**W23: Underactive bladder and Voiding Dysfunction: New Insights**

**Workshop Chair:** Gommert van Koeveringe, Netherlands

**15 September 2016 14:35 - 16:05**

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

**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**

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.

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.

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

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

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

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

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
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.

Bladder Outlet Resistance
Bladder Contractility

Detrusor Underactivity

Epidemiology

- Detrusor underactivity:
  - in up to 40% of men aged >65 years ¹
  - 48% of men aged >70 years ²
  - approximately ⅓ of continent 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

Parameters to Judge Voiding

Invasive Indicators of DU

Measurement of Bladder Contractile Function in Men

<table>
<thead>
<tr>
<th>Table</th>
<th>Summary of diagnostic methods</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Schäfer Nomogram</td>
</tr>
<tr>
<td>2.</td>
<td>van Koeveringe GA et al.</td>
</tr>
<tr>
<td>3.</td>
<td>Osman et al.</td>
</tr>
<tr>
<td>4.</td>
<td>Schäfer W.</td>
</tr>
</tbody>
</table>


10 | 20 | 30 | 40 | 50 | 60 | 70 | 80 | 90 | 100 | 110 | 120 | 130 | 140 | 150

Copyrights Life-Thy, Inc. - 1999-2007

Contractile Function in Men

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

Solution for Defining Men with Detrusor Underactivity
- Defining threshold values for the entire range of outlet resistance
- Analysis of a urodynamic database of treatment naive men aged 440 years ($n=822$)
- Exclusion criteria: suspicion of prostate or bladder cancer, radiotherapy, pelvic surgery, neurological disorder, UTI, prostatectomy, bladder stones, bladder diverticula
- Plotting of $\text{BOOI} - W_{\text{max}}$ values in a diagram, calculation of percentiles ($10^{th}$, $25^{th}$, $50^{th}$, $75^{th}$, $90^{th}$) and analyzing differences between the percentiles

Defining Threshold Values

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 $Q_{\text{max}}$ and voided volume + increase of PVR with aging (data of the German epidemiological LUTS study)

Aging
Treatment Effects

- man with BOO and normal/low contractility receives TURP
- Reduction of BOO in 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


Patient Data pre-post TURP

Clinical Consequences of DU

- Fate of bladder emptying ($Q_{\text{max}}$, $P_{\text{detQmax}}$, 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 BOO 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.

Contractility-Obstruction Nomogram

- Sacral neuromodulation data -

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

Sacral neuromodulation 53

- treatment success 86% vs. treatment success 20%

Non-Invasive Indicators of DU

- man with BOO of 80 (30) cm H$_2$O uses an $\alpha$-blocker
  - reduction of BOO by 16% (67.5 or 25.5 cm H$_2$O)

• man with detrusor underactivity ($W_{\text{max}}$ 7.5 W/m$^2$) will most likely remain having PVR, whereas a man with equivocal detrusor contractility may improve

• man with BOO of 80 cm H$_2$O uses an antimuscarinic
  - reduction of BOO by 12% (70.4 cm H$_2$O) and $W_{\text{max}}$ by 20%

• man with contractility of $W_{\text{max}}$ 14 W/m$^2$ is likely to develop PVR or retention, whereas a patient with better contractility (20 W/m$^2$) is unlikely to develop PVR or retention
Non-invasive indicators

- Evaluation of symptoms – patient history
- Ultrasound measurement of detrusor wall thickness (DWT)
- Measurement of isovolumetric bladder pressure with the penile cuff test?
  
Non-invasive Indicators: Symptoms

- Non-invasive indicators: Symptoms
- 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

Ultrasound DWT Measurement for DU Diagnosis

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

Methods:
- Cross-sectional study; men with uncomplicated LUTS
- IPSS, free flow parameters ($Q_{\text{max}}$ and $Q_{\text{ave}}$), PVR, bladder capacity, detrusor wall thickness measurement (DWT)
- DU clinically defined based on PVR + exclusion of BOO / dysfunctional voiding after pressure-flow analysis
- Classification And Regression Tree analysis (CART)
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-Hannover) nomogram defines threshold values for all obstruction grades; points below the 25th percentile indicate detrusor underactivity
- The nomogram can predict the outcome of treatment in men
- Non-invasive parameters are potentially able to replace computer-urodynamic evaluation in clinical practice; until now, only DWT in combination with bladder capacity has been evaluated

- 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
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 Oelke²

¹Maastricht University Medical Centre (MUMC+)
²Hannover Medical School (MHH)
Funding Astellas Europe fund 2012
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 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 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 with specific 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 the highest and 10 patients with the lowest symptom score were analysed
## Characteristics

- Median (IQR)

### Voiding effectiveness:

93% vs. 16%
Study females with voiding dysfunction.

<table>
<thead>
<tr>
<th></th>
<th>Post-void residual</th>
<th>W max</th>
<th>Voiding Efficiency</th>
</tr>
</thead>
<tbody>
<tr>
<td>N=182</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Feeling of incomplete bladder emptying</td>
<td>0.363</td>
<td>&lt;0.001</td>
<td>n.s.</td>
</tr>
<tr>
<td>Intermittency on bladder emptying</td>
<td>0.215</td>
<td>0.042</td>
<td>-0.241</td>
</tr>
<tr>
<td>Weak stream</td>
<td>n.s.</td>
<td>n.s.</td>
<td>n.s.</td>
</tr>
<tr>
<td>Applying abdominal pressure during voiding</td>
<td>n.s.</td>
<td>n.s.</td>
<td>n.s.</td>
</tr>
</tbody>
</table>
Can we differentiate between different causes of voiding dysfunction by symptoms alone?

- **Maybe:**
  - Gammie et al. Eur Urol. 2015

- **No:**

  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

contractility

obstruction
Precipitating factors?

- Dysfunctional voiding
- Urinary retention
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.

Therapeutic margins

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

• Diagnostic tools need to be developed to determine the contractile reserve or the subvesical relaxation capacity. A stress test
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 toileting
  • Allow children to go to clean bathrooms at school

Van Koevearence, Rahnamai’i, Berghman’s; BJU Int 2010; 105(4): 101
Rademakers KL, Drossaerts JM, Rahnama’i MS, van Koevearence GA.
Maastricht Urology Team

Team Urologie
Uw zorg heeft onze aandacht