W23: Underactive bladder and Voiding Dysfunction: New Insights

Workshop Chair: Gommert van Koeveringe, Netherlands
15 September 2016 14:35 - 16:05

Start	End	Topic	Speakers
14:35	14:50	Detrusor underactivity, when should we consider this condition in patients with LUTS?	Christopher Chapple
14:50	15:05	What is new concerning detection of detrusor underactivity in LUTS patients?	Matthias Oelke
15:05	15:20	What is new concerning diagnosis of detrusor underactivity in male patients with LUTS?	Matthias Oelke
15:20	15:35	When do we have to consider, and what do we need to diagnose detrusor underactivity in Female patients?	Gommert van Koeveringe
15:35	15:50	Discussion	All
15:50	16:05	What future steps are necessary to detect and confirm the condition, develop therapies, and follow-up after treatment?	All

Aims of course/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 of this bladder condition. However, no consensus on the diagnosis or evaluation approach has been reached. The speakers will present and discuss the latest information and key facts concerning UAB/DU. How do we define the LUTS patients with UAB/DU and what are differences in assessment of male and female patients? Which are invasive or non-invasive tools to assess contractility? How can we differentiate detrusor underactivity from bladder outlet obstruction? How to manage our patients?

Learning Objectives

After this workshop participants should be able to:

1. Define underactive bladder and detrusor underactivity and when to consider this in patients with LUTS
2. Select tools to detect and diagnose detrusor underactivity in males and females in a population with LUTS symptomatology.
3. Have insight in what is necessary to confirm the condition, to evaluate existing therapies and to develop new therapies.

Learning Outcomes

After the course, the participant will be able to:

- Know current working definitions of underactive bladder and detrusor underactivity.
- Recognize the possibilities and limitations of current non invasive tools and invasive tools to detect and diagnose detrusor underactivity.
- Recognize the similarities and differences in symptomatology of the different voiding dysfunctions: obstruction, dysfunctional voiding, detrusor underactivity.
- Have an updated knowledge on new developments for detection and diagnosis of the underactive bladder.
- Develop new research ideas for detection and diagnosis of , and therapeutic approaches to, the underactive bladder

Target Audience

Urologists, Gynaecologists, researchers, epidemiologists, colleagues interested in urodynamics

Advanced/Basic

Advanced

Conditions for learning

The course will be informative and interactive. It will contain interactive discussions on what is known and not known yet concerning this subject.

Suggested Learning before workshop attendance

Read the review articles of which the references are indicated 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.
- Neurourol Urodyn. 2016 Feb; 35(2):312-7. Detrusor underactivity and the underactive bladder: Symptoms, function, cause-what do we mean? ICI-RS think tank 2014. Smith PP, Birder LA, Abrams P3, Wein AJ, Chapple CR.
- Eur Urol. 2016 Feb; 69(2):361-9. Signs and Symptoms of Detrusor Underactivity: An Analysis of Clinical Presentation and Urodynamic Tests from a Large Group of Patients Undergoing Pressure Flow Studies. Gammie A, Kaper M, Dorrepaal C, Kos T, Abrams P.

Prof C.H. 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.

Prof M. Oelke

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. 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.

Prof G.A. 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.

What is new concerning the diagnosis of detrusor underactivity in male patients with LUTS?

Matthias Oelke; MD, PhD, FEBU
Department of Urology
Hannover Medical School

Workshop 23: Detrusor Underactivity
International Continence Society, Tokyo, 15th September 2016

Conflict of Interest

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

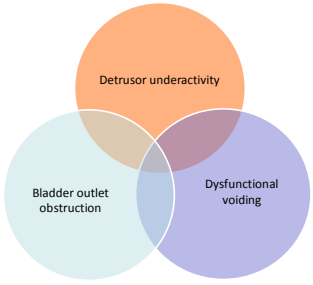
Travel to the ICS in Tokyo was partially self-funded and partially institution-funded

Objectives of the Lecture

- to learn about the definition of detrusor underactivity
- to distinguish between detrusor underactivity and bladder outlet obstruction in men
- to know the invasive and non-invasive tests to diagnose detrusor underactivity in men
- to become aware of the clinical value of detrusor underactivity

Reasons for Impaired Bladder Emptying

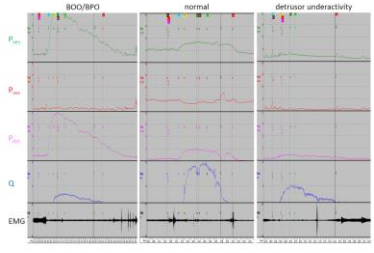
(increased PVR, decreased VE, decreased flow)



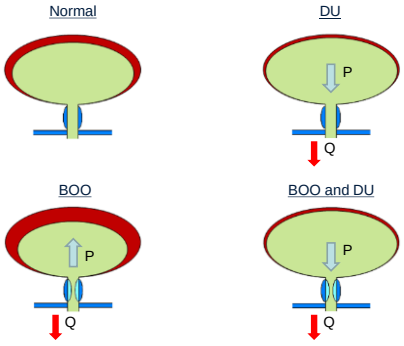
Abrams P et al. *Neurourol Urodyn.* 2002; 21: 167 – 178.

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

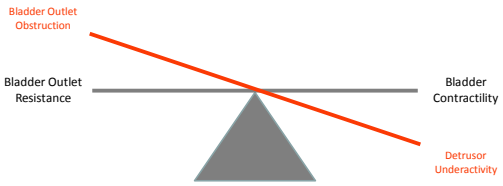


Abrams P et al. *Neurourol Urodyn.* 2002; 21: 167 – 178.



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

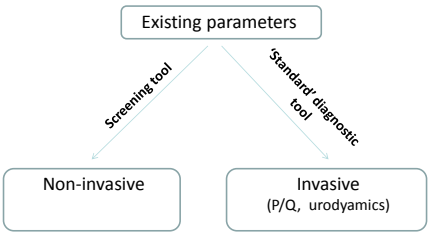


Epidemiology

- Detrusor underactivity:
  - in up to 40% of men aged >65 years [1]
  - 48% of men aged ≥70 years [2]
  - approximately ⅔ of incontinent institutionalised elderly individuals [3]
- Bladder outlet obstruction:
  - in approximately 60% of symptomatic, non-neurogenic men aged ≥50 years [4,5]
- No information about men with detrusor underactivity and bladder outlet obstruction

1. Jeong SJ et al. *Korean J Urol.* 2012; 53: 342 - 348.
2. Abarbanel J, Marcus EL. *Urology.* 2007; 69: 436 - 440.
3. Resnick NM et al. *N Engl J Med.* 1989; 320: 1-7.
4. Reynard JM et al. *Br J Urol.* 1998; 82: 619 - 623.
5. Oelke M et al. *Eur Urol.* 2008; 54: 419 - 426.

Parameters to Judge Voiding



Invasive Indicators of DU

Hannover Medical School

Measurement of Bladder Contractile Function in Men

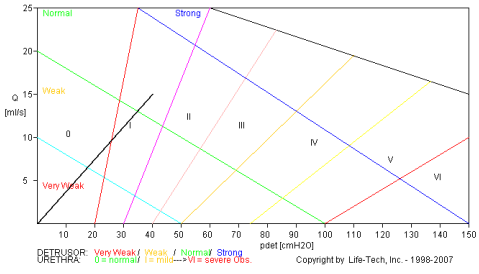
Table 3 – Summary of diagnostic methods

Type	Method	Advantages	Limitations
Mathematical calculations	Watts factor	1. Measure of bladder power 2. Minimally dependant 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
	Detrusor shortening velocity	May identify early stage DU	
Indexes	Detrusor contraction coefficient	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
	Bladder Contractility Index		
Occlusion testing	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		
Ranges of urodynamic measurements	$P_{det}@Q_{max}$ (eg, <40) Q_{max} (eg, <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; $P_{det}@Q_{max}$ = detrusor pressure at the time of maximum flow; Q_{max} = maximum flow rate.

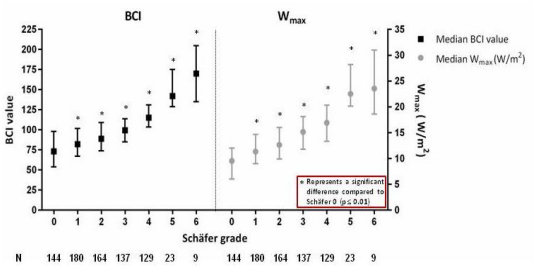
Osman et al. *Eur Urol.* 2014; 65(2): 389 – 98.
van Koeveringe GA et al. *Neurourol Urodyn.* 2011; 30(5): 723 – 8.

Schäfer Nomogram



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

Contractile Function in Men



$BCI = P_{det.Qmax} + 5\ Q_{max}$

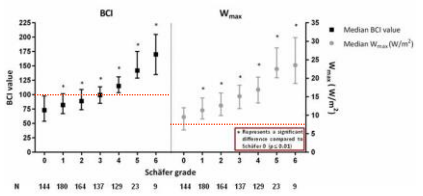
$$W = (P_{det} \cdot V_{det} + a \cdot V_{det} + b \cdot P_{det}) / 2\pi$$

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

Oelke M, Rademakers KL, van Koeveringe GA. *World J Urol.* 2014; 32: 1177 – 1183.

Problem with Defining Men with Detrusor Underactivity

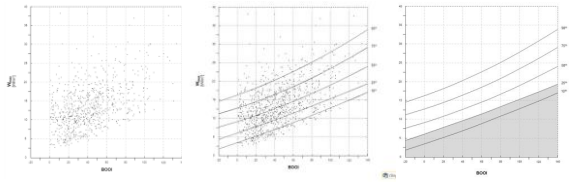
- Proposed threshold values: BCI <100 or W_{max} <7 W/m² do not seem to be correct for all men
- No single threshold value for the characterization of men with detrusor underactivity for the entire range of men with different bladder outlet resistance



Oelke M, Rademakers KL, van Koeveringe GA. *World J Urol.* 2014; 32: 1177 – 1183.

Solution for Defining Men with Detrusor Underactivity

- Defining threshold values for the entire range of outlet restistance
- 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 Koeveringe GA. *Neurourol Urodyn.* 2016; in press: doi: 10.1002/nau.22841.

Defining Threshold Values

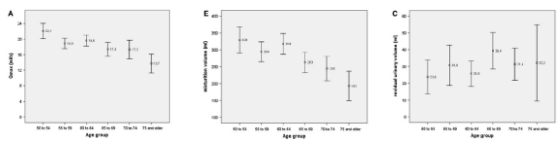
	< 25th percentile n=208	25th-50th percentiles n=204	p-value
Age [years]	66 (65-67)	63 (62-64)	**0.006**
Prostate volume [cc]	40 (36-45)	40 (37-44)	0.929
Height [cm]	175 (174-176)	175 (174-176)	0.831
Weight [kg]	80 (78-81)	80 (78-82)	0.963
IPSS	15 (14-17)	15 (13-16)	0.639
IPSS storage sub-score	7 (6-8)	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 uroflowmetry			
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 (236-273)	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)	**0.015**
Multichannel urodynamics			
Cystometric bladder capacity [ml]	503 (470-536)	442 (410-473)	**0.009**
$P_{det.Qmax}$ [cm H_2O]	56.7 (53.2-60.1)	57.1 (53.2-61.0)	0.869
BOOI [cm H_2O]	44 (40-48)	45 (41-49)	0.742
Bladder Contractility Index	88.6 (85.1-92.1)	89 (85-94)	0.829
W_{max} [W/m²]	7.9 (7.5-8.3)	11.7 (11.3-12.1)	**<0.001**

Oelke M, Rademakers KL, van Koeveringe GA. *Neurourol Urodyn.* 2016; in press: doi: 10.1002/nau.22841.

Aging of the Male Lower Urinary Tract

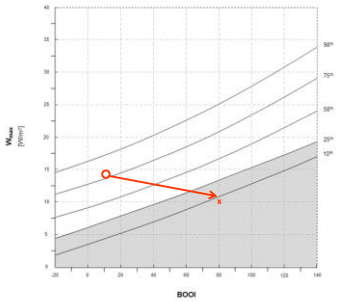
- Experimental animals with BOO develop detrusor underactivity and urinary retention over time (+ renal insufficiency due to bilateral hydronephrosis)
- Patients with diabetes mellitus also develop detrusor underactivity due to detrusor muscle cell degeneration and damage of afferent/efferent bladder nerves
- In men, decrease of Q_{max} and voided volume + increase of PVR with aging (data of the German epidemiological LUTS study)

Q_{max} voided volume PVR



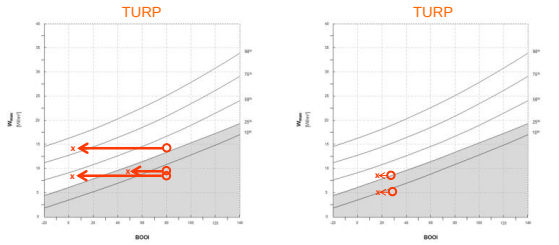
Berges R, Oelke M. *World J Urol.* 2011; 29: 171 – 178.

Aging



Rademakers KL, van Koeveringe GA, Oelke M. *Curr Opin Urol.* 2016; 26: 3 – 10.

Treatment Effects

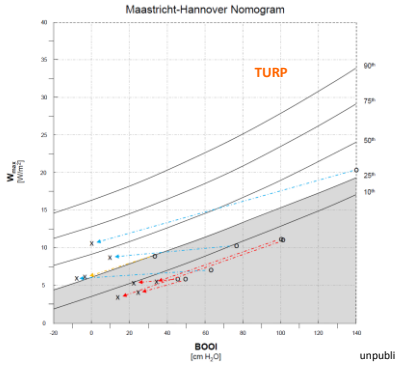


- man with BOO and normal/low contractiltiy receives TURP
- Reduction of BOOI man with sufficient contractility or detrusor underactivity will most likely have reduced PVR
- Patient with incomplete resection may remain with PVR

- man without BOO but with detrusor underactivity receives TURP
- Reduction of BOO will most likely not result in improved voiding or PVR
- However, some patients with equivocal detrusor contractility may benefit from prostate surgery

Rademakers KL, van Koeveringe GA, Oelke M. *Curr Opin Urol.* 2016; 26: 3 – 10.

Patient Data pre-post TURP



unpublished data

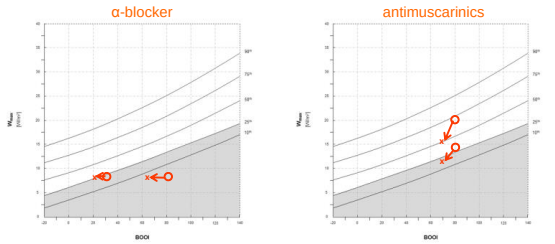
Clinical Consequences of DU

- Fate of bladder emptying (Q_{max}, $P_{det.Qmax}$), PVR, voiding efficiency, BCI and LUTS have been determined in long-term studies in men with detrusor underactivity
- Clinical and urodynamic evaluation at baseline and follow- up (>10 years)
  - in men treated with TURP, all parameters remained unchanged after mean follow-up of 14.5 ± 3.2 years
  - in untreated men, all parameters also remained unchanged after a mean follow-up of 13.6 ± 3.3 years
  - in men with or without active treatment, patients with TURP had significantly lower BOOI but PVR was significantly higher, voiding efficiency was significantly lower and more men had chronic retention

➢ Conclusion: TURP is not an adequate treatment of detrusor underactivity; therefore, assessment of voiding function with computer-urodynamic studies is indicated

Thomas AW et al. *BJU Int.* 2004; 93:745 – 750.
Thomas AW et al. *BJU Int.* 2005; 96:1301 – 1306.

Treatment Effects

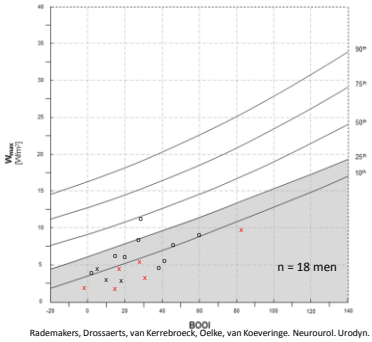


- man with BOOI of 80 (30) cm H_2O uses an α-blocker
- reduction of BOOI by 16% (67.5 or 25.5 cm H_2O)
- man with detrusor underactivity (W_{max} 7.5 W/m²) will most likely remain having PVR, whereas a man with equivocal detrusor contractility may improve

- man with BOOI of 80 cm H_2O uses an antimuscarinic
- reduction of BOOI by 12% (70.4 cm H_2O) and W_{max} by 20%
- man with contractility of W_{max} 14 W/m² is likely to develop PVR or retention, whereas a patient with better contractility (20 W/m²) is unlikely to develop PVR or retention

Contractility-Obstruction Nomogram

- Sacral neuromodulation data -



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

↓

Sacral neuromodulation S3

↓

treatment success 86%
vs.
treatment success 20%

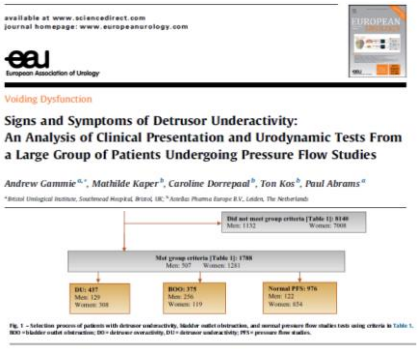
Rademakers, Drossaerts, van Kerrebroeck, Oelke, van Koeveringe. Neurourol. Urodyn. 2016; in press: DOI 10.1002/nau.23010

Non-Invasive Indicators of DU

Non-invasive indicators

- Evaluation of symptoms – patient history
- Ultrasound measurement of detrusor wall thickness (DWT)
- Measurement of isovolumentric bladder pressure with the penile cuff test?
- ……..?

Non-invasive Indicators: Symptoms



available at www.sciencedirect.com
journal homepage: www.europeanurology.com

European Association of Urology

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,], Mathilde Kaper [b], Caroline Dorrepaal [b], Ton Kos [b], Paul Abrams [a]*

[a] Bristol Urological Institute, Southmead Hospital, Bristol, UK; [b] Astellas Pharma Europe B.V., Leiden, The Netherlands

Non-invasive Indicators: Symptoms

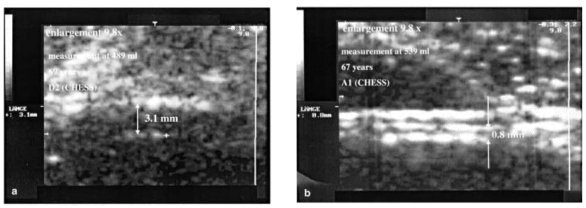
Table 5 – Summary of symptoms with statistically significant differences reported for patients with detrusor underactivity compared with those with normal pressure flow studies or with bladder outlet obstruction

Men		Women	
Higher occurrence for DU vs normal PFS	Higher occurrence for DU vs BOO	Higher occurrence for DU vs normal PFS	Higher occurrence for DU vs BOO
Decreased urinary stream	Abnormal sexual function	Decreased urinary stream	Decreased urinary stream
Interrupted urinary stream	Stress incontinence	Interrupted urinary stream	Stress incontinence
Hesitancy	Enuresis	Hesitancy	Enuresis
Incomplete bladder emptying	Palpable bladder	Incomplete bladder emptying	Absent and/or decreased sensation
Palpable bladder	Absent and/or decreased sensation	Palpable bladder	
Absent and/or decreased sensation	Always strain to void	Absent and/or decreased sensation	
Always strain to void	Bowel strain	Enuresis	
Incomplete bowel emptying	Incomplete bowel emptying	Impaired mobility	
	Poor bowel control		
Lower occurrence for DU vs normal PFS	**Lower occurrence for DU vs BOO**	**Lower occurrence for DU vs normal PFS**	**Lower occurrence for DU vs BOO**
None	Decreased urinary stream Hesitancy Urgency	None	None

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

Detrusor Wall Thickness measurement

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



Adopted from: Oelke, 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)

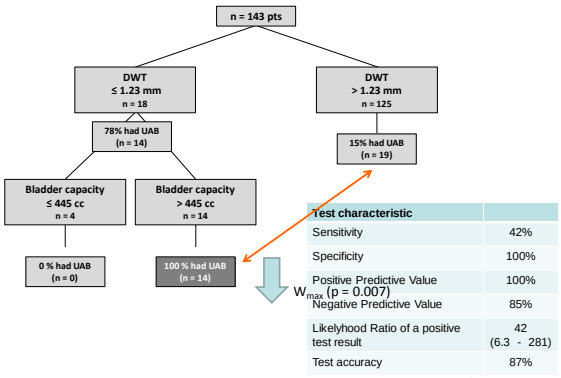
Rademakers KL et al. *World J Urol.* 2016; in press: DOI 10.1007/s00345-016-1902-7.

Table 1. Patient characteristics. *Variables are presented as median with interquartile range*

Characteristic	*Total group n=143*	*UAB n=33*	*No-UAB n=110*	*p-value*
Age (yr)	62 (59-70)	62 (59-73)	62 (57-68)	
IPSS	16 (10-21)	14 (10-20)	16 (10-22)	
Bladder capacity (ml)	406 (300-541)	560 (390-718)	385 (288-462)	<0.001
Detrusor Wall Thickness (mm)	1.70 (1.40-2.20)	1.30 (1.10-1.75)	1.90 (1.50-2.33)	<0.001
Free uroflowmetry				
Q_{max} (ml/s)	10.3 (7.4-14.3)	10.7 (6.4-17.3)	10.3 (7.8-14.0)	
PVR * (ml)	100 (30-201)	130 (100-250)	71 (30-200)	0.027
Voided volume	224 (153-324)	318 (205-416)	212 (149-292)	0.003
VE * (%)	70.7 (51.7-88.4)	63.8 (51.3-84.4)	74.5% (52.1-89.6)	
Pressure flow study				
DO ‡ (n)	85 (59.4%)	17 (51.5%)	68 (61.8%)	
Q_{max} (ml/s)	6.9 (4.0-10.4)	6.9 (3.8-10.2)	6.9 (4.1-10.4)	
$PdetQ_{max}$ (cmH_2O)	48.7 (34.9-71.3)	27.2 (19.8-39.8)	58.2 (45.6-76.6)	<0.001
Bladder Contractility Index	93.3 (76.2-110.4)	67 (45-82)	103 (84-117)	<0.001
W_{max} (W/m^2)	9.8 (6.1-13.1)	4.9 (3.7-6.0)	11.4 (8.2-14.8)	<0.001
Abrams Griffiths-number	33.5 (18.0-53.2)	15.6 (5.2-27.2)	39.2 (22.9-63.1)	<0.001

*PVR: Post-void residual
* VE: Voiding Efficiency
‡ DO: Detrusor Overactivity

Rademakers KL et al. *World J Urol.* 2016; in press: DOI 10.1007/s00345-016-1902-7.



Test characteristic	
Sensitivity	42%
Specificity	100%
Positive Predictive Value	100%
Negative Predictive Value	85%
Likelyhood Ratio of a positive test result	42 (6.3 - 281)
Test accuracy	87%

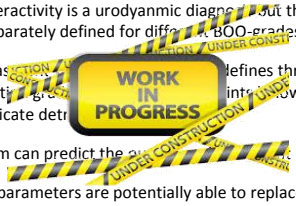
Rademakers KL et al. *World J Urol.* 2016; in press: DOI 10.1007/s00345-016-1902-7.

- DWT ≤1.2 mm + bladder capacity >445 ml can sufficiently identify UAB with likelihood ratio of a positive test result (LR^+) of 42
  - selecting the extremes
- An independent study should validate our preliminary results

Rademakers KL et al. *World J Urol.* 2016; in press: DOI 10.1007/s00345-016-1902-7.

Take-Home Messages

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



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, Ramona Hohnen, Matthias Oelke[2]
[1]Maastricht University Medical Centre (MUMC+)
[2]Hannover Medical School (MHH)
Funding Astellas Europe fund 2012

FORCE
Focus On Redefining detrusor Contractility and Effectiveness
Research Group

Conflicts of Interest:

G.A. Van Koeveringe

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

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)

Studies in female patients

- Our pelvic care database counts > 6000 patients
  - General questionaire: 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 discriminitave ability of the selected combination of questions

Study on general Pelvic floor complaints

Moosdorf et al Abstract # 7 IC,S 2017

- 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, Feacal incontinence
  - No correlation with POP

  - Significant correlations also withspecific symptoms like: feeling of incomplete emptying, weak stream, intermittancy, 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 he highest and 10 patients with the lowest symptom score were analysed

- Characteristics
  - Median (IQR)

	Low symptom score (n=10)	*High symptom score (n=10)*
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)
pdetQmax (cmH_2O)	19.5 (15.0-34.8)	23.5 (15.0-33.0)
pmax (cmH_2O)	34.5 (22.8-51.0)	31.0 (15.3-48.5)
Blaivas obstruction model	1 (-)	1 (-)
W_{max} (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)

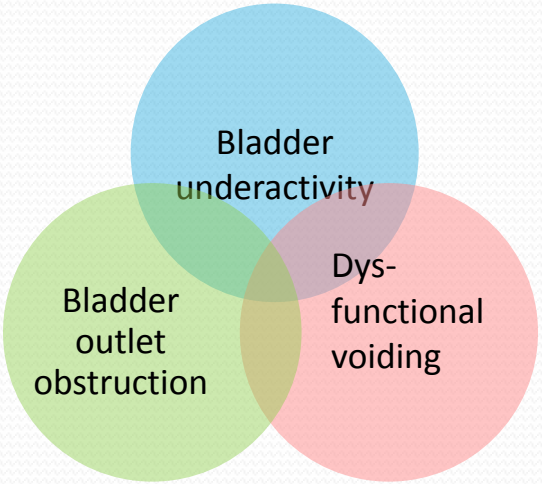
[+]patients with urinary retention are excluded from calculations of flow related parameters

Voiding effectiveness:
93% vs. 16%

Study females with voiding dysfunction.

	Post-void residual		**W max**		**Voiding Efficiency**	
N=182	*Correlation coefficient*	*p-value*	*Correlation coefficient*	*p-value*	*Correlation coefficient*	*p-value*
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?



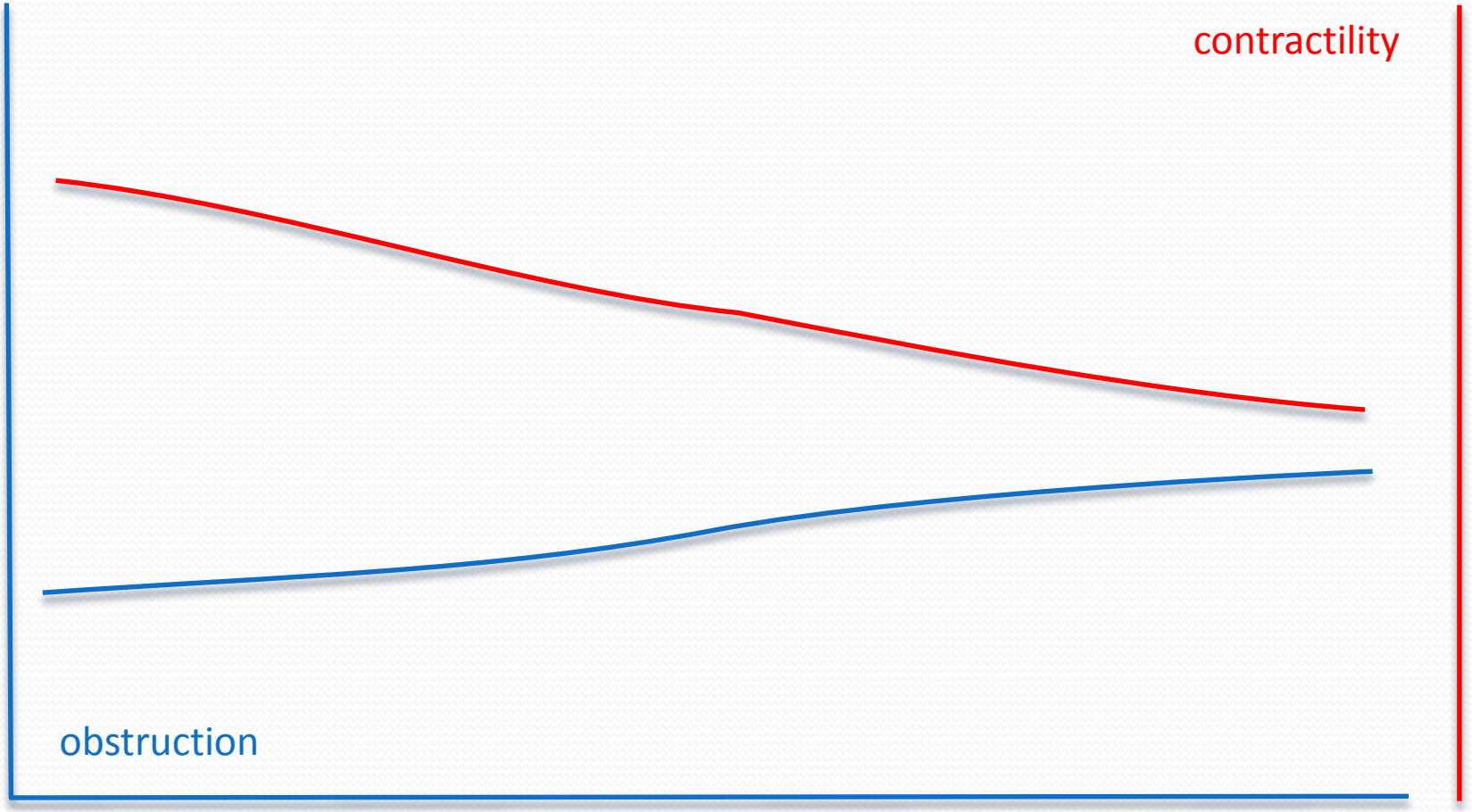
- Maybe:
  - Gammie et al. Eur Urol. 2015
- No:
  - Brown et al. Neurourol.Urodyn. 2016
  - Faraj et.al. Int.Urol.Nefrol. 2016
  - Conn et.al. Curr.op.Urol.2016
    - However, all of these measures may be more relevant to research than clinical practice, where numbers matter less than overall clinical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

Possible precipitating factors

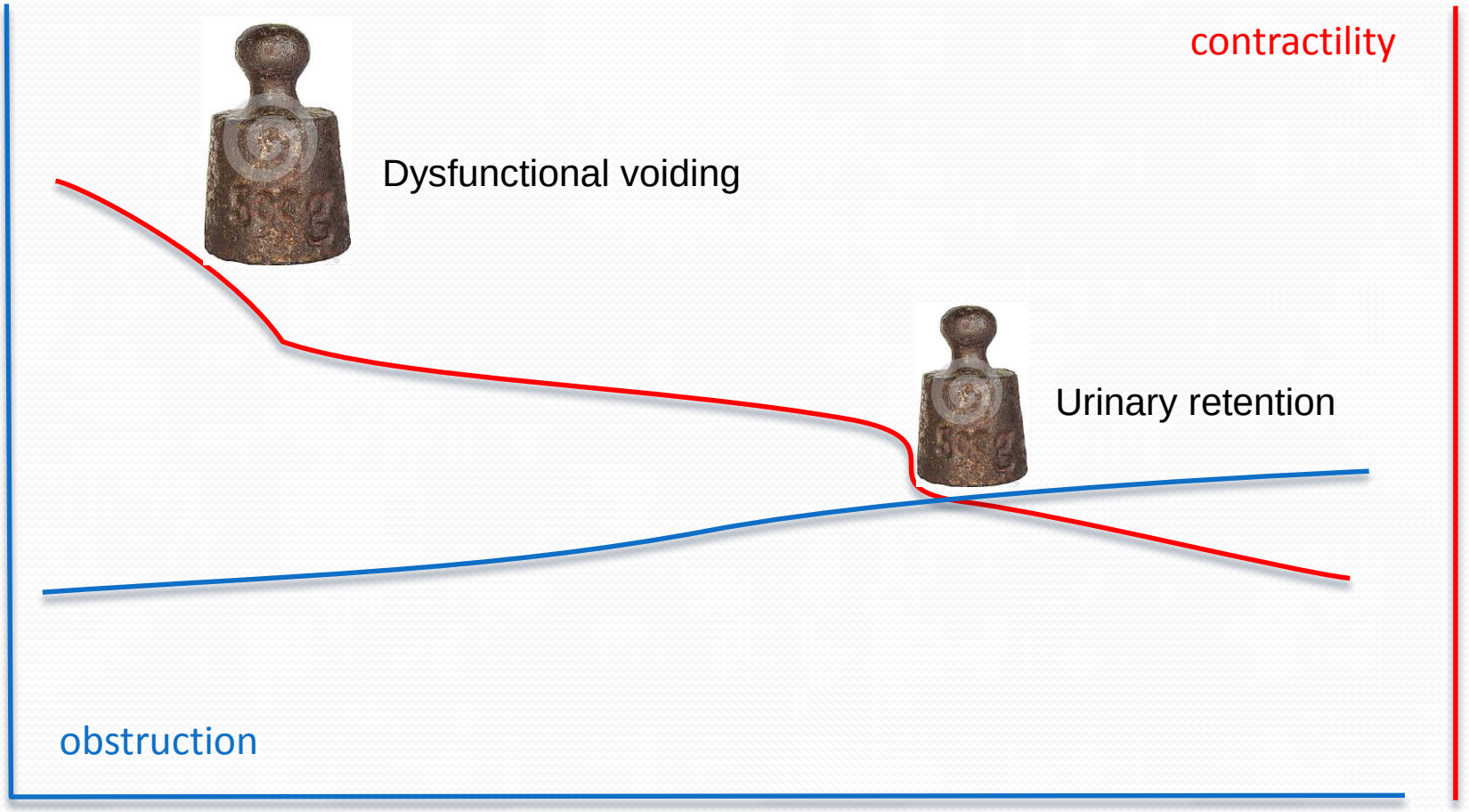
Ageing ? + ?

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

Aging and lower urinary tract function precipitating factors



Precipitating factors ?



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 Koeveringe, Rademakers, Birder, Korstanje, Daneshgari, Ruggieri, Igawa, Fry, Wagg.
ICI-RS 2013, acc. Neurourol Urodyn. 2014

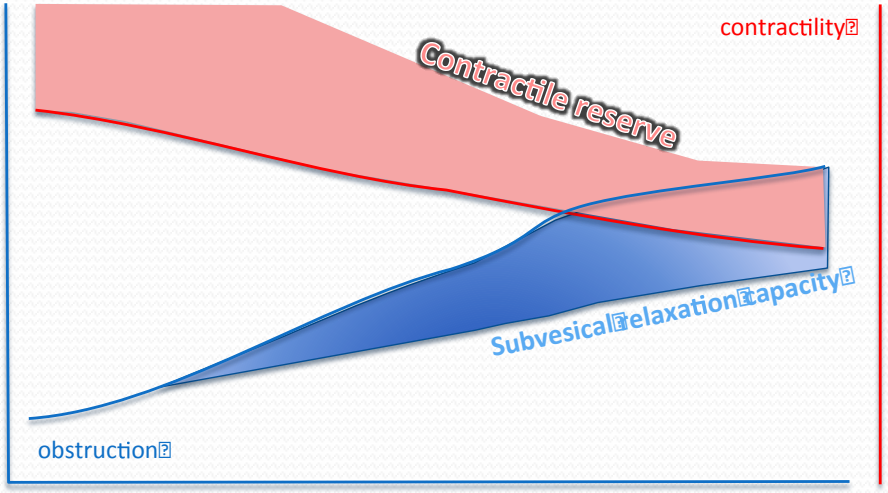
Therapeutic margins

New therapies should aim at either increasing:

- contractile reserve

and/or increasing:

- the subvesical relaxation capacity.



Van Koeveringe et al. Neurourol Urodyn. 2014

- 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 myoplasy
   - Continue CICS

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

Van Koeveringe, Rahnamai', Berghmans; BJUint 2010; 105(4): 101
Rademakers KL, Drossaerts JM, Rahnama'i MS, van Koeveringe GA. Int J Urol. 2015 May;22(5):503-7.

Maastricht Urology Team

Maastricht UMC+
azM | Maastricht University