

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

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 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

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

- Neurourol Urodyn. 2011 Jun;30(5):723N8. Detrusor underactivity: a plea for new approaches to a common bladder dysfunction. van Koeveringe GA, Vahabi B, Andersson KE, Kirschner-Herrmans R, Oelke M.
- Neurourol Urodyn. 2014 Jun;33(5):591-6. Detrusor underactivity: Pathophysiological considerations,

models and proposals for future research. ICI-RS 2013. van Koeveringe GA, Rademakers , Birder , Korstanje , Daneshgari , Ruggieri , Igawa , Fry , Wagg

- Neurourol Urodyn. 2015 Jul 31. (EPub) Detrusor underactivity: Development of a bladder outlet resistance-bladder contractility nomogram for adult male patients with lower urinary tract symptoms. Oelke M, Rademakers KL, van Koeveringe GA
- Eur Urol. 2015 Sep;68(3):351-3. The underactive bladder: a new clinical concept? Chapple CR, Osman NI, Birder L, van Koeveringe GA, Oelke M, Nitti VW, Drake MJ, Yamaguchi O, Abrams P, Smith PP.
- Eur Urol. 2014 Feb;65(2):389-98. Detrusor underactivity and the underactive bladder: a new clinical entity? Osman, Chapple CR, Abrams, Dmochowski, Haab, Nitti, Koelbl, van Kerrebroeck, Wein.
- Nat Rev Urol. 2014 Nov;11(11):639-48. Contemporary concepts in the aetiopathogenesis of detrusor underactivity. Osman NI, Chapple CR.
- World J Urol. 2014 Oct;32(5):1177-83. Detrusor contraction power parameters (BCI and W max) rise with increasing bladder outlet obstruction grade in men with lower urinary tract symptoms Oelke M, Rademakers, van Koeveringe.
- Curr Opin Urol. 2016 Jan;26(1):3-10. Detrusor underactivity in men with lower urinary tract symptoms/benign prostatic obstruction: characterization and potential impact... Rademakers, van Koeveringe, Oelke M.

Speaker 1: Prof Christopher Chapple

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 2: Kevin Rademakers, MD

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 3: Prof Matthias Oelke

For the diagnosis of Detrusor underactivity, several urodynamic parameters have been developed mainly for male patients. Cut-off 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. If there is a consensus on diagnosing DU, then, non-invasive tools can be developed such as for example Detrusor wall thickness. A less complicated non-invasive tool is, of course, a questionnaire. These have been studied recently too but their differentiating capacity from, for example, obstruction is still not clear.


Speaker 4: Prof. Gommert van Koeveringe

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

*All financial and non-financial interests with respect to the subject presented during your presentation.

Funding for speaker to attend:

Self-funded

Institution (non-industry) funded

Sponsored by:

Standardisation and Terminology 2016-17 (2022)
DOI: 10.1052/sum.12022

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

Paul Abrams, Linda Cardozo, Magnus Fall, Derek Griffiths, Peter Rosier, Ulf Ulmsten, Philip van Kerrebroeck, Arne Victor, and Alan Wein

- 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

Lower Urinary Tract Symptoms

Weak stream ?

Dysuria ?

Incontinence ?

Frequency ?

Incomplete emptying

Hesitancy ?

Nocturia

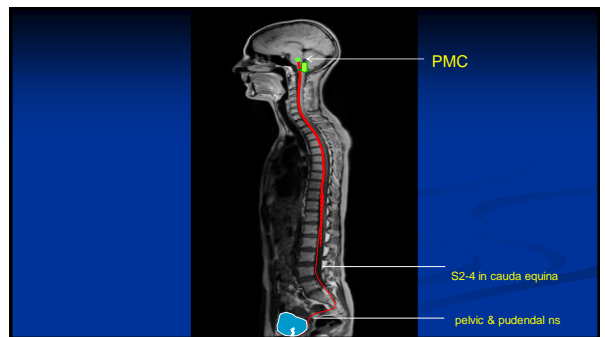
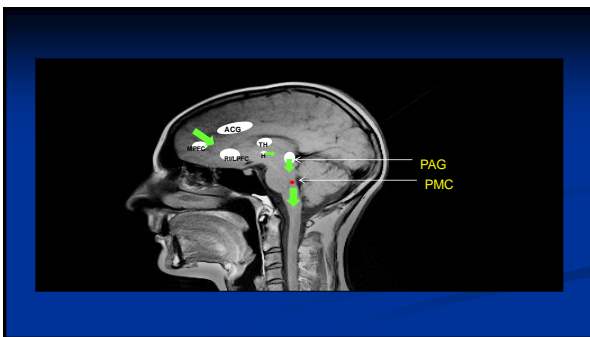
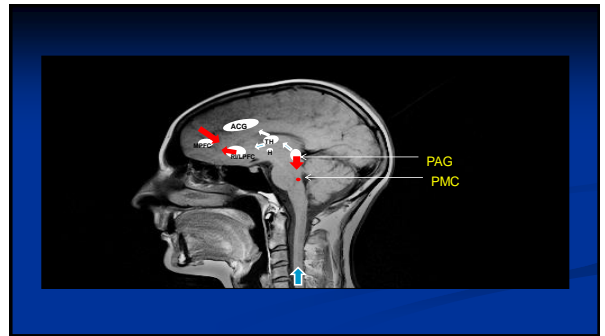
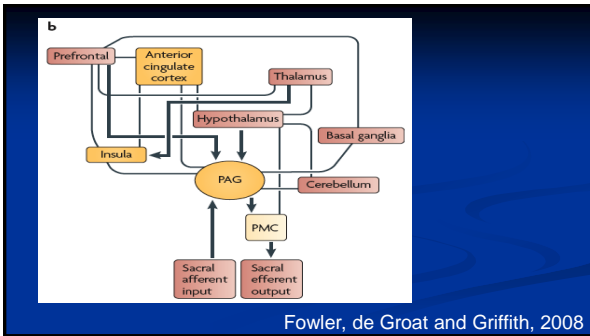
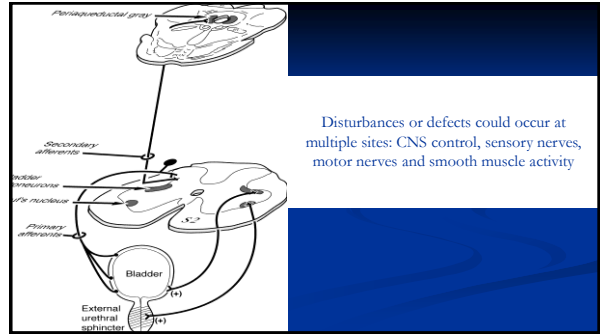
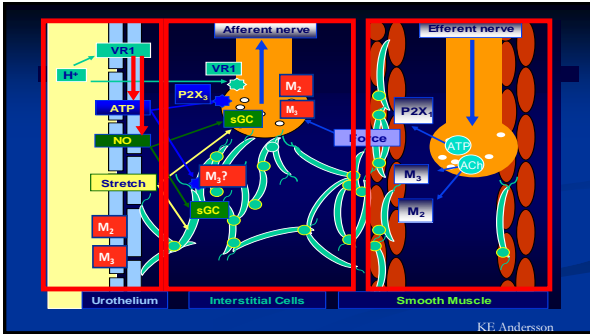
Urgency ?

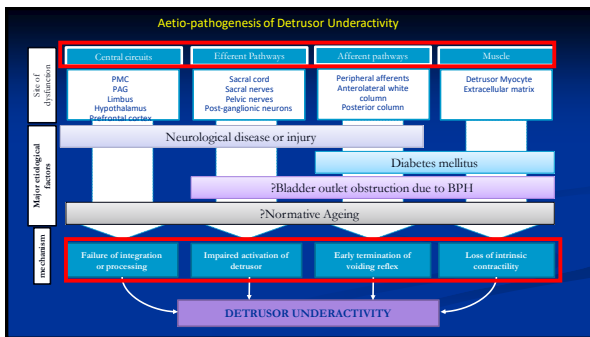
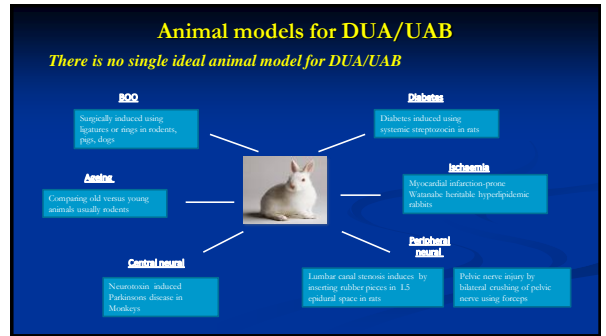
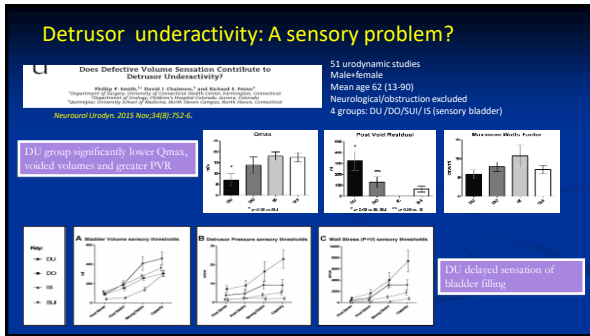
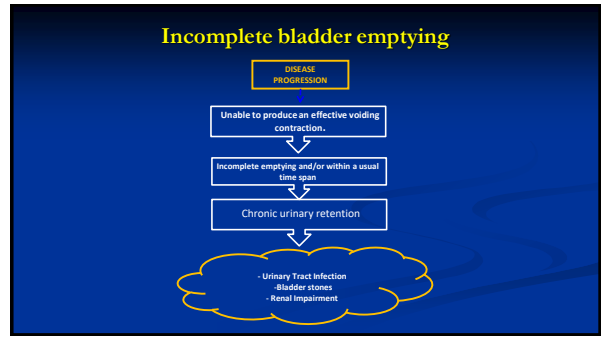
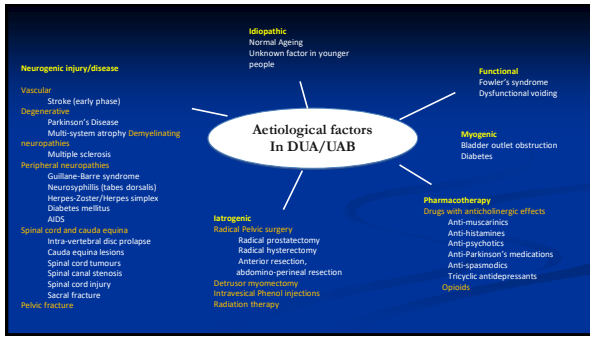
“The Bladder is an Unreliable Witness”¹

- 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

¹ Turner Warwick 1979 Urol Clin N America







Neurology and Urodynamics 36:1151-1154 (2017)

Phenotyping Women With Detrusor Underactivity by Presumed Etiology: Is It Plausible?

Elizabeth T. Brown, Joshua A. Cohn, Melissa R. Kaufman, Roger E. Dmochowski, and William S. Reynolds
Department of Urologic Surgery, Vanderbilt University Medical Center, Nashville, Tennessee

Aims: Underactive bladder (UAB) is a symptom complex with poorly characterized causation. The aim of this study was to determine if clinical and UDS parameters differed between categories of presumed detrusor underactivity (DU) etiologies. **Methods:** A retrospective review was performed at a single institution from 2011 to 2015 to identify patients with symptoms of UAB. Patients were excluded if they were male, had anti-incontinence, or pelvic organ prolapse (POP) surgery within 1 year, or the UDS did not demonstrate DU as defined within. Subjects were stratified by etiology into four cohorts: cardiovascular disease manifestations (CV), cardiac risk factors (CVR), neurologic (N), or idiopathic (I). Patient demographics, comorbidity, symptomatology, physical exam, and UDS parameters were compared. **Results:** A total of 200 patients met inclusion criteria (CV, n = 53 [26.5%], CVR, n = 44 [22%], N, n = 81 [40.5%], I, n = 22 [11%]). Women in the CV cohort were significantly older and more likely to be post-menopausal ($P < 0.001$). There were no differences between cohorts for BMI ($P = 0.48$), recurrent UTI ($P = 0.63$), history of urinary retention (AUR) ($P = 0.65$), POP ($P = 0.49$), American Urological Association Symptom Score (AUA-SS) ($P = 0.06$), presenting symptomatology (urgency, frequency, urgency urinary incontinence, AUR, incomplete emptying, hesitancy, LTI) ($P = 0.97$), or UDS parameters (first sensation [$P = 0.25$], normal desire [$P = 0.88$], strong desire [$P = 0.58$], capacity [$P = 0.11$], Qmax [$P = 0.60$], PVR at Qmax [$P = 0.22$], post-void residual [$P = 0.82$]). **Conclusions:** Though differences were observed between cohorts for age and menopausal status, clinical or urodynamic parameters did not demonstrate distinct differences across presumed categories of etiology, suggesting that the etiologies of DU may be multifactorial. Neurology. Urodynamics. 36:1151-1154, 2017. © 2016 Wiley Periodicals, Inc.

	Mean (SD)
Age	61.9 (15.8)
BMI	28.2 (6.6)
AUA-SS	21.4 (7.4)
	n (%)
Diabetes mellitus	49 (24.5)
Bowel dysfunction	86 (43.0)
Constipation	37 (43.0)
IBS	35 (40.7)
Other	14 (16.3)
Cardiovascular disease:	53 (26.5)
CAD/PVD/MI	32 (60.4)
Arrhythmias	6 (11.3)
Structural/valve disease	7 (13.2)
CVA	8 (15.1)

UDB	Urodynamic parameters mean (SD)				P-value
	Cardiovascular manifestations (%)	Cardiac risk factors (%)	Neurologic etiology (%)	Idiopathic etiology (%)	
Post-void sensation	349 (387)	310 (348)	342 (387)	340 (376)	0.25
Normal desire	210 (230)	210 (231)	208 (231)	208 (230)	0.89
Strong desire	366 (22)	418 (230)	418 (211)	392 (230)	0.59
Capacity	471 (206)	579 (225)	545 (209)	552 (225)	0.11
Post-void Res.	11.3 (13.2)	9.9 (13.2)	12.0 (17.9)	18.5 (26)	0.22
Flow	18.8 (6)	17.8 (6)	17.8 (6)	14.8 (6)	0.09
PIV	192 (232)	178 (248)	166 (241)	162 (236)	0.82

Terminology

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

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

Paul Abrams, Linda Cardozo, Magdal Fell, Derek Griffiths, Peter Hennes, Ulf Chalmers, Philip van Kerrebroeck, Anne Viciano, and Alan Wein

- 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)

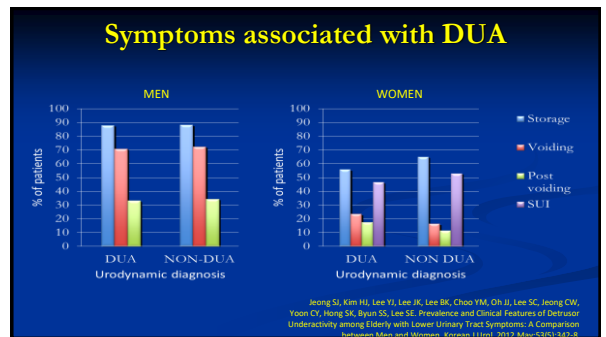
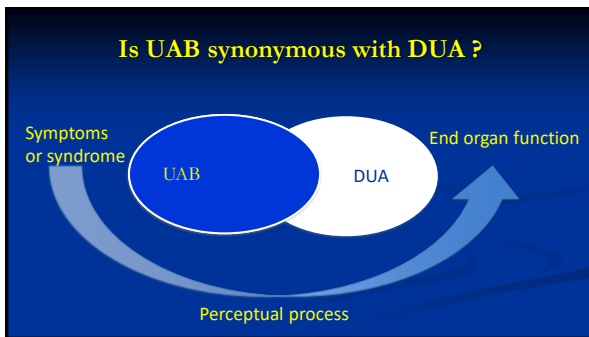
- DU is diagnosed urodynamically and has an ICS definition
 - Based on pressure-flow
 - Characterized by low-pressure, and/or poorly sustained detrusor contraction in combination with low urinary flow
- UAB has no ICS definition
 - “The clinical syndrome that accompanies DU”

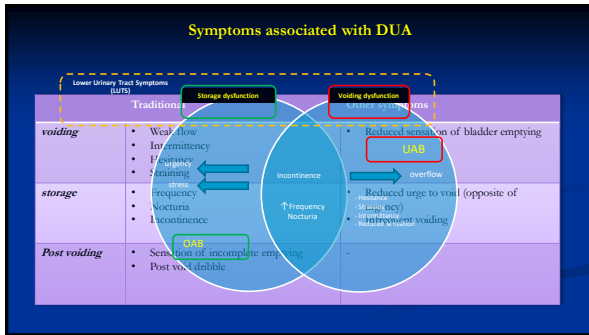
Anderson KE. Curr Opin Urol. 2014

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.





Signs and Symptoms of Detrusor Underactivity: An Analysis of Clinical Presentation and Urodynamic Tests From a Large Group of Patients Undergoing Pressure-Flow Studies

-Retrospective analysis
-Prospective database
-1788 patients (men+women)

Confirms symptoms associated with DUA

Men	Women
High occurrence for DU vs BOO Decreased urinary stream Intermittent urinary stream Hesitancy Urgency Abnormal and/or decreased sensation Abnormal urine to void Incomplete voiding Post void dribble	High occurrence for DU vs BOO Decreased urinary stream Intermittent urinary stream Hesitancy Urgency Abnormal and/or decreased sensation Abnormal urine to void Incomplete voiding Post void dribble
DU vs BOO Decreased urinary stream Intermittent urinary stream Urgency	DU vs BOO Decreased urinary stream Intermittent urinary stream Urgency

Suggest some symptoms may differentiate DUA from BOO

Eur Urol. 2016 Feb;69(2):361-9.

The patient experience of underactive bladder

A. Urens, N. Cottenif, C. Harding, C. Hillary, C. Chapple, M. Klawer, D. Bongert, Z. Hakonar, P. Abrams
 *British Urological Institute, UK; *Protona Hospital, Newcastle; *Royal Hallamshire Hospital, Sheffield; *Nestlé Pharma B.V., Leiden, The Netherlands

Background

- Detrusor underactivity (DU) is a common but poorly understood lower urinary tract dysfunction, diagnosed following urodynamic testing.
- The working definition of underactive bladder (UAB) is currently proposed as:

"A symptom complex suggestive of detrusor underactivity and is 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."

Methods

- 47 concept elicitation interviews conducted (32 male, 15 female, mean age 64 years)

In-depth, semi-structured interviews → Qualitative analysis of the transcripts → 1st version of the PRO generated

Abstract 995 EAU 2016

Results

More than 30 symptoms, signs or impacts were reported.

Sample or diagnostic group	Total number of patients (n)	Males n (%)	Females n (%)	Mean age and range (years)	Currently or historically catheterised n (%)	Uroodynamically confirmed DU/BOO n (%)
DU (only)	39	12 (31%)	27 (69%)	69 (28-88)	13 (33%)	15 (38%)
DU with other co-existing urological conditions (DU, BOO, BOO+DU)	25	12 (48%)	13 (52%)	68 (38-87)	13 (52%)	20 (80%)
BOO	3	2 (67%)	1 (33%)	67 (66-72)	0	1 (33%)

Abstract 995 EAU 2016

Proposed Definition

Underactive bladder is characterised 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**.

- * Underactive bladder occurs in association with diverse pathophysiology and based on current knowledge there is no single distinguishing symptom.
- ** Storage symptoms are varied and may be highly prevalent, including nocturia, increased daytime frequency, reduced sensation of filling, and incontinence. Underlying mechanisms of storage symptoms are diverse, and are often related to a significant post voiding residual urine volume.

Chapple CR, Ooms NI, Binder L, van Kooyck G-A, Oude M, Nitti V-P, Drake MJ, Dmochowski R, Yamaguchi O, Abrams D, Smith LP, Wix A.

- Associated factors
 - Gender
 - Age
 - Neurogenic versus Non-Neurogenic
- Associated Investigation
 - Bladder Diary
 - Flow rate/ Post Void Residuals
 - Pressure/Flow Urodynamics

Refining the definition

There needs to be:

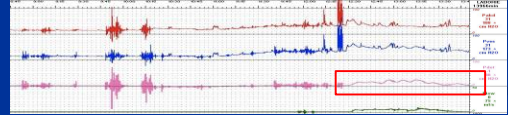
- Qualitative research to look for characteristic symptoms
- Quantitative research in uroodynamically defined DU patients

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

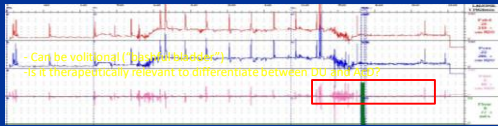
DU - ICS Definition (2002)

“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**”



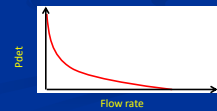
Acontractile detrusor (AcD) – ICS (2002)

“(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: Q_{max} and $P_{det}@Q_{max}$
- Urodynamic estimation of isometric contraction strength based on Bladder outlet relation (BOR) (Griffiths 1972)



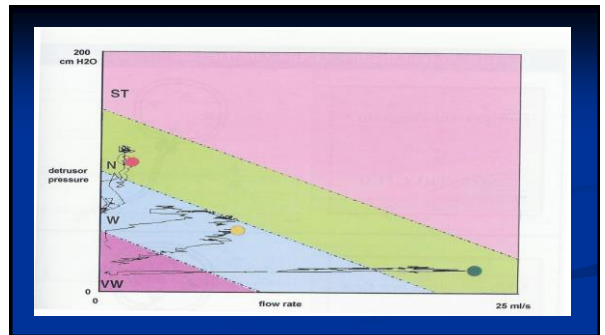
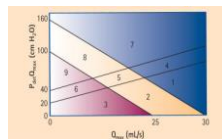
The Bladder Outflow Obstruction Index (BOOI)

Most authors use ranges for $P_{det}@Q_{max}$ (e.g. <40) and Q_{max} (e.g. <15)

BOOI (Abrams Griffiths Number)

$P_{det}@Q_{max} - 2 \times Q_{max}$

- Unobstructed :- $\leq 20 \text{ cmH}_2\text{O}$
- Equivocal $\leq 20-40 \text{ cmH}_2\text{O}$
- Obstructed $> 40 \text{ cmH}_2\text{O}$



Assessing bladder voiding function: Strength

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)

PIP can be calculated using formula:
 $PIP = Pdet @ Qmax + kQmax$
 K: fixed constant, represents slope of BOR
 in older men = $5cmH2O/ml/s$ / $(12-3cmH2O)$
 (in older women $1cmH2O/ml/s$)

>150 strong contractility
 100-150 normal contractility
 50-100 weak contractility
 <50 very weak contractility

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

BCI
 Strong >150
 Normal 100-130
 Weak <100

ORIGINAL CLINICAL ARTICLE | WILEY | © ICS 2017

Comparison of three methods to analyze detrusor contraction during micturition in men over 50 years of age

Celine ten Donkelaar S MD | Peter Rosier FWM, MD, PhD | Laetitia de Kort MO, MD, PhD

Aims: To grade detrusor voiding contraction three parameters are used: the Schäfer pressure-flow nomogram (LinPURR), the bladder contractility index (BCI) and the maximum Watt factor (W_{max}). Because these methods to quantify detrusor contraction and/or to diagnose detrusor underactivity (DU) have not yet been mutually compared, this study compares these three methods of grading detrusor contraction.

Materials and Methods: Evaluated were 1420 urodynamic pressure-flow studies from 1222 men (aged >50 years) with lower urinary tract symptoms (LUTS). Excluded were patients with evidence of urethral stricture and W_{max} making contraction. We compared the BCI, LinPURR, and W_{max} .

Results: The comparison showed a high agreement between the methods.

Assessing bladder voiding function: Strength

Occlusion tests

Isovolumetric pressure can be measured directly by mechanically obstructing the flow of urine

- (1) Stop test: interruption of urine flow after it has begun (voluntary or mechanical)
- (2) Continuous occlusion test: urine outflow blocked before and during the course of the voiding contraction.

Advantages:-

- Real time indication of isovolumetric strength
- Good test retest reliability
- No calculations

Limitations:-

- Impractical and painful and impossible in some patients
- Can underestimate contraction strength (voluntary stop test)
- Need to repeat voiding phase (continuous occlusion)

Interventions for DUA/UAB

- Bladder Related (Increasing intravesical pressure or facilitating bladder contractility)**
 - External compression, Valsalva
 - Promotion / initiating reflex contraction
 - Pharmacologic therapy
 - Electrical stimulation
 - Reduction cystoplasty
 - Bladder myoplasty
- Outlet Related (Decreasing outlet resistance)**
 - At a site of anatomic obstruction
 - Pharmacologic therapy
 - Transurethral resection
 - V-V. ptery
 - At level of smooth sphincter
 - Pharmacologic therapy
 - Transurethral resection
 - V-V. ptery
 - At level of striated sphincter
 - Behavioural therapy @ Biofeedback
 - Pharmacologic therapy
 - Intermittent catheterisation
 - Continuous catheterisation
 - Urinary diversion (conduit)
- Circumventing the Problem**
 - Intermittent catheterisation
 - Continuous catheterisation
 - Urinary diversion (conduit)

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 10-year urodynamic follow up of men diagnosed with DU ($Q_{max} < 15 \text{ ml/s}$, $P_{det} @ Q_{max} < 40 \text{ cmH}_2\text{O}$) initially managed with watchful waiting (no catheterisation)
- Sixty-nine men who initially opted for watchful waiting were followed-up with PFS (mean follow up 13.6 years).
- No significant deterioration in symptomatic or urodynamic parameters over time.
- Only eleven patients failed the initial watchful waiting approach and underwent TURP, 8 (11.6%) due to worsening LUTS and 3 (4.35%) due to acute retention.

Thomas AW, Cannon A, Bartlett E, BJU International. 2005 Dec; 96:1295-300

Monitoring

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

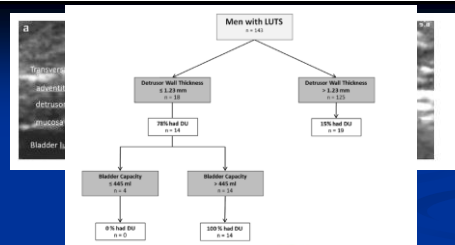
World J Urol (2017) 35:153-159
DOI 10.1007/s12005-016-1902-7

ORIGINAL ARTICLE

Ultrasound detrusor wall thickness measurement in combination with bladder capacity can safely detect detrusor underactivity in adult men

Kevin L. J. Rademakers¹, Gommert A. van Kooijevaar¹, Matthias Oelke², on behalf of the FORCE Research Group, Maastricht and Hannover

Results The study population consisted of 143 consecutive men with medians of 62 years, IPSS 16, and prostatic volume 35 ml. In total, 33 patients (23.1 %) had DU. CART analysis showed that all men with DWT $\leq 1.23 \text{ mm}$ plus bladder capacity $> 445 \text{ ml}$ had DU. This multivariate model has a sensitivity of 42 %, specificity of 100 %, positive predictive value of 100 %, and negative predictive value of 85 %.



Conclusions This study showed that all men with ultrasound DWT $\leq 1.23 \text{ mm}$ + bladder capacity $> 445 \text{ ml}$ have DU. Combination of these two tests could help physicians to diagnose DU noninvasively in clinical practice. A prospective independent study should confirm these results.

Epidemiology

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

Potential epidemiological measure of DU:	For	Against
LUTS	• Feasible to collect large scale data using questionnaires or surveys	• Confounding found in other LUTS questionnaires. • Impossible to differentiate from BPOC.
Flow measurement	• Non-invasive and easy to perform • Objective data • Positive findings in DU	• Does not distinguish DU from BPOC.
Postvoid Residual	• Non-invasive and easy to perform • Objective data	• Flow test across reliability • No accepted threshold for abnormal PVR • May not be a consistent feature of DU
Urinary retention	• Feasible to collect large scale data	• Variable definitions • No accepted threshold for PVR for retention • Multifactorial aetiology

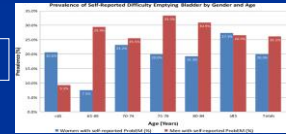
Prevalence of DUA in clinical studies

Study	Population	Size	Age range (yrs)	Prevalence of DUA (% of asymptomatic detrusors)
Peters et al 2001		541	26-89	10%
Kane et al 2007	Male	1487	46-96	16.6%
Wong et al 2013	M/F	139	43-85	17%
Mean	<ul style="list-style-type: none"> DUA affects 9-28% of men under the age of 50 years 48% in those over 70 years undergoing urodynamics 			
Mean	<ul style="list-style-type: none"> DUA is found in 12-45% of women undergoing urodynamic studies is more prevalent amongst the institutionalized elderly. 			
Jung et al 2012	Male	812	94	40.2%
	Female	547	94.5	13.3%
Bonvicini et al 2009	Male	17	87	30% Male
	Female	77		
Bonvicini et al 2016	Female	97	87.6*	45%*
Greuter et al 1999	Female	206	82.6 ± 10.8 yrs*	19%
Volinniet et al 2011	Female	442	92.0	13.8%

How common are UAB symptoms?

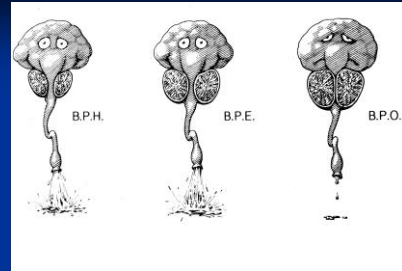
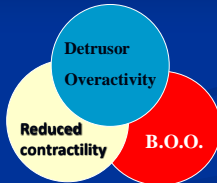
Survey 633 subjects (54 % men, 46 % women)
 Age range 33 to 92 years old, 97 % > 60, mean of 74.3 years

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



Epidemiology and demographics of the underactive bladder: a cross-sectional survey. *Int J Urol Nephrol*. 2014;5(4):56-60. Sengul LS, Topolcan S, Ciftci D, Dulfener C, Chancellor D, Okanisi J, Verzeckar A, Dao E, Lajiness M, Diskara A, Chancellor M.

Patho-physiology of LUTS



Definition of Benign Prostatic Hyperplasia

- Prostate Histology (BPH)
 - Anatomy of the prostate: McNeal 1978 *Invest Urol* 15;340-345
 - Age related prevalence
 - 'Common in men over 50 years of age, histological criteria for BPH are present in 88% of men over 80 yrs'
 - Lytton B. 1968 *J Urol* 99; 639-645, Berry SJ et al. 1984 *J Urol* 132; 474-9, Boyle et al 2001 5th *Int Cons BPH* 19-48
- Prostate Size (BPI)
 - 'Poor correlation between prostate size, urinary flow rate & symptoms' Barry MJ et al 1993 *J Urol* 150; 351-358

Definition of Benign Prostatic Hyperplasia

- Urodynamics
 - Frequency volume charts
 - Frequency/ Nocturia/ Volume voided
 - Flow rate
 - 'Uroflowmetry in general and Qmax in particular, lack specificity for a reliable urodynamic diagnosis of the cause of abnormal voiding'

Qmax <10ml/sec	90% BOO
Qmax 10-14ml/sec	67% BOO
Qmax >15ml/sec	30% BOO

Abrams P et al 2001 5th *Int Cons BPH* p236

Definition of Benign Prostatic Hyperplasia

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

Abrams P et al 2001 5th Int Congr BPH p266-268

What is a significant post voiding residual?

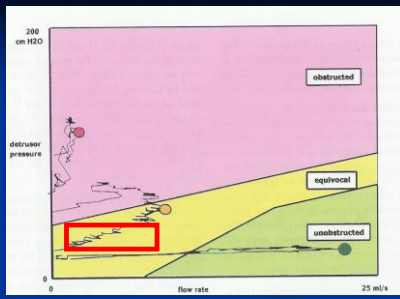
The concept of Bladder Voiding Efficiency
>40% of the Functional Bladder Capacity (volume voided +residual)

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 Congr BPH p261



Original Article
doi:10.1016/j.urocl.2015.12.001
http://dx.doi.org/10.1016/j.urocl.2015.12.001
pubmed 26061-4777 - abstract 26061-4841

Underactive Bladder: Clinical Features, Urodynamic Parameters, and Treatment

Methods: A retrospective chart review of consecutive urodynamic studies performed on voiding dysfunction between 2012 and 2014 was conducted to identify patients with detrusor underactivity. Detrusor underactivity was defined by a bladder contractility index of less than 100. Charts and urodynamic tracings were examined for patient demographics, suspected risk factors, presenting symptoms, urodynamic parameters, and treatment undertaken. Descriptive statistics were utilized to analyze the data.

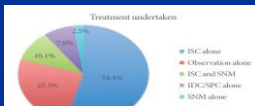
Results: The prevalence of detrusor underactivity in this study was 23% (79 of 341). Average age of the patients was 59.2 years (range, 19–90 years). Women represented 68.4% (54 of 79) of the patients. The most common reported symptoms were urinary urgency (63.3%), weak stream (61.6%), straining (57.0%), and urinary frequency (57.0%). Urinary incontinence, urinary urgency, and straining were noted in 46.5% and 19.0% of the patients, respectively. The most common management was intermittent self-catheterization in 54.4%, followed by observation/conservative treatment in 25.3% and sacral neuromodulation in 12.7%.



Fig. 1. Bar graph demonstrating prevalence of urinary symptoms among identified underactive bladder patients. UTI, urinary tract infection.

Original Article
doi:10.1016/j.urocl.2015.12.001
http://dx.doi.org/10.1016/j.urocl.2015.12.001
pubmed 26061-4777 - abstract 26061-4841

Underactive Bladder: Clinical Features, Urodynamic Parameters, and Treatment



Pie chart demonstrating treatment undertaken by underactive bladder patients in study cohort. ISC, intermittent self-catheterization; SNM, sacral neuromodulation; ISC, intermittent self-catheterization; SPN, suprapubic catheter.

Original Article - Lower Urinary Tract Dysfunction
Inquiry Clin Med 2017;5(6):247-254
http://dx.doi.org/10.1177/20755824177058247
ISSN 2466-0893 - eISSN 2466-054X

INVESTIGATIVE AND CLINICAL UROLOGY
ICUROLOGY

How do we diagnose detrusor underactivity? Comparison of diagnostic criteria based on an urodynamic measure

Seong Jin Jeong^{1,2}, Jung Keun Lee^{1,2}, Kwang Mo Kim^{1,2}, Harim Kook^{1,2}, Sung Yong Cho^{1,2}, Seung-June Oh^{1,4}
Department of Urology, Seoul National University College of Medicine, Seoul, Department of Urology, Seoul National University Bundang Hospital, Seongnam, Department of Urology, Seoul Metropolitan Government Seoul National University Borame Medical Center, Seoul, Department of Urology, Seoul National University Hospital, Seoul, Korea

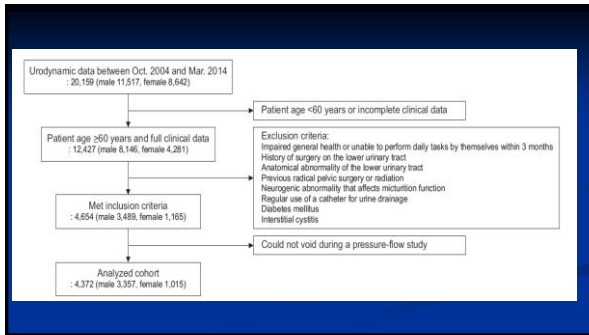


Table 1. Previously proposed urodynamic criteria for diagnosing detrusor underactivity in the literature

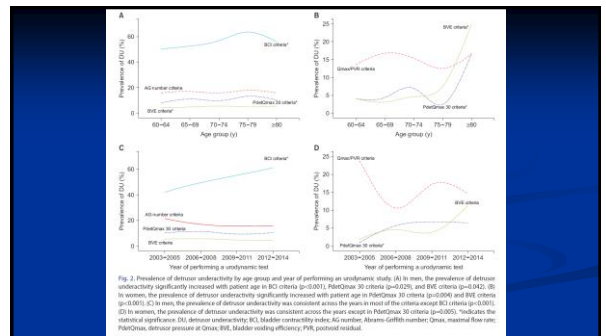
Study	Target population	Diagnostic criteria	Byname in the present study
Abrams (1999) [4]	Male	BCI <100	BCI criteria
Nitti et al. (2002) [5]	Male	AG number <20 and free outflow Qmax <12 mL/s	AG number criteria
Alarabanel and Marcus (2007) [6]	Male	PdetQmax <30 cmH ₂ O and PFS Qmax <10 mL/s	PdetQmax 30 criteria
Gammie et al. (2016) [8]	Male	BCI <100 and AG number <20 and BVE% <90	BVE criteria
Grouzet et al. (1999) [7]	Female	Qmax <12 mL/s with ≥100 mL voided or PVR volume >150 mL on 2 or more free flow readings	Qmax/PVR criteria
Alarabanel and Marcus (2007) [6]	Female	PdetQmax <30 cmH ₂ O and PFS Qmax <10 mL/s	PdetQmax 30 criteria
Gammie et al. (2016) [8]	Female	PdetQmax <30 cmH ₂ O and PFS Qmax <15 mL/s and BVE% <90 and absence of clinical obstruction	BVE criteria

BCI, bladder contractility index; AG, number, Abrams-Griffith number; Qmax, maximum flow rate; PdetQmax, detrusor pressure at maximal flow rate; PFS, pressure-flow study; BVE, bladder voiding efficiency; PVR, postvoid residual.

Age (y)	No. of patients	3,357 (96.6)	1,015 (23.2)
60-64	789 (23.5)	327 (32.2)	
65-69	1,055 (31.4)	301 (29.7)	
70-74	874 (26.0)	245 (24.1)	
75-79	467 (13.9)	106 (10.4)	
≥80	172 (5.1)	36 (3.5)	

Urodynamic criteria	No. (%)
Men (n=3,357)	
BCI criteria	1,873 (55.8)
AG number criteria	557 (16.6)
PdetQmax 30 criteria	181 (5.4)
BVE criteria	345 (10.3)
Women (n=1,015)	
Qmax/PVR criteria	151 (14.9)
PdetQmax 30 criteria	97 (9.6)
BVE criteria	65 (6.4)

BCI, bladder contractility index; AG, number, Abrams-Griffith number; Qmax, maximal flow rate; PdetQmax, detrusor pressure at Qmax; BVE, bladder voiding efficiency; PVR, postvoid residual.



Catheterisation

Indwelling catheter

Suprapubic catheter

Intermittent catheter

Clean intermittent self-catheterisation:

- Most prevalent method of bladder management in patients with UAB
- Complications rare compared with indwelling/suprapubic catheters
 - UTI, 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

Increasing intravesical pressure/bladder contractility

- Parasympathetic agents (bethanechol, distigmine)
- Prostaglandins
- Blockers of inhibition
- Opioid receptor antagonists

Decreasing outlet resistance

- α₁-adrenergic receptor antagonists (phenoxybenzamine, prazosin, terazosin / doxazosin, alfuzosin / tamsulosin, silodosin)
- Benzodiazepines
- Baclofen
- Dantrolene
- Botulinum toxin
- [anti-androgens for reducing prostatic size, e.g. finasteride]

- Available studies do not support the use of parasympathomimetics¹
 - Specifically when frequent and/or serious possible side effects are taken into account
- Combination therapy with a cholinergic drug and an alpha-blocker appears to be more useful than monotherapy²

1. Ransohoff JF. *Am J Surg* 2017;199:12. 2. Yamada H. *Int J Urol* 2004;11:69-92.

Pharmacological Reports

Pharmacotherapy in detrusor overactivity: A new challenge for urologists and pharmacologists (from lab to clinic)

ABSTRACT

Higher incidence of functional urinary bladder dysfunction (detrusor overactivity – DO and detrusor underactivity – DU) occurs in elderly people. Effective therapy is widely used in patients with DO, in contrast DU seems to be a serious burden for the older population due to the lack of successful treatment. The aim of the study was to review the potential pharmacological targets in DU treatment in the animal model. This review is based on systemic literature research. The Medline/Pubmed, Scopus, Embase, and Web of Science databases were searched in order to identify original and review articles, as well as editorials relating to underactive bladder, detrusor underactivity. The following Medical Subject Headings (MeSH) were used: detrusor underactivity, detrusor underactivity, detrusor underactivity models, humans and therapy. 19 papers met the criteria and were included for this review. 19 papers met the criteria and were included for this review. The pathophysiology of DU and its animal models were described. Moreover, the potential pharmacological targets in DU therapy were discussed, such as bombesin receptors, prostaglandin-, ATP-, NO-, CGRP-, SP-, Dopamine-, NGR-, M2-, and agrin-dependent pathways. In conclusion, due to the lack of effective treatment strategies in DU, further research is necessary. Close cooperation between urologists and pharmacologists should be maintained for optimal research on DU pharmacotherapy.

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Intravesical Electrical Stimulation (IVES)

- Establishes conscious control of the initiation and completion of a micturition reflex
- Activates specific mechanoreceptors in the bladder wall
- Lowers the micturition threshold and enhances reflex amplitude
- Randomised placebo-controlled trials lacking
- Achieved long-term normalisation of voiding in 20/24 (83%) children with idiopathic, and 8/20 (40%) with neurogenic, underactive detrusor!
- 10 daily 60 min session (5 b.t.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 6-815) 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

IVES induced change in residual urine volume of individual responsive children*

J. Urol. Neuro. Urodyn. 2016;35(2):271-274

Electrical stimulation

Intravesical stimulation (IVES)

Brindley device (S2, S3, S4 nerve roots)

Sacral nerve modulation

- Used for idiopathic urinary retention
- Effective, but invasive

Brindley device!

- Ventral root stimulation +/- dorsal root section / sacral deafferentation
- 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
- Emitting voiding may occur in spurts at above-normal bladder pressures

Sacral nerve modulation

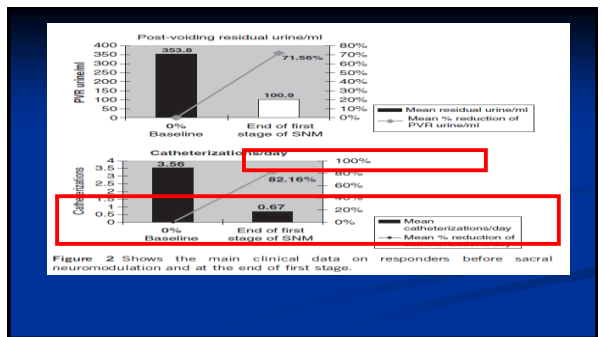
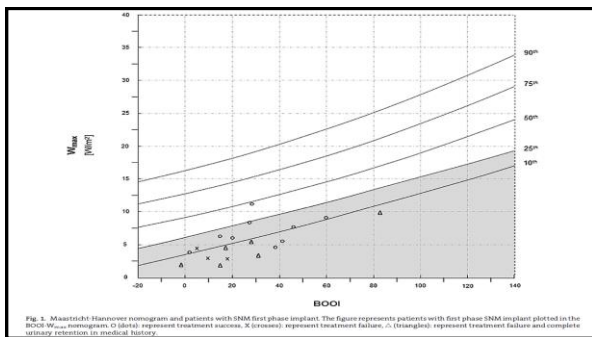
- In patients with retention (n=31), achieved decrease in:
 - mean volume per catheterisation (379.9 ± 183.8 to 109.2 ± 184.3 mL)
 - mean number of catheterisations (5.3 ± 2.8 to 1.9 ± 2.8)

J. Urol. Neuro. Urodyn. 2012;31(2):271-274. Copyright © 2012 Wolters Kluwer Health | Lippincott Williams & Wilkins. All rights reserved.

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

Kevin L. Rademakers, Jamie M. Drossaers, Philip E. van Keghelbroeck, Matthias Oelke, and Gormet A. van Kesterling

Methods and Evidence: The aim of this study was to assess whether the use of the new BOO-contraction (Maastricht-Hannover) nomogram can identify and predict SNM non-responders. Our results in 18 men showed that only 20% of patients below the 10th percentile, but 86% of men between the 10 and 25th percentiles of the nomogram can be treated successfully with SNM. All successfully treated patients voided without needing self-catheterisation. **Conclusions:** This pilot study showed for the first time that SNM treatment response in male patients with impaired bladder emptying can be predicted with the BOO-contraction (Maastricht-Hannover) nomogram. Men below the 10th percentile are likely to be treatment non-responders, whereas the majority of men above the 10th percentile are responders. *Neurourol. Urodyn.* © 2016 Wiley Periodicals, Inc.



Surgical options

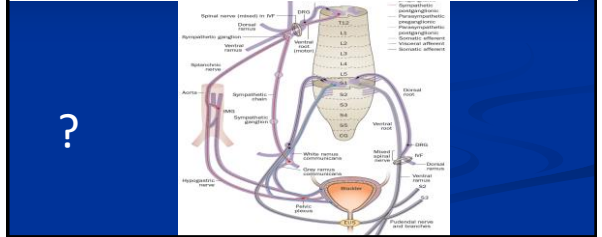
- Trans-urethral resection of prostate
- Intrasphincteric Botulinum Toxin
- Reduction cystoplasty
- ? Stem cells/ Tissue engineering
- Neural Reconstruction
- Detrusor Myoplasty—bladder wrap



Neural reconstruction methods of restoring bladder function

Sandra M. Gomez-Ariza, Mary F. Barbo, William C. de Groat, Justin M. Brown, Gerald F. Tuto, Jacques Corcos, Susan B. Fedro, Alan S. Grovesman and Michael R. Roggiani Sr

Gomez-Ariza, S. M. et al. Nat. Rev. Urol. 12, 100–118 (2016); published online 10 February 2015; doi:10.1038/nrurol.2015.4



Functional Detrusor Myoplasty for Bladder Acontractility: Long-Term Results

The Latissimus Dorsi Detrusor Myoplasty for Functional Myoplasty for Functional Treatment of Bladder Acontractility

Functional Urinary Bladder Wall Substitute Using a Free Innervated Latissimus Dorsi Muscle Flap

Restoration of voluntary emptying of the bladder by transplantation of innervated free skeletal muscle

Latissimus Dorsi Detrusor Myoplasty to Restore Voiding in Patients with an Acontractile Bladder – Fact or Fiction?

FREE NEUROVASCULAR TRANSFER OF LATISSIMUS DORSI MUSCLE FOR THE TREATMENT OF BLADDER ACONTRACTILITY: II. CLINICAL RESULTS

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

Multicenter Study: n=24

- Participating Centers:
- Maastricht, Netherlands
 - Mumbai, India
 - Munich Germany
 - Tuebingen, Germany

Functional Detrusor Myoplasty in Bladder Acontractility: Long-Term Results

Georgios Gakis,* Milomir Ninkovic, Gommert A. van Koeveering,† Shailesh Raina, Gustavo Sturtz, Karl-Dietrich Sievert and Arnulf Stenzl

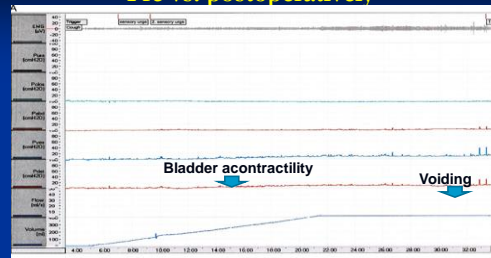
Eberhard-Karls University, Tuebingen (GG, KDS, AS) and Department of Plastic and Reconstructive Surgery, Hospital Munich-Bogenhausen, Munich (MN, GDS), Germany; Department of Urology, Massachusetts General Hospital, Boston, MA (MS), USA; Department of Urology, JSSM Hospital & Research Centre, Mumbai, India (SR)

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Causes for bladder acontractility (n=24)

Etiology	Number of patients
Traumatic spine fracture (Th12 or L1)	9
Tethered-cord syndrome	4
Lumbar hernia of nuclei pulposi	3
Megacystis and benign outlet obstruction	2
Voiding dysfunction post hysterectomy	1
Sacral myelomeningocele	1
Idiopathic	4

Voiding under urodynamic assessment Pre vs. postoperatively



Complications

Table 5. Major postoperative complications by voiding result

	No.	Grade*	Complete	Partial	None
Pt ₁	8	---	5	1	2
Complication	9	---	6	1	2
Deep vein thrombosis	1	I	1		
Pulmonary embolism	1	II		1	
Pelvic abscess requiring temporary drainage	3	IIIa (2), IIIb (1)	2		1
Congruent syndrome of nonoperated shoulder	1	IIIa	1		
Wound healing disorder	1	IIIa			1
Persistent seroma of operated shoulder requiring surgical intervention	2	IIIb	2		

* According to Clavien classification.

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 aetiopathogenesis
- There is a lack of any simple and effective treatments

The Question is - to what extent can we *trust* the Current Evidence?



Workshop schedule

09:00	DETRUSOR UNDERACTIVITY, WHEN SHOULD WE CONSIDER THIS CONDITION IN PATIENTS WITH LUTS ?
	CHRISTOPHER R CHARLIE
09:15	WHAT IS NEW CONCERNING DETECTION OF DETRUSOR UNDERACTIVITY IN LUTS PATIENTS ?
	KEVIN RADMAGERS
09:30	WHAT IS NEW CONCERNING DIAGNOSIS OF DETRUSOR UNDERACTIVITY IN MALE PATIENTS WITH LUTS ?
	MATTHIAS DELLE
09:45	WHEN DO WE HAVE TO CONSIDER, AND WHAT DO WE NEED TO DIAGNOSE DETRUSOR UNDERACTIVITY IN FEMALE PATIENTS ?
	GERMERT A VAN KODERENGE
10:00	DISCUSSION
	ALL
10:15	WHAT FUTURE STEPS ARE NECESSARY TO DETECT AND CONFIRM THE CONDITION, DEVELOP THERAPIES, AND FOLLOW UP AFTER TREATMENT ?
	CHRISTOPHER R CHARLIE MATTHIAS DELLE KEVIN RADMAGERS GERMERT A VAN KODERENGE

Maastricht UMC+

Affiliations to disclose[†]:

No disclosures

† All financial ties (over the last year) that you may have with any business organization with respect to the subjects mentioned during your presentation

Funding for speaker to attend:

Self-funded

Institution (non-industry) funded

Sponsored by:

Maastricht UMC+

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

Maastricht UMC+

Literature overview 2017: the numbers

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

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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

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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

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Introduction

DU UAB vs. DO OAB

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PROs Subjective outcomes

FVC Physiological measurement

Objective outcomes

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

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Symptoms

Total research from 1995-2007 and 2011-15, 18, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 197, 198, 199, 200, 201, 202, 203, 204, 205, 206, 207, 208, 209, 210, 211, 212, 213, 214, 215, 216, 217, 218, 219, 220, 221, 222, 223, 224, 225, 226, 227, 228, 229, 230, 231, 232, 233, 234, 235, 236, 237, 238, 239, 240, 241, 242, 243, 244, 245, 246, 247, 248, 249, 250, 251, 252, 253, 254, 255, 256, 257, 258, 259, 260, 261, 262, 263, 264, 265, 266, 267, 268, 269, 270, 271, 272, 273, 274, 275, 276, 277, 278, 279, 280, 281, 282, 283, 284, 285, 286, 287, 288, 289, 290, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304, 305, 306, 307, 308, 309, 310, 311, 312, 313, 314, 315, 316, 317, 318, 319, 320, 321, 322, 323, 324, 325, 326, 327, 328, 329, 330, 331, 332, 333, 334, 335, 336, 337, 338, 339, 340, 341, 342, 343, 344, 345, 346, 347, 348, 349, 350, 351, 352, 353, 354, 355, 356, 357, 358, 359, 360, 361, 362, 363, 364, 365, 366, 367, 368, 369, 370, 371, 372, 373, 374, 375, 376, 377, 378, 379, 380, 381, 382, 383, 384, 385, 386, 387, 388, 389, 390, 391, 392, 393, 394, 395, 396, 397, 398, 399, 400, 401, 402, 403, 404, 405, 406, 407, 408, 409, 410, 411, 412, 413, 414, 415, 416, 417, 418, 419, 420, 421, 422, 423, 424, 425, 426, 427, 428, 429, 430, 431, 432, 433, 434, 435, 436, 437, 438, 439, 440, 441, 442, 443, 444, 445, 446, 447, 448, 449, 450, 451, 452, 453, 454, 455, 456, 457, 458, 459, 460, 461, 462, 463, 464, 465, 466, 467, 468, 469, 470, 471, 472, 473, 474, 475, 476, 477, 478, 479, 480, 481, 482, 483, 484, 485, 486, 487, 488, 489, 490, 491, 492, 493, 494, 495, 496, 497, 498, 499, 500, 501, 502, 503, 504, 505, 506, 507, 508, 509, 510, 511, 512, 513, 514, 515, 516, 517, 518, 519, 520, 521, 522, 523, 524, 525, 526, 527, 528, 529, 530, 531, 532, 533, 534, 535, 536, 537, 538, 539, 540, 541, 542, 543, 544, 545, 546, 547, 548, 549, 550, 551, 552, 553, 554, 555, 556, 557, 558, 559, 560, 561, 562, 563, 564, 565, 566, 567, 568, 569, 570, 571, 572, 573, 574, 575, 576, 577, 578, 579, 580, 581, 582, 583, 584, 585, 586, 587, 588, 589, 590, 591, 592, 593, 594, 595, 596, 597, 598, 599, 600, 601, 602, 603, 604, 605, 606, 607, 608, 609, 610, 611, 612, 613, 614, 615, 616, 617, 618, 619, 620, 621, 622, 623, 624, 625, 626, 627, 628, 629, 630, 631, 632, 633, 634, 635, 636, 637, 638, 639, 640, 641, 642, 643, 644, 645, 646, 647, 648, 649, 650, 651, 652, 653, 654, 655, 656, 657, 658, 659, 660, 661, 662, 663, 664, 665, 666, 667, 668, 669, 670, 671, 672, 673, 674, 675, 676, 677, 678, 679, 680, 681, 682, 683, 684, 685, 686, 687, 688, 689, 690, 691, 692, 693, 694, 695, 696, 697, 698, 699, 700, 701, 702, 703, 704, 705, 706, 707, 708, 709, 710, 711, 712, 713, 714, 715, 716, 717, 718, 719, 720, 721, 722, 723, 724, 725, 726, 727, 728, 729, 730, 731, 732, 733, 734, 735, 736, 737, 738, 739, 740, 741, 742, 743, 744, 745, 746, 747, 748, 749, 750, 751, 752, 753, 754, 755, 756, 757, 758, 759, 760, 761, 762, 763, 764, 765, 766, 767, 768, 769, 770, 771, 772, 773, 774, 775, 776, 777, 778, 779, 780, 781, 782, 783, 784, 785, 786, 787, 788, 789, 790, 791, 792, 793, 794, 795, 796, 797, 798, 799, 800, 801, 802, 803, 804, 805, 806, 807, 808, 809, 810, 811, 812, 813, 814, 815, 816, 817, 818, 819, 820, 821, 822, 823, 824, 825, 826, 827, 828, 829, 830, 831, 832, 833, 834, 835, 836, 837, 838, 839, 840, 841, 842, 843, 844, 845, 846, 847, 848, 849, 850, 851, 852, 853, 854, 855, 856, 857, 858, 859, 860, 861, 862, 863, 864, 865, 866, 867, 868, 869, 870, 871, 872, 873, 874, 875, 876, 877, 878, 879, 880, 881, 882, 883, 884, 885, 886, 887, 888, 889, 890, 891, 892, 893, 894, 895, 896, 897, 898, 899, 900, 901, 902, 903, 904, 905, 906, 907, 908, 909, 910, 911, 912, 913, 914, 915, 916, 917, 918, 919, 920, 921, 922, 923, 924, 925, 926, 927, 928, 929, 930, 931, 932, 933, 934, 935, 936, 937, 938, 939, 940, 941, 942, 943, 944, 945, 946, 947, 948, 949, 950, 951, 952, 953, 954, 955, 956, 957, 958, 959, 960, 961, 962, 963, 964, 965, 966, 967, 968, 969, 970, 971, 972, 973, 974, 975, 976, 977, 978, 979, 980, 981, 982, 983, 984, 985, 986, 987, 988, 989, 990, 991, 992, 993, 994, 995, 996, 997, 998, 999, 1000.

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Voiding Dysfunction

Signs and Symptoms of Detrusor Underactivity: An Analysis of Clinical Presentation and Urodynamic Tests From a Large Group of Patients Undergoing Pressure Flow Studies

Andrew Gammie^{a,c}, Mathilde Kaper^a, Caroline Dorrepaal^b, Ton Kos^b, Paul Abrams^a

^aBritish Urological Institute, Southampton Hospital, Southampton, UK; ^bAlexion Pharma Europe B.V., Leiden, The Netherlands

Fig. 1 - Selection process of patients with detrusor underactivity. Multiple urodynamic, bladder outlet obstruction, and normal pressure flow studies took using criteria in Table 1. **BOO** = bladder outlet obstruction; **DU** = detrusor underactivity; **PPS** = pressure flow studies.

Maastricht UMC+ Gammie et al. Eur Urol 2016

Symptoms

Table 1 - Summary of symptoms with statistically significant differences reported for patients with detrusor underactivity compared with those with normal pressure flow studies or with bladder outlet obstruction

Symptoms	None		Symptoms	
	Higher occurrence for DU vs normal PPS	Higher occurrence for DU vs BOO	Higher occurrence for DU vs normal PPS	Higher occurrence for DU vs BOO
Decreased urinary stream	Abnormal urethral flow time	Decreased urinary stream	Decreased urinary stream	Decreased urinary stream
Intermittent urinary stream	Spasms on micturition	Intermittent urinary stream	Intermittent urinary stream	Intermittent urinary stream
Straining	Straining	Straining	Straining	Straining
Neurogenic bladder symptoms	Neurogenic bladder symptoms	Neurogenic bladder symptoms	Neurogenic bladder symptoms	Neurogenic bladder symptoms
Urgency	Urgency	Urgency	Urgency	Urgency
Post-void dribble	Post-void dribble	Post-void dribble	Post-void dribble	Post-void dribble
Abnormal and/or decreased sensation	Abnormal and/or decreased sensation	Abnormal and/or decreased sensation	Abnormal and/or decreased sensation	Abnormal and/or decreased sensation
Always starts to void	Always starts to void	Always starts to void	Always starts to void	Always starts to void
Always starts to void	Always starts to void	Always starts to void	Always starts to void	Always starts to void
Intermittent voiding	Intermittent voiding	Intermittent voiding	Intermittent voiding	Intermittent voiding
Post-void dribble	Post-void dribble	Post-void dribble	Post-void dribble	Post-void dribble
Lower occurrence for DU vs normal PPS	Lower occurrence for DU vs BOO	Lower occurrence for DU vs normal PPS	Lower occurrence for DU vs BOO	Lower occurrence for DU vs BOO
None	Decreased urinary stream	None	None	None
None	Urgency	None	None	None
None	Urgency	None	None	None

BOO = bladder outlet obstruction; DU = detrusor underactivity; PPS = pressure flow studies.

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EUROPEAN UROLOGY 72 (2017) 402–407

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Platinum Priority - Voiding Dysfunction
Editorial by Mikkel Faer and Jens Sanden on pp. 400–401 of this issue

Qualitative Exploration of the Patient Experience of Underactive Bladder

Alan D. Uren^{a,c}, Nikki Cotterill^b, Christopher Harding^a, Christopher Hillary^a, Christopher Chapple^a, Monique Klaver^a, Dominique Bongers^a, Zalmat Hakim^d, Paul Abrams^a

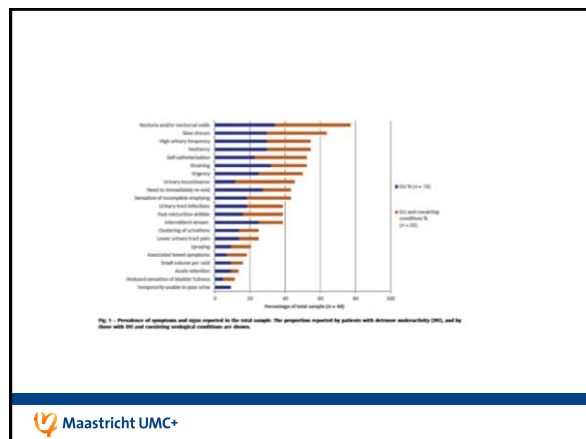
^aDepartment of Urology, British Urological Institute, Southampton, UK; ^bDepartment of Urology, Freeman Hospital, Newcastle, UK; ^cDepartment of Urology, Royal Holloway Hospital, Surrey, UK; ^dAlexion Pharma B.V., Leiden, The Netherlands

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Table 3 - Sample demographic and clinical characteristics

Clinical or demographic characteristic	Total sample	DE†	DE + remaining urological conditions
n	44	19	25
Mean age and range (yr)	64 (27-88)	59 (27-88)	64 (28-87)
Sex, male n (%)	29 (66)	12 (63)	17 (68)
Intermittent self-catheterisation, n (%) (biological or remote)	23 (52)	10 (53)	13 (52)
PVR > 30 mL ^a , n (%)	14 (32)	14 (74)	0 (0)
PVR > 30 mL ^b (ML median and interquartile range)	189 (146-402)	203 (149-402)	179 (146-360)
ICI (median and interquartile range)	62 (49-79)	62 (49-82)	62 (50-77)
BOO (median and interquartile range)	18 (8-26)	13 (8-16)	25 (9-44)
Res _{max} (median and interquartile range)	25 (12-35)	24 (12-29)	26 (12-36)
Res _{void} (median and interquartile range)	9 (6-16)	9 (6-14)	8 (5-16)

ICI = bladder contractility index; BOO = Bladder Outlet Obstruction Index; ICI = detrusor underactivity; PVR = postvoid residual.
^a In the absence of any evidence base for the lower limit of a "significant" PVR we chose > 30 mL.
^b Main only.



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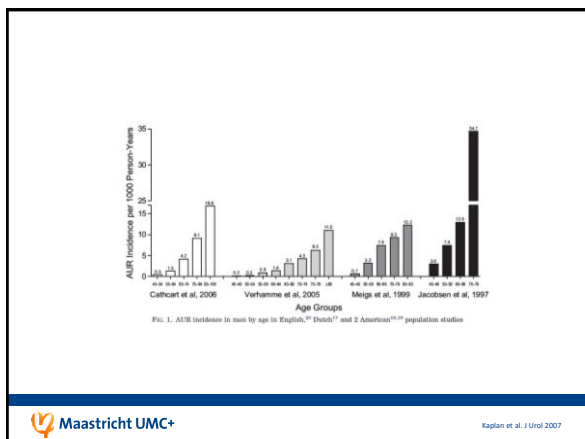
**Non-catheter detection methods:
2. The utility of post-void residual**

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EAU Guidelines on PVR in men

	LE	GR
Measurement of post-void residual (PVR) in male LUTS should be a routine part of the assessment.	3	B

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PVR and risk of AUR

Study	Study name (if given)	Patient group	Age (yr)	PVR cut-off (mL)	N	% AUR	PVR related to development of AUR?
Blarstov 1987	-	AUR patients	-	>50	228	-	>50mL had 3.6x risk for 2nd AUR
Thomas 2005	-	LUTS/BPO	>45	-	-	4%	No
Crawford 2006	ALTOPS	LUTS, pseudoBPH	>50	30	737	0.6%	No
Roehrborn 2006	ALTESS	LUTS/BPO	>55	350	Afluzon (757) Afuzonin (749)	1.8% 2.1%	No
Wicker 2006	-	BPH patients	>50	300	914	1.5%	No
Roehrborn 2010	COMBAT	LUTS/BPO	>50	-	Tamoxifen (1613) Dutasteride (1623) Combination (1610)	6.8% 2.7%	No
Cahn 2014	-	BPH patients	45-71	100	44	2.2% 9.3%	No

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Kaplan et al. J Urol 2007

PhD Thesis Rademakers

Residual Urinary Volume and Urinary Tract Infection—When are They Linked?

José Carlos L. Truzzi,* Flávia Miotto R. Almeida, Eduardo Caputi Nunes and Marcus V. Sall
From the Division of Urology, UNMSM Medical School, University of São Paulo, São Paulo, Brazil

Purpose: Large post-void residual urinary volume may be related to the development of urinary tract infection. However, the maximum post-void residual volume that predisposes patients to a higher risk of urinary tract infection is not known. In this prospective study we determined the cutoff value for post-void residual volume that allows early antibiotic treatment.

Materials and Methods: Data were obtained from 196 consecutive healthy adult men (median age 56 years) who presented symptoms of acute urinary tract infection. Right after symptom onset, a voiding study was performed under normal aseptic conditions, and the post-void residual volume was measured. Urinary tract infection was confirmed by culture from each patient and the results were compared to the various post-void residual volumes.

Results: Overall 27% of the patients presented with a positive urine culture. The mean post-void residual volume was 357 mL (range 100 to 900) compared to 123 mL (range 10 to 340) for the group with negative urine culture. The post-void residual volume of 180 mL was determined to have the best specificity and predictive value for bacterial growth of a post-void residual volume of 180 mL or greater was 87.6% as value was 96.7%.

Conclusions: Clinically asymptomatic adult men with a post-void residual volume of 180 mL or greater may require close medical attention since it may be necessary to introduce early antibiotic treatment to improve the bladder emptying.

Fig. 3. ROC curve of PVR showing best correlations with positive urine culture.

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EAU guidelines on PVR in women (UI)

Summary of evidence	LE
Lower urinary tract symptoms coexisting with UI are associated with a higher rate of PVR compared to asymptomatic subjects.	2

Recommendations	GR
When measuring post void residual urine volume, use ultrasound.	A
Measure post-voiding residual in patients with urinary incontinence who have voiding symptoms.	B
Measure post-voiding residual when assessing patients with complicated urinary incontinence.	C
Post-voiding residual should be monitored in patients receiving treatments that may cause or worsen voiding dysfunction, including surgery for stress urinary incontinence.	A*

*Recommendation based on an expert opinion.

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Study	Group	N	Cut-off (mL)	% above the upper limit
Dwyer 1994	Suggestive of VO	165	350	34%
Haylen 1999	LUTS	250	30	5 vs 9% (non- vs symptomatic)
Fitzgerald 2001	Urgency, frequency	336	100	5%
Constantin 2003	LUTS and/or incontinence	348	150	
Millerman 2004	OAB	201	100	19%
Luback 2007	Pelvic floor disorders	1399	100	11%
Gehrich 2007	Asymptomatic (mostly) postmenopausal women	96	50 100	15% 5%
Haylen 2008	Pelvic floor dysfunction	1140	0-10 11-30 31-50 51-100 >100	76% 5% 5% 8% 6%
Lowenstein 2008	LUTS	636	150	Low correlation with obstructive voiding symptoms
Tsang 2008	SUI + no previous pelvic surgery or prolapse	902	50 100	36% 16%
Saaby et al 2012	Urological complaints	396	100	71.14%, 72.3-1-2%
Khayami 2015	VO based on PF study	205	150	2/20-150 with voiding dysfunction 18/20-150 with voiding dysfunction
Park 2016	>65 yrs + OAB	151	100	36%
Lu 2016	POP-Q in IV and reconstruction	1370	>200cc	OR 2.15 for post-op VO

TA vs TV vs catheterisation!

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

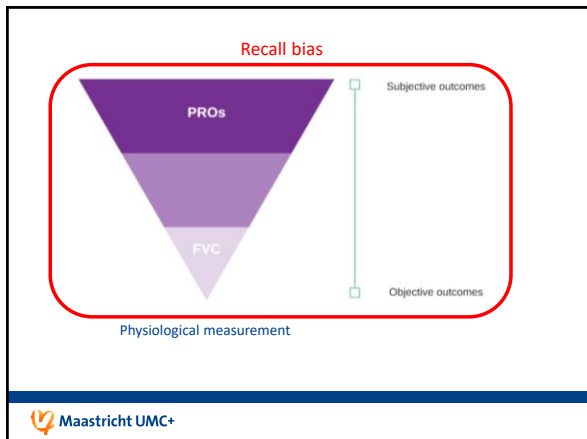
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Non-catheter detection methods: 3. Bladder filling sensation

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Sensation Related Bladder Diaries (SR-BDs)

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Time to change measurement methods?

- Real-time data ca
- Momentary Assessment
 - Ecological Moments
 - Repeated states in the
 - Experience Sampling
 - Time-sampled
- Diaries, behaviour
 - Development of
 - Acceptance by cl

part's momentary

Take Home Messages

- Symptoms have not yet been proved beneficial in the detection of DU patients
- Voiding efficiency ((voided volume / bladder capacity) x 100): 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

Obvious	Less obvious (grey area)
Bladder capacity	Bladder capacity
Volume filling sensation (SRBDs)	'Normal' filling sensation
Voiding efficiency (rec UTIs with response to CIC)	Voiding efficiency
	Irritative and/or voiding LUTS

Thank you for your attention!

Targeted (central) processes involved in bladder control:

- Cerebral cortex
- Basal ganglia
- Prefrontal cortex
- Amygdala
- Cerebellum
- Spinal cord

Targeted (central) processes involved in voiding control:

- Prefrontal cortex
- Amygdala
- Hypothalamus
- Hypothalamic-pituitary-adrenal (HPA) axis
- Adrenal medulla

Targeted (central) processes within the Central Nervous System:

- Gamma-aminobutyric acid (GABA)
- Glutamate
- Dopamine

Targeted (central) processes involved in voiding control:

- Cerebral cortex
- Basal ganglia
- Prefrontal cortex
- Amygdala
- Cerebellum

Targeted (central) processes within the Central Nervous System:

- Gamma-aminobutyric acid (GABA)
- Glutamate
- Dopamine

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



Conflict of Interest

Parts of the presented work have been accomplished with money provided by the Astellas European Foundation Grant 2012

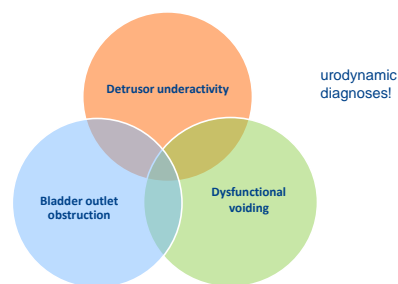
Travel to the ICS in Florence was partially self- and partially institution-funded



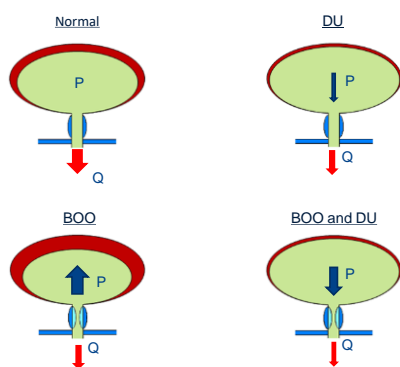
Objectives of the Lecture

- 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)

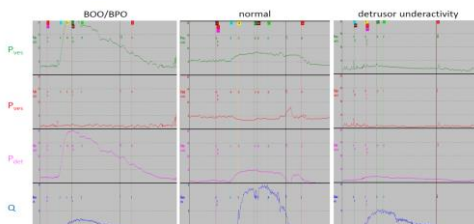


Abrams P et al. *Neurourol Urodyn.* 2002; 21: 167 – 178.



Definition of Detrusor Underactivity

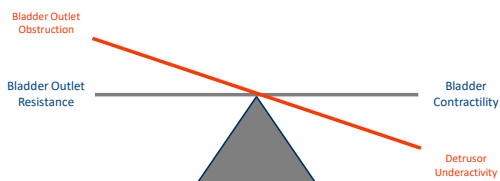
- contraction of reduced strength and/or duration, resulting in prolonged bladder emptying and/or failure to achieve complete bladder emptying with a normal time span
- urodynamic diagnosis characterized by decreased detrusor pressure and decreased urinary flow rate



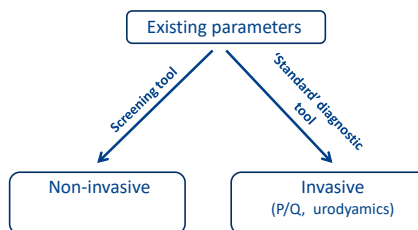
Abrams P et al. *Neurourol Urodyn.* 2002; 21: 167 – 178.

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



Invasive Indicators of DU



Measurement of Contractility in Men

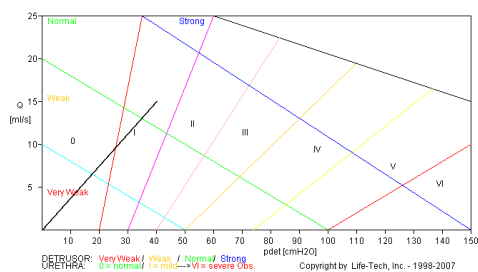
Table 3 - Summary of diagnostic methods

Type	Method	Advantages	Limitations
Mathematical calculations	Watts factor	1. Measure of bladder power 2. Minimally dependent on volume of urine 3. Not affected by presence of BOO	1. Lengthy and complex calculation 2. No validated thresholds 3. Does not measure sustainability of contraction
Indices	Detrusor shortening velocity Detrusor contraction coefficient	May identify early stage DU 1. Simple to use 2. Measurement easy to obtain 3. Estimation of isovolumetric contraction	1. Does not measure sustainability of contraction 2. May not be applicable to other groups 3. Does not conceptually consider coexistence of BOO and DU
Occlusion testing	Bladder Contractility Index Voluntary stop test	1. Real-time indication of isovolumetric contraction strength 2. No calculations	1. Uncomfortable or painful for patients 2. Impractical 3. No information on sustainability of contraction in continuous occlusion 4. May underestimate isovolumetric pressure (stop test) 5. Unusable in some patient groups
	Mechanical stop test Continuous occlusion	1. Real-time indication of isovolumetric contraction strength 2. No calculations	1. Uncomfortable or painful for patients 2. Impractical 3. No information on sustainability of contraction in continuous occlusion 4. May underestimate isovolumetric pressure (stop test) 5. Unusable in some patient groups
Ranges of urodynamics measurements	$P_{det} @ Q_{det}$ (Pg. 48) Q_{det} (Pg. 15)	Simple to use	1. No widely accepted "normal" ranges 2. Underestimates contraction strength 3. Does not conceptually consider coexistence of BOO and DU

BOO = bladder outlet obstruction; DU = detrusor underactivity; $P_{det} @ Q_{det}$ = detrusor pressure at the time of maximum flow; Q_{det} = maximum flow rate.

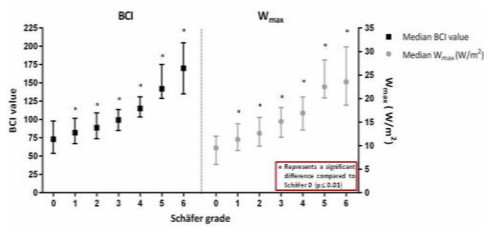
Osman et al. *Eur Urol.* 2014; 65(2): 389 – 98.
van Koeveering GA et al. *Neurourol Urodyn.* 2011; 30(5): 723 – 8.

Schäfer Nomogram



Schäfer W. *Urol Clin North Am.* 1990; 17(3): 553 – 66.

Contractile Function in Men



$$BCI = P_{det, Q_{max}} + 5 Q_{max}$$

$$W = P_{det} \cdot V_{det} + a \cdot V_{det} + b \cdot P_{det} / 2\pi$$

$$[V_{det} = Q/2(3/(4n)) \cdot (V_{ves} + V_{l}) - 2/3]$$

van Koeveering GA et al. *Neurourol Urodyn.* 2011; 30(5): 723 – 8.
Oelke M, Rademakers KL, van Koeveering GA. *World J Urol.* 2014; 32: 1177 – 83.

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

Oelke M, Rademakers KL, van Koeveering GA. *World J Urol.* 2014; 32: 1177 – 83.

Solution for Defining Men with Detrusor Underactivity

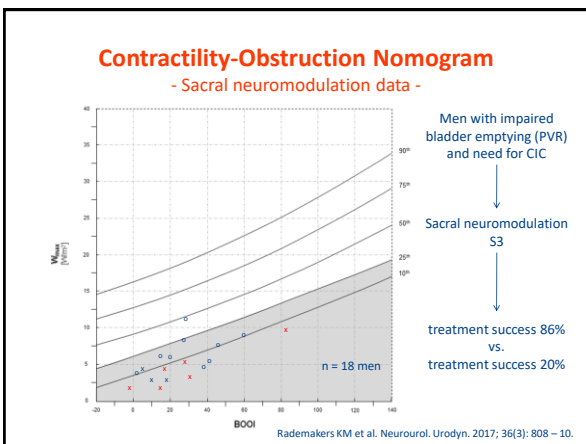
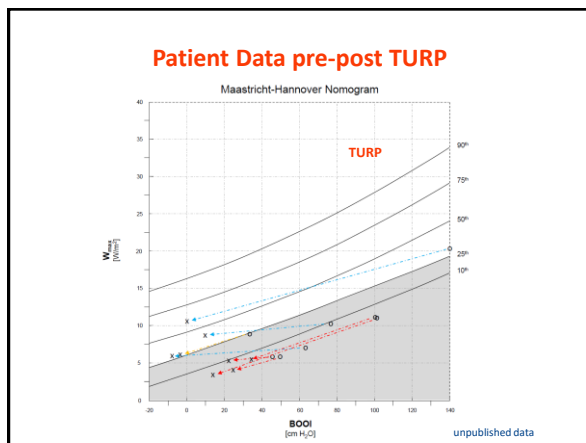
- Defining threshold values for the entire range of outlet resistance
- Analysis of a urodynamic database of treatment naive men aged ≥ 40 years (n=822)
- Exclusion criteria: suspicion of prostate or bladder cancer, radiotherapy, pelvic surgery, neurological disorder, UTI, prostatitis, bladder stones, 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

Oelke M, Rademakers KL, van Koeveering GA. *Neurourol Urodyn.* 2016; 35(8): 980 - 6.

Defining Threshold Values

	< 25 th percentile n=208	25 th -50 th percentiles n=204	p-value
Age [years]	66 (65-67)	63 (62-64)	0.006
Prostate volume [cc]	40 (36-45)	40 (37-44)	0.929
Height [cm]	175 (174-176)	175 (174-176)	0.831
Weight [kg]	80 (78-82)	80 (78-82)	0.963
IPSS	15 (14-17)	15 (13-16)	0.639
IPSS storage sub-score	7 (6-8)	6 (6-7)	0.260
IPSS voiding sub-score	8 (7-9)	8 (7-9)	0.917
IPSS QoL score	4 (3-4)	3 (3-4)	0.164
Free outflowmetry			
Q _{max} [ml/s]	9.7 (9.1-10.4)	10.2 (9.5-10.9)	0.338
Q _{ave} [ml/s]	5.1 (4.7-5.5)	4.8 (4.4-5.2)	0.291
Voided volume [ml]	247 (230-264)	254 (246-273)	0.557
Bladder capacity [ml]	431 (372-490)	369 (345-393)	0.063
PVR [ml]	167 (142-193)	116 (99-134)	0.001
Voiding efficiency [%]	67 (63-70)	72 (69-75)	0.019
Multichannel anrodynamics			
Cystometric bladder capacity [ml]	619 (475-810)	442 (410-473)	0.009
P _{max} [cm H ₂ O]	56.2 (53.4-60.1)	57.1 (53.4-61.0)	0.960
BOOI [cm H ₂ O]	44 (40-48)	45 (41-48)	0.742
Bladder Contractility Index	88.6 (85.1-92.1)	89 (85-94)	0.829
W_{max} [W/m ²]	7.9 (7.5-8.3)	11.7 (11.3-12.1)	<0.001

Oelke M, Rademakers KL, van Koeveering GA. *Neurourol Urodyn.* 2016; 35(8): 980 - 6.



Non-Invasive Indicators of DU

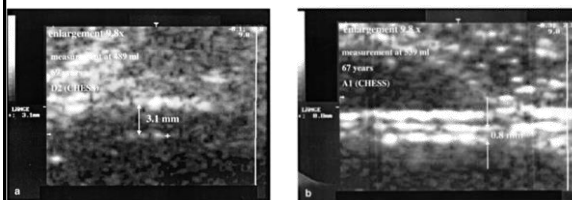
Maastricht UMC+

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



Adopted from: Gelle, World J Urol 2002

Ultrasound DWT Measurement for DU Diagnosis

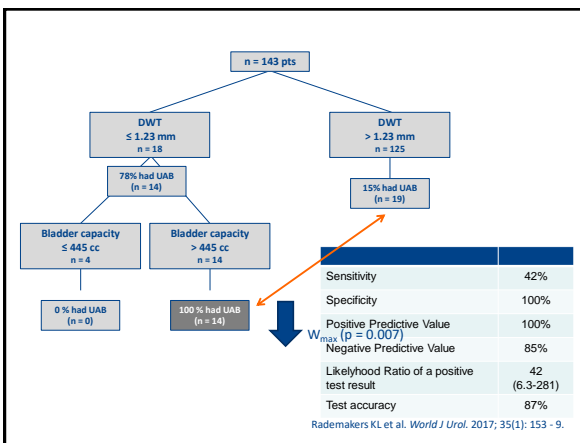
Study aim:

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

Methods:

- Cross-sectional study; men with uncomplicated LUTS
- IPSS, free flow parameters (Q_{max} and Q_{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)

Rademakers KL et al. World J Urol. 2017; 35(1): 153 - 9.



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, $p = 0.130$).

Chen SF et al. Int Urol Nephrol. 2017; published online Aug 2017; doi: 10.1007/s11255-017-1666-z.

Take-Home Messages

- The balance between bladder outlet resistance and contractile function of the bladder is responsible for sufficient voiding
- Detrusor underactivity is a urodynamic diagnosis but threshold values have to be separately defined for different BOO grades
- The new (Maastricht) nomogram defines threshold values for all obstruction grades. The 25th percentile indicate detrusor underactivity
- The nomogram can predict the outcome of treatment in men with BOO
- Non-invasive parameters are initially able to replace computer-urodynamic evaluation in clinical practice; until now, only DWT in combination with bladder capacity has been evaluated

When do we have to consider, and what do we need to diagnose: Detrusor Underactivity in Female patients ?

Gommert van Koeveringe, MD, PhD, Fellow EBU
Maastricht University Medical Center, the Netherlands
And Pelvic Care Center Maastricht

On behalf of the Force research team:
GvK,¹ Kevin Rademakers, Matthias Oelke²
¹Maastricht University Medical Centre (MUMC+)
²Hannover Medical School (MHH)
Funding Astellas Europe fund 2012



Gommert van Koeveringe



Affiliations to disclose[†]:

Astellas: Consultancy, Clinical trial
Solace therapeutics: Consultancy, Clinical trial
Allergan: Clinical trial
Boston Scientific: Consultancy

† All financial ties (over the last year) that you may have with any business organization with respect to the subjects mentioned during your presentation

Funding for speaker to attend:

- Self-funded
 Institution (non-industry) funded
 Sponsored by:

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:

Acontractile 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.
- Rademakers et al. (ICI-RS 2014) NeuroUrol. Urodyn 2016
 - Normative age matched data necessary
 - New nomograms to be developed for use in females
- Gammie et al. Curr. Op. Urol 2015
 - 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 NeuroUrol 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

Moosdorf et al. Submitted NeuroUrol.Urodyn.

- 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, Faecal incontinence
 - No correlation with POP
- Significant correlations also with specific symptoms like: feeling of incomplete emptying, weak stream, intermittency, straining.
- This advocates for 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

Characteristics

- Median (IQR)

	Low symptom score (n=120)	High symptom score (n=20)
General data		
Age (yr)	58 (43-69)	47 (43-57)
Urinary retention (n)	0	1
Urodynamic data		
First desire (ml)	162 (110-206)	176 (140-206)
Normal desire (ml)	210 (119-274)	238 (156-351)
Strong desire (ml)	228 (166-296)	258 (192-348)
Bladder capacity (ml)	293 (217-353)	362 (261-492)
Voided volume (ml)	266 (165-398)	59 (36-178)
Calculated post-void residual (ml)	19 (0-77)	250 (181-462)
Voiding effectiveness (%)	93 (75-100)	16 (11-46)
Flow time (sec)	40 (30-67)	27 (19-41)
Voiding time (sec)	105 (64-144)	210 (56-382)
Lack time (sec)	11 (4-27)	28 (25-68)
Qmax (ml/sec)	18.0 (11.0-21.0)	13.0 (4.0-16.0)
postQmax (cmH ₂ O)	19.5 (15.0-34.8)	23.5 (15.0-38.0)
pmax (cmH ₂ O)	34.5 (22.8-51.0)	31.0 (15.3-48.5)
Blavas obstruction model	1 (-)	1 (-)
Wmax (W/m ²)	8.12 (5.60-15.78)	4.84 (3.28-9.79)
Bladder Contractility Index (BCI)	108 (80-128)	83 (62-106)

patients with urinary retention are excluded from calculations of flow related parameters

Voiding effectiveness: 93% vs. 16%

Study females with voiding dysfunction.

	Post-void residual		W max		Voiding Efficiency	
	Correlation coefficient	p-value	Correlation coefficient	p-value	Correlation coefficient	p-value
N=182						
Feeling of incomplete bladder emptying	0.363	<0.001	n.s.		-0.296	0.005
Intermittency on bladder emptying	0.215	0.042	-0.241	0.035		n.s.
Weak stream		n.s.		n.s.		n.s.
Applying abdominal pressure during voiding		n.s.		n.s.		n.s.

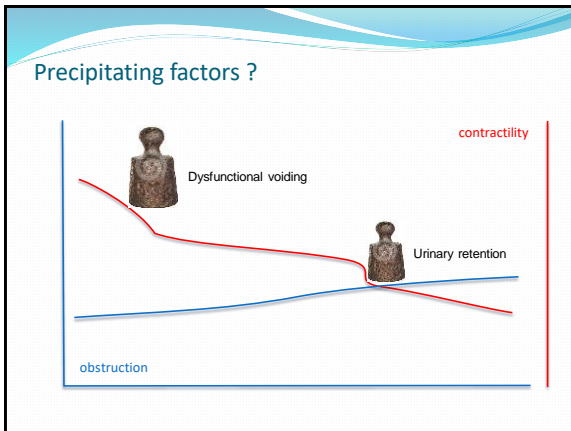
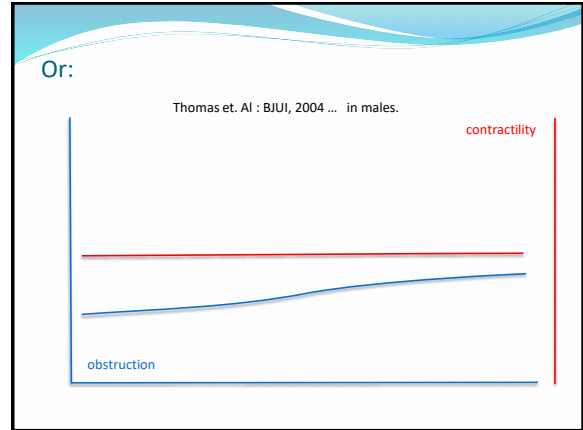
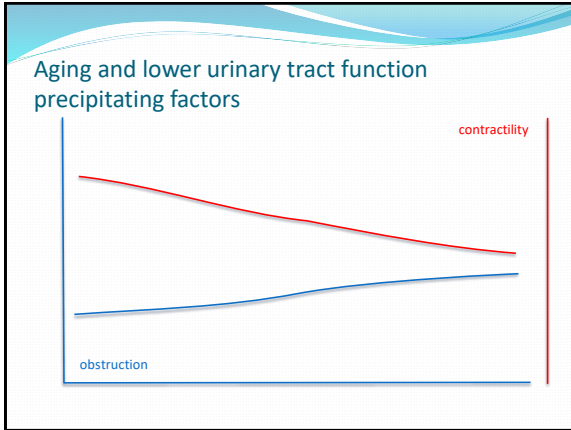
Can we differentiate between different causes of voiding dysfunction by symptoms alone?

- **Maybe:**
 - Gammie et al. Eur Urol. 2015
- **No:**
 - Brown et al. NeuroUrol.Urodyn. 2017
 - Faraj et al. Int.Urol.Nefrol. 2016
 - Conn et al. Curr.op.Urol.2016
 - However, all of these measures may be more relevant to research than clinical practice, where numbers matter less than overall clinical impression. In many cases where the clinical diagnosis remains unclear, UDS can assist in distinguishing UAB from other LUTS-associated conditions.

Possible precipitating factors

Ageing ? + ?

1. Diabetes?
2. Neurogenic disorders?
3. Hypertension chronic >> acute
4. UTI's ?
5. Obstruction?
6. Psychogenic, sociogenic constitution.



- ### The Future: What else do we need
1. Adequate diagnostics to identify the condition (for example with specialized or ambulatory urodynamics)
 2. Longitudinal studies, to understand what the symptoms really imply.
 3. Identification of precipitating factors
 - Role of dysfunctional voiding that started at young age.
 - Role of multiple urinary tract infections/pelvic pain
 4. Development of a stress test to identify people at risk by estimation of the compensatory capacity of bladder and sphincter for example before pelvic surgery.
- Van Koeveeringe, Rademakers, Binder, Korstanje, Daneshgari, Ruggieri, Igawa, Fry, Wagg, ICI-RS-2013, acc. NeuroUrol Urodyn. 2014

Therapeutic margins

New therapies should aim at either increasing:

- contractile reserve
- and/or increasing:
- the subvesical relaxation capacity.

The graph shows a red shaded area labeled 'Contractile reserve' and a blue shaded area labeled 'Subvesical relaxation capacity'. The x-axis is labeled 'obstruction' and the y-axis is labeled 'contractility'.

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

- ### 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 neuromodulation
 - 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
- Van Koeveeringe, Rahnamaï, Berghmans; BJUInt 2010; 105(4): 101
 Rademakers KL, Drossaerts JM, Rahnamaï MS, van Koeveeringe GA. Int J Urol. 2015 May;22(5):503-7.

Maastricht Urology Team

