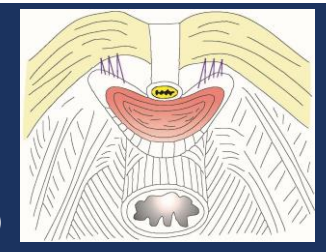
Colposuspension



Reiteration of good long term data as primary procedure
(Was designed by a gynaecologist for failed Kelly plication)

Cochrane Lapitan et al 2017
PVS versus open colposuspension
Cure: RR 1.19 (95% CI 1.03- 1.37)

Because procedure changes angle of anterior vaginal wall,
Consistent 9 – 13% chance of rectocele/ enterocoele post-op long term

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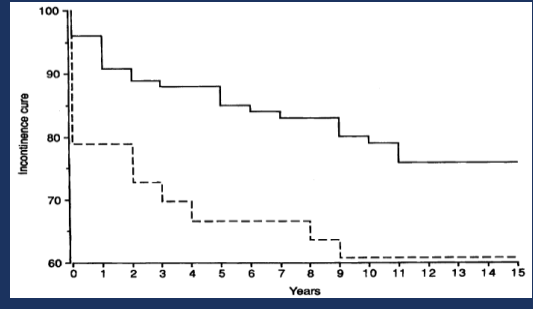
Need to Re-iterate this important study; Colposuspension better for primary surgery

Survival analysis of objective incontinence cure comparing patients with primary colposuspensions and secondary colposuspensions. The curves are significantly different (Log rank test, ***P*** = 0.02).
Solid line = primary surgery; dotted line=secondary surgery.



Original 14 year FU study by Alcalay, Monga, Stanton, 1995

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Laparoscopic Colposuspension

Different morbidity profile, much shorter time in hospital, 6-8% risk bladder perforation needing formal suturing

No new studies (very disappointing) – previous meta analyses

- 10 English RCTs, 1 Turkish, of Lap Colpo versus open
- Objective cure at 18 m; Lap colpo lower RR 0.91, 95% CI 0.86-0.96
- Objective cure 18 m – 5 years; RR 1.01, 95% 0.88 – 1.16
- At 2 years; **Kitchener et al 2006** Lap colpo 80% cure versus open 70% cure
  Carey et al 2006 Lap Colpo 72% cure versus open 78%

Long term results need more data !!!!

Procedure is becoming more popular with patients due to fear of mesh.

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NEW COCHRANE, DEAN et al (2017)

DATA AND ANALYSES

Comparison 1. Laparoscopic urethropexy vs open colposuspension

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Subjective cure	8		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
1.1 Within 18 months	7	1025	Risk Ratio (M-H, Fixed, 95% CI)	0.95 [0.90, 1.00]
1.2 Between 18 months and 5 years	1	263	Risk Ratio (M-H, Fixed, 95% CI)	1.00 [0.81, 1.25]
1.3 After 5 years	1	64	Risk Ratio (M-H, Fixed, 95% CI)	1.53 [1.00, 2.35]
2 Incontinent episodes over 24 hours within 18 months	2	133	Mean Difference (IV, Fixed, 95% CI)	-0.12 [-0.92, 0.68]
3 Objective cure on clinical testing	10		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
3.1 Within 18 months	9	1087	Risk Ratio (M-H, Fixed, 95% CI)	0.91 [0.86, 0.96]
3.2 Between 18 months and 5 years	2	290	Risk Ratio (M-H, Fixed, 95% CI)	1.01 [0.88, 1.16]
3.3 After 5 years	2	107	Risk Ratio (M-H, Fixed, 95% CI)	0.94 [0.69, 1.27]

Still only two studies with data after 5 years

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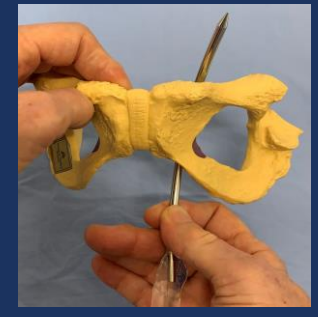
Retropubic Mid Urethral Sling

Robust first line procedure, even for women with ISD
Hundreds of trials



1. Four good quality trials of TVT versus open colpo, all no sig. diff
2. Five good quality trials of TVT versus Lap Colpo,
   3 trials = identical cure,
   2 trials show TVT has approx. 10% higher cure than lap colpo

New study **Karmakar et al 2021**

- 13 year FU of matched cohort
- 336 Burch, versus 100 TVT, all patients had no ISD
- Cure = 83% open colpo, versus 85% TVT, p = 0.038

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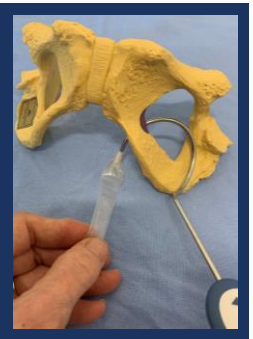
Trans-obturator Sling



Developed to reduce risk of bladder/urethral perforations

(Finland registry risk = 3.8%, Austrian registry 2.7%)

Schierlitz et al (2019) long term data, poor outcome in ISD

Hundreds of trials

2017 LR Maggiore Systematic review of ≥5 year data

TVT versus TVTO: objective cure OR 0.87 (95% CI 0.49-1.53)

Serati et al 2020 FU 156 months, n= 157 women, objective cure TVTO 92%

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Constantini et al 2016: TVT versus TVTO

Kaplan Meyer curve

Continence rate decreased for up to 25 months post-op,

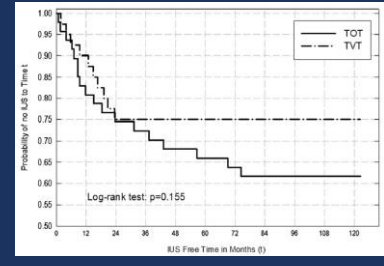
then TVT continence rate stabilised

but TVTO rate continued to fall.

Recent evidence suggests:

"Learning Curve" :

Trans Obturator tapes should be used in well selected population, with no ISD, not obese



Free survival times from UI subdivided according to surgical techniques

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Difficult data analysis of Trans Obturator Tape re: groin pain/ reoperation

Groin pain not systematically reported in all studies

The 2017 Cochrane review of TVT versus TOT (Ford et al) found a significantly higher risk of groin pain after the trans obturator procedures (RR 4.12, 95% CI 2.71 – 6.27).

Several meta-analyses have demonstrated a significantly higher risk of thigh/groin pain with TOT compared with TVT. This applies particularly for the inside-out technique (3.1% TOT vs 15.7% TVT-O) where the trocar is directed more laterally in this critical area thus getting much closer to the nerve stem. More serious complications in this area include myositis, fascitis, and abscess formation" [37]

Reoperation rates difficult;

Mesh exposure versus extrusion not always accurately reported

In the medium term, more women required repeat incontinence surgeries in the TOT group RR 21.89 (95% CI 4.36 – 109.8),

with a similar trend in long term studies RR 8.97 (95% CI 3.36-23.00).

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Single Incision Slings

Further attempt to reduce morbidity

Some have not stood the test of time.

- TVT Secur withdrawn
- MiniArc withdrawn

TVT Abbrevo two recent studies;

- **Melendoz Munz 2018:** Objective cure 96% at 12 months
- **Braga et al 2020:** Objective cure 92.5% at 3 years
- Altis / Solyx accumulating data

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OBESITY : NEGATIVE IMPACT UPON SURGERY FOR STRESS INCONTINENCE

BECOMING VERY APPARENT; Level I Evidence

- **Barco-Castillis et al 2020:**
- meta-analysis of obesity as a risk factor for poor outcomes after RP MUS
- 4 RCTs, objective (pad test, CST, Urodynamics) failure RR 1.62
- **Laterza (2018 Austrian group, n = 554):** TVT versus TVTO secondary analysis at 5 years
- high BMI 35 failure = 30%, versus BMI 25 failure = 10% RR 1.62 (1.26-2.07)
- **Brennand et al 2015:** obese cure 68% versus cure 85.6% non obese (sig)

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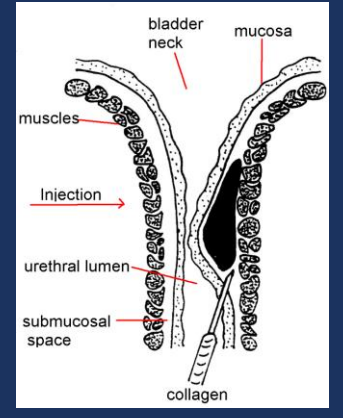
Bulking Agents

Many clinicians feel that injection of urethral bulking agents is generally more successful when the urethra is non-mobile (fixed by previous surgery), but the urethral closure pressure / VLPP is normal.

However, most studies do not analyse the data in this way.

MANY NEW STUDIES SINCE LAST ICI



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Macroplastique (PDMS)

Prospective database; *Rosenfeld 2016*

(from University of Texas)	At 9 months FU	At 20 months FU	Completely Dry
a) Naive patients	93%	41%	a) 4%
b) Prior continence surgery	70%	40%	b) 15%
c) Prior bulking + c surgery	69%	65%	c) 29%

Hoe et al 2021: 56 articles; meta-analysis difficult to interpret success

- Macroplastique ; cases of erosion

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Many New Studies:

Rodriguez 2020 Macroplastique after MUS removal for sling complications

Success = UDI Q6 = 0 or 1, no additional treatment

- Success of 46% at 46 months
- Success after repeat injection 69%

Serati 2019: 85 women age 75 + Macroplastique after 3 years = 47% objective cure

Plotti etal 2018 PDMS / Macroplastique

63 women with mean follow-up 8.3 years:

- Cure = 24%
- Improved = 19%
- Failed = 57%

But do we really expect bulking agents to last more than 10-12 months?

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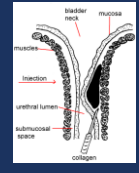
Bulkamid (PAHG)

2016 systematic review, difficult to summarise 12 studies, only 6 = dry rate

Zivanovic 2017: 60 women who had recurrent SUI after previous MUS

- Cure = negative cough stress tests + pad test < 2g + VAS
- Improved = few drops on cough stress test, PT 2-10 g
- Cure + improve rate = 84% at 12 months



Durasphere (carbon coated zirconium)

Hoe et al (2021) reported migration into lymph nodes

Futyma 2016: Urolastic; 66 women with recurrent SUI

- Objective "success" = 33% at 24 months
- Completely dry = 22%
- Oval shaped mass inside bladder = 4.5%

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Other New Studies: Bulking agents vs surgery

Itknoen Frietas 2020

- Large non-inferiority study, n= 224: TVT vs PAHG
- Cough test negative, 95% TVT versus 66% PAHG
- "Non - inferiority" criteria not met

Bach + Toozs-Hobson 2020

Bulking in elderly

Bulking after failed sling 2019: 73 women: 66% MUS, 27% PVS, 7% both

- Cure rate not given! 71% had "partial symptom response"

Daly et al 2021

- 38 women "salvage" procedure
- PGII outcome at 33 months, "success" 75%

Capobianco 2020: Systematic review up to December 2018

- Cure rate = 26% ≤ 1 year, 21% > 1 year

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Comparison of Surgical Treatments for SUI – Cure

Imamura M at al BMJ. 2019 Jun 5;365:l1842. doi: 10.1136/bmj.l1842.

"We also estimated the ranking probabilities of the different surgical treatments for cure and improvement using the surface under the cumulative ranking curves (SUCRA), which gives probabilities of each intervention being ranked the best (ie, having the highest proportion of women cured or improved)."

Note: "cure" was defined by patient subjective response or pad tests, cough stress test and bladder diaries not used

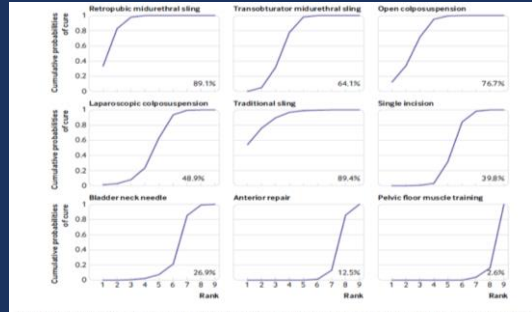

Fig 3 | Surface under cumulative ranking curves (SUCRA) for number of women showing cure of urinary incontinence symptoms

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Artifical Urinary Sphincter for Women

Performed as Open Procedure x 45 years.

In last ICI:

- Small studies of laparoscopic procedure
- Early reports of Robotic procedure

Several new studies since last ICI - 6

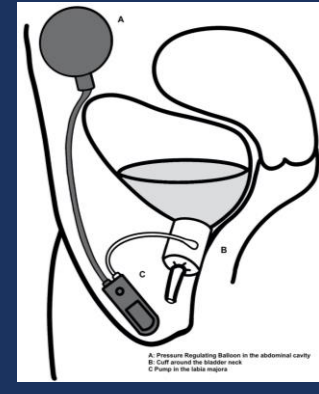

Figure thanks to B Peyronnet and C Richard, France

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Overview of Use:

- Widely used in France
- Selected use in UK, Canada, Europe
- No FDA approval: seldom used in USA / Asia
- Available in Australia, re-imbursed

- Mainly used for ISD and
- selected Neuropathic Incontinence

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Laparoscopic Approach

Schroeder et al 2021 n=49

- FU 4 years
- 84% socially continent (0-1 pads/day)
- 14% explantations

Bracchitta 2019 n=74

- FU 3.6 years
- 78% totally dry (no pads)
- 10% explantations

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Robotic Approach

Peyronnet et al 2019 (Eur Urol) n=49

- Median FU 18.5 months
- 81.6% fully continent
- 2% explantations

Peyronnet et al n=123, 4 countries

- FU 13 months
- 3.3% explantations

Overall, useful option for end stage ISD

Only in certain countries

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Other surgery for Female SUI: Buccal Mucosal Grafts

Remove triangular shaped graft from inner aspect of the patients mouth

Transplant it to dorsal urethra, for deficient urethra after mesh removal

- First reported in 2014
- Further recent reports Scholler 2018
- Lane et al 2020
- Little objective outcome data

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Stem Cell Technology

Preclinical studies

10 animal studies in rats/ monkeys/ pigs – small numbers, confirms stem cells improves urethral tissue in short term

Clinical Study

Jankowski 2018 - Double blind placebo controlled RCT for SUI/ MUI

- N=143 , intrasphincter injection of autologous muscle -derived cells
- Primary outcome of >50% reduction in daily SUI episode/ 12month follow up
- Study stopped at 61% recruitment due to 90% efficacy in placebo group

2 Other small prospective studies n=10, 70-80% improvement of SUI at 12months (one with mesenchmyal stem cell , one with muscle derived cell)

(Garcia-Arranz 2020, Sharifiaghdas 2016)

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Sacral Nerve Stimulation SNS (now Neuromodulation)

New insights into mechanism of action:

Functional MRI or PET scanner studies-

SNS affects activity in somatosensory areas of brain that integrate sensation of bladder filling/ detrusor contraction

Varying the intensity SNS may affect different brain areas

Predictors of Success:

Improvement during test phase is main predictor;
tined lead superior to PNE

Age: conflicting results

Obesity: no effect

Prior back surgery/ Psychiatric conditions: No Effect

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Insite Study of SacroNeuromodulation; now reported for 5 years (Siegel et al, 2018)
At 5 years, >50% benefit occurred in 82%
- Mean reduction of 2.0 leaks/ day
- Mean reduction of 5.4 voids/ day
- Implant site pain 15%
- SNS ineffective 13%
- Device explantation 19%

Currently running: SOUNDS study for 5 years (Chartier-Kastler, 2021)
French government re-imbursement requirement
So far, 3 year data available
- OAB Wet; 30% completely dry
- Implant pain 6%
- Implant infection 4%
- Failure 7%

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Interstim II SNM system works on *constant voltage basis*
Inter-stim Microsystem and Axonics are *current-controlled systems* , that adjust voltage to automatically give stable stimulation of S3.
No evidence that either system is superior

Both Axonics and InterStim™ Micro system are rechargeable and conditional MRI safe

(recent report of 13 MRIs done with SNS in situ, no ill effects)

Dudding et al (2021) new systematic review
Regarding reprogramming of lead configuration, pacing amplitude, pulse rate , pulse width

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ARTISAN study (using Axonics system; Pezzella et al 2021)

Prospective, multicenter, pivotal study performed to gain FDA approval.

- Results for 24 months available
- OAB Wet: 37% completely dry
- Uncomfortable stimulation 9%
- Device explantation 4%
- Surgical revision 9%
- 94% reported recharging frequency and duration were acceptable.

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PTNS; new Implantable tibial nerve stimulator

BLUEWIND DEVICE

Study	Design	Intervention	Results	Comments
Breda et al. (2017)	3-month prospective study	Bluewind implantable device (n=15)	Decrease in 24-hr frequency (11.8 to ->8.1), urgency episodes (6.5->2.0), severe incontinence episodes (2.8->0.3), urinary loss (243->55gm)	AE: prolonged antibiotic treatment (20%), pain (20%). Removal of implant in 1 patient (7%)
Heesakkers et al. (2018)	6-month multicentre prospective study	BlueWind implantable device (n=34)	**71%** of participants had >50% reduction in Number of leaks/day OR number of voids/day OR episodes with degree of urgency>2	AE: Implant site pain (13.9%), suspected infection (22.2%), wound complications (8.3%)
Dorsthorst et al. (2020)	3-year follow-up prospective study	BlueWind implantable device (n=20)	**75%** overall treatment success rate. 73% of patients reported improvement in QoL scores	Removal of 1 implant **No reports of implant migration.** *Treatment frequency varied from once every 4-6 wks to 1-2 per day.*

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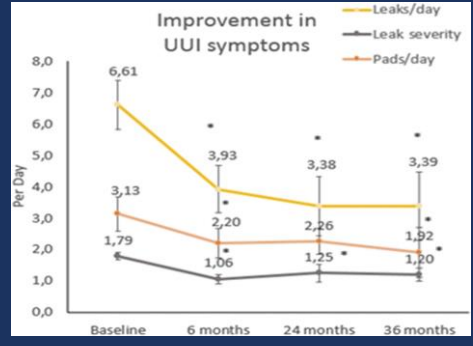
Dorsthorst, M. J. T., Digesu, G. A., Tailor, V., Gore, M., van Kerrebroeck, P. E., van Breda, H. M. K., Heesakkers, J. (2020). 3-Year Followup of a New Implantable Tibial Nerve Stimulator for the Treatment of Overactive Bladder Syndrome. *J Urol, 204*, 545-550. doi:10.1097/ju.0000000000001024



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E Coin device

Study	Design	Intervention	Results	Comments
MacDiarmid et al. (2019)	6-month multicentre prospective study	eCoin implantable device (n=46)	**70%** of participants had ≥50% decrease in episodes of UUI. 20% were continent. I-QOL scores improved by mean of 48%.	1 participant developed wound cellulitis treated with antibiotics.
Gilling et al. (2021)	12-month follow-up prospective study	eCoin implantable device (n=46)	**65%** of participants had ≥50% decrease in episodes of UUI. **26% were continent.** I-QOL scores improved by a mean of 86%.	1 participant experienced 1cm posterior migration of implant
Janssen et al. (2013)	9-year follow-up study	Urgent-SQ implant (n=8)	7 patients still had implant. **6 out of 7** patients had response on stimulation.	Implants were intact with no migration and/or displacement. 1 participant reported localised ankle discomfort.

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Augmentation 'Clam" Cystoplasty

- As SNS/Botox are more widely used for urge incontinence , clam cystoplasty less common because of risk of
  - excess mucous production,
  - recurrent UTI ,
  - metabolic acidosis etc and
  - rare cancer
- Budzyn et al 2019
- Generally only used in rare cases of urge incontinence with very small bladder capacity

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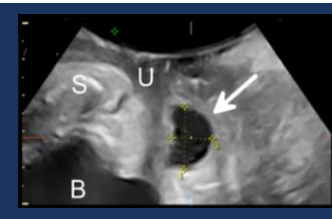
Urethral Diverticuli



Recommendations:

- Patients with UD should be carefully questioned and investigated for co-existing voiding dysfunction and urinary incontinence. (Grade C)
- Patients with UD without SUI should not be offered concomitant prophylactic SUI surgery at the time of urethral diverticulectomy. (Grade C)
- Following appropriate counselling, patients with UD and bothersome SUI may be offered concomitant non-synthetic sling or may be offered an anti-incontinence surgery following urethral diverticulectomy if bothersome SUI persists postoperatively (Grade C)
- Patients should be counselled regarding the possibility of de novo or persistent lower urinary tract symptoms including urinary incontinence despite technically successful urethral diverticulectomy. (Grade C)

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Clinical Trial Outcomes

- Cochrane reviews describe our data quality as “modest at best”
- Severe heterogeinity

- UK Parliamentary review 2020 –
- no reliable information on true number of women who suffered complications, et pain, sexual dysfunction, surgical site infection

- Term “subjective Cure” = more than 20 different terms used.

- OVERALL, NEED CORE DATA OUTCOME SET

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Reiterate message from ICI 2 Chair: Tony Smith

“The medical press is still publishing case series of surgical procedures for stress incontinence that are scientifically flawed... This may mislead, often presenting an over-optimistic view of the outcome. A minimum data set of information should be included in the assessment of any surgical procedure: ”

- Anatomical/ physiological-structured physical examination + urodynamics
- Symptoms (Validated questionnaire)
- Urine loss (pad test)
- Quality of Life (Validated questionnaire)
- Full documentation of all confounding variables
- Economic costs

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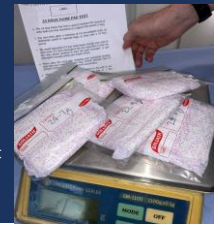
Recent Trends

"Patient reported outcome measures" ; need to have four domains:

1) Symptoms, 2) Functioning, 3) General Health Perception and 4) HRQOL.

- "Composite" outcomes; give a very low success rate, researchers need to report all the items in the composite to allow separate analysis
- PGII/ PGIS Patient Global Assessment of Improvement/ Satisfaction
  - Only give discrete values ("very satisfied", etc)
  - Difficult to correlate with other outcomes as to construct validity



Objective measures of leakage;
1 hour or 24 hour pad test give pre and post surgery data

Cough Stress Test must be at standard volume (> 300 ml); only gives "yes/no" result
3 day bladder diary must include column for leakage episodes

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Summary

ICI 7

- Some older procedures lacking long term data (especially lap colpo and "sling on string")
- Retropubic MUS obviously robust over time, effective, v. large amount of data
- Trans-obturator tape controversial
- Bulking agents : substantial new data
- New implantable PTNS very promising
- Artificial sphincter; new robotic results
- SNS : exciting new developments/ refinements

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