

Detrusor underactivity

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Valorisation

Lower urinary tract symptoms (LUTS), including urinary incontinence, are major and important quality of life issues within urology. It has been estimated that approximately 1 million people in the Netherlands suffer from LUTS in general and urinary incontinence in particular, and both LUTS and incontinence are responsible for health care seeking behaviour and health care expenditure. With an increasingly ageing population, LUTS, particularly voiding LUTS, become more prominent in society and are responsible for substantial morbidity and quality of life deterioration. The presence of voiding LUTS may precipitate urinary retention and can cause urinary tract infections (UTIs), overflow incontinence, and renal failure. It is estimated that voiding dysfunction occurs in up to two-thirds of the institutionalised elderly and is related to high rates of catheter use¹. For the last decades, research with regard to voiding dysfunction in both men and women has focused on bladder outlet resistance as the main source of voiding LUTS, increased post-void residual urine, urinary retention, overflow incontinence, and UTIs. However, the role of the bladder as the major cause of voiding dysfunction has become increasingly apparent during the recent years, mainly by decreasing bladder outlet obstruction (BOO) in patients with benign prostatic hyperplasia (e.g. by transurethral resection of the prostate) or increasing obstruction in patients with stress urinary incontinence (e.g. by with slings or tapes) has resulted in a number of treatment failures.

Voiding dysfunction caused by a bladder unable to produce sufficient contraction strength and/or adequate duration resulting in incomplete bladder emptying is termed 'detrusor underactivity' (DU) by the International Continence Society². DU may be related to a number of other voiding LUTS and development of UTIs in specific populations. As antibiotic resistance increases rapidly and has become a serious threat, UTIs could even be lethal, as pointed out by the WHO in February 2017³. This health alert on antibiotic treatment, with particular attention to UTIs, emphasises the importance of adequate analysis of potential aetiological factors such as DU in order to diagnose and treat the underlying cause correctly. However, in an era when humans even develop artificial intelligence only little is known about something seemingly simple such as voiding physiology and pathophysiology.

This PhD thesis investigates and discusses DU in broad perspective. DU reflects the result of failure of multiple regulatory systems of the bladder. As the bladder is not only the 'mirror of the soul' but also a reflection of function of different organ systems, failure of these systems and systemic diseases should be taken into account. For example, the presence of DU is related to highly prevalent diseases such as diabetes mellitus or atherosclerosis. Knowledge on the interaction between the bladder (voiding function) and systemic diseases is of major importance and, therefore, reflects an emerging basic research area within urology.

A major part of this thesis covers assessment tools and algorithms to screen and diagnose DU patients among other causes of voiding dysfunction. Diagnosis of DU is highly challenging because all types of voiding dysfunction (i.e. DU, BOO, and detrusor-sphincter dysfunction) often result in the same symptoms and signs. As DU prevalence rate is estimated as high as 45% in the LUTS outpatient department, identifying and categorising these patients is of key importance. Until recently, there has not been a non-invasive or invasive tool available to adequately assess DU and separate it from other types of voiding dysfunctions. The publications included in this thesis have opened a new field of research within functional urology. Several articles form the basis for new research with regard to diagnostic challenges and possibilities to assess voiding function. In addition, this thesis emphasises the importance of differences in voiding function between men and women, something that has been ignored in the past. The output of my research and content of this thesis may help a large group of urological patients and urologists to (1) protect a group of patients to be assessed and treated in the wrong way (e.g. women who receive a transvaginal tape but are unable to void after surgery), (2) raise awareness to urologists to adequately assess a patient with a large post-void residual or urinary retention, and (3) stimulate new treatment options for DU. At present, there are only limited treatment options for DU. Consequently, this PhD thesis on DU aims to initiate research with regard to new pharmacological compounds or smart devices such as neuro-modulators to improve voiding function at various levels.

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2. Abrams P, Cardozo L, Fall M, Griffiths D, Rosier P, Ulmsten U, van Kerrebroeck PE, Victor A, Wein A. The standardisation of terminology of lower urinary tract function: report from the Standardisation Sub-committee of the International Continence Society. *Neurourology and Urodynamics* 2002;21:167-178.
3. Global priority list of antibiotic-resistant bacteria to guide research, discovery, and development of new antibiotics. *World Health Organization*, February 2017.