Tzu Chi Medical Journal 27 (2015) 1–6

Contents lists available at ScienceDirect

Tzu Chi Medical Journal

journal homepage: www.tzuchimedjnl.com

Review Article

Clinical presentation and underlying pathophysiology of an underactive bladder

Jia-Fong Jhang, Yuan-Hong Jiang, Cheng-Ling Lee, Hann-Chorng Kuo*

Department of Urology, Buddhist Tzu Chi General Hospital and Tzu Chi University, Hualien, Taiwan

ARTICLE INFO

Article history:
Received 23 July 2014
Received in revised form
5 August 2014
Accepted 7 August 2014
Available online 24 September 2014

Keywords:
Detrusor underactivity
Diagnosis
Neurogenic bladder
Treatment
Urinary retention

ABSTRACT

Detrusor underactivity (DU) is frequently encountered in elderly patients with chronic medical or neurological diseases. DU causes chronic urinary retention or large postvoid residual urine that is usually difficult to manage. The pathophysiology of DU may involve neurogenic, myogenic, and bladder outlet pathologies. Recent studies also reveal that urothelial dysfunction of the urinary bladder may be associated with impaired bladder sensation as well as impaired detrusor contractility. This article reviews recent research on the prevalence, pathophysiology, and clinical management of DU. Comprehensive clinical investigations and basic research may provide a better understanding and effective treatment for this common but difficult bladder disorder.

1. Introduction

Chronic urinary retention is a debilitating bladder disorder that negatively impacts quality of life and also threatens health. Chronic urinary retention is frequently encountered and is difficult to manage in elderly patients with chronic medical diseases, such as diabetes mellitus (DM), and chronic heart failure or neurological diseases, such as cerebrovascular accident, Parkinson's disease, and dementia. Urinary tract infection (UTI) and renal function deterioration will develop if the bladder condition is not properly managed with clean intermittent catheterization or an indwelling Foley catheter. The pathophysiology of chronic urinary retention may involve neurogenic, myogenic, and bladder outlet pathologies [1]. Recent studies have also revealed that urothelial dysfunction of the urinary bladder may be associated with impaired bladder sensation as well as impaired detrusor contractility [2]. Furthermore, urethral mucosal dysfunction and smooth muscle hyperactivity of the bladder neck and the urethra might also play important roles in the initiation of micturition. Research is needed to explore the pathophysiology of detrusor underactivity (DU) and underactive bladder (UAB).

2. Definition of underactive bladder

The International Continence Society defines DU as a contraction of reduced strength and/or duration, resulting in prolonged bladder emptying and/or failure to achieve complete bladder emptying within a reasonable time [3]. Patients with UAB/DU usually have a diminished sensation of bladder fullness or urgency and cannot contract the detrusor sufficiently to complete bladder emptying. Urodynamic study of UAB/DU may be characterized by a noncontractile detrusor, low pressure, or poorly sustained detrusor contraction in association with a poor flow rate with or without a large post-void residual (PVR) volume [4]. Patients with UAB/DU usually void with abdominal straining and an intermittent flow pattern is noted. The bladder sensation may be normal or reduced in sensing a first or urge sensation [5]. Some patients with UAB/DU may have both detrusor hyperactivity and inadequate contractility (DHIC), resulting in urgency incontinence and a large PVR [6]. In patients with UAB/DU, the intrinsic detrusor contraction speed is more compromised than intrinsic strength. Patients with UAB/DU can be divided into the following three groups according to the urodynamic findings: (1) low maximum detrusor contraction velocity, low isovolumetric detrusor pressure, and bladder emptying efficiency of <67%; (2) low maximum detrusor contraction velocity, low isovolumetric detrusor pressure, and bladder emptying efficiency of ≥67%; and (3) low maximum contraction velocity, normal isovolumetric detrusor pressure, and bladder emptying efficiency of ≥67% [7]. These urodynamic findings are also found in women

Conflicts of interest: none.

* Corresponding author. Department of Urology, Buddhist Tzu Chi General Hospital, 707, Section 3, Chung-Yang Road, Hualien, Taiwan. Tel.: +886 3 8561825x2117; fax: +886 3 8560794.
E-mail address: hck@tzuchi.com.tw (H.-C. Kuo).

http://dx.doi.org/10.1016/j.tcmj.2014.08.001

with idiopathic UAB/DU [8]. The underlying pathophysiology for each group might be different and can be attributed to varying detrusor muscle contractility and bladder outlet resistance in individual patients.

3. Prevalence of UAB/DU

UAB/DU is a common urological problem in elderly patients presenting with urinary retention and lower urinary tract symptoms (LUTS). DU has been found in nearly two-thirds of incontinent institutionalized elderly people [9]. The incidence and prevalence of UAB/DU is highly dependent on the definition and the availability of diagnostic tests. In a retrospective study, 40.2% of men and 13.3% of women undergoing urodynamic study for LUTS were classified as having DU [10]. In urodynamic evaluation of patients with non-neurogenic LUTS, DU was found in 9–48% of men and 12–45% of older women [11]. One urodynamic pressure flow study revealed that 41% of elderly men with symptoms of difficult bladder emptying had an obstructive high pressure low flow pattern, 28.2% had an underactive detrusor contractility pattern, 20.5% had a mixed obstructive and underactive detrusor type, and 10.3% had a normal pattern [12]. The prevalence of bladder outlet obstruction (BOO) voiding difficulty and DU in female urology patients who visited several urology clinics in nine hospitals was 87.2% and 12.8%, respectively [13]. Gotoh et al [14] found impaired detrusor contraction in 81.9% and BOO in 14.8% of women with impaired bladder emptying.

UAB/DU usually occurs in patients with spinal cord injury (central neuropathy) or post pelvic surgery (peripheral neuropathy). In 100 women with urinary retention, Sakakibara et al [15] found the underlying diseases included multiple system atrophy, multiple sclerosis, cervical/thoracic tumors, and lumbar spondylosis. DU is also common in older patients, in those with general weakness and medical diseases such as DM, debilitating disease, and cancer in the terminal stages, and after major surgery [16]. Women with diabetic voiding dysfunction were found to have a longer duration of DM than those with an overactive bladder. Ageing and UTI are two independent factors contributing to impaired voiding function and diabetic bladder dysfunction [17]. A large proportion of patients with diabetic cystopathy were found to have electrophysiological (EP) evidence of neuropathy, which can moderately predict the presence of cystopathy [18]. DM can affect the bladder, presumably via peripheral pathogenetic mechanisms that induce DHIC. Patients with DU showed impaired emptying function and decreased sensation on cystometry and intravesical current perception threshold testing [19].

UAB/DU and DHIC were also common (15% and 1%, respectively) in patients with recent ischemic stroke [20]. Although UAB/DU may occur in any age group, both conditions have an age-associated prevalence. The actual contribution of ageing on detrusor contractility, however, has not been conclusively demonstrated. In one study, UAB/DU was observed in 41% of patients presenting with urinary incontinence or LUTS following radical prostatectomy [21]. UAB/DU may be chronic or temporary. In clinical practice, we have observed patients with BOO and normal detrusor contractility who have developed transient UAB/DU after transurethral resection of the prostate or immediately after a minor stroke. These patients may regain spontaneous voiding within 1–3 months. However, some patients might develop chronic DU and spontaneous voiding may not return in the short term. There must be some underlying pathogenesis for the development of transient UAB/DU, such as detrusor muscle damage or neurological inhibition, which interferes with the integration of musculomucosal mechanoreceptors, mucosal mechanoreceptors, and chemoreceptors [22].

We have previously investigated videourodynamic characteristics in men and women with LUTS refractory to conventional medication. DU was noted in 146 (5.2%) of 2,831 men with LUTS and DHIC in 150 (5.3%) of 2,831 men with LUTS. The incidence of DHIC increased with ageing; however, the incidence of DU with age was not significantly different from that in other vesicourethral dysfunctions such as detrusor overactivity, bladder neck dysfunction and benign prostatic obstruction. DU was noted in 108 (36.1%) of 299 patients with a PVR >250 mL and DHIC in 44 (14.7%) of 299 patients with a PVR >250 mL. The bladder sensation of filling and fullness were significantly reduced compared with that in patients with BOO. The incidence of DU in 1,333 female patients with LUTS was 11.4% and DHIC was noted in 4.3% (Table 1). The medical comorbidity in 118 women presenting with chronic urinary retention or a large PVR included DM (43, 30.7%), hypertension (52, 37.1%), coronary arterial disease (17, 12.1%), chronic obstructive pulmonary disease (3, 2.1%) and chronic kidney disease (25, 17.9%) [23].

4. Pathophysiology of UAB/DU

The pathogenesis of UAB/DU is likely to be multifactorial [1]. UAB/DU may be classified into myogenic and neurogenic mechanisms [24]. The causes of UAB/DU include DM, BOO, ageing, neurological diseases, spinal cord lesions, and pelvic plexus and infectious neurological problems [25]. UAB/DU can result from damage to the bladder afferent pathways, bladder efferent pathways, or lumbosacral spinal cord or be due to pure detrusor failure [26]. There is a need for longitudinal patient data to define risk factors, develop screening tools, and establish an animal model for translational research into UAB/DU [27].

4.1. UAB/DU in patients with chronic urinary retention may be caused by latent neuropathy

In videourodynamic study (VUDS), patients with chronic urinary retention usually have low voiding pressure or DU without significant BOO, defined as non-obstructive voiding dysfunction. We retrospectively collected 60 patients, who were diagnosed with nonobstructive voiding dysfunction on VUDS and had received lower urinary tract EP studies. EP studies included examination of the bulbocavernous reflex by electrical stimulation, electromyography of the external urethral sphincter (EUS), and nerve conduction velocity (NCV) study of the internal pudendal nerve. In electromyography study, denervation, reinnervation changes, and reduced recruitment of the EUS was observed in 21.7%, 71.7%, and 86.7% of patients, respectively. Decreased amplitude of the internal pudendal nerve was noted in NCV study in 73.3% of the patients. Significant sacral neuropathy (e.g., saddle anesthesia) was present on neurological examination in 19 out of 60 patients (31.7%).

Table 1
Prevalence of detrusor underactivity in women with lower urinary tract symptoms.

Normal findings	272 (16.9)
Sensory disorders (459)	
• Bladder oversensitivity	289 (18.0)
• Suggestive of interstitial cystitis/painful bladder syndrome	170 (10.6)
Motor disorders (560)	
• Idiopathic detrusor overactivity	308 (19.2)
• Detrusor hyperactivity and inadequate contractility	69 (4.3)
• Detrusor underactivity	183 (11.4)
Bladder outlet disorders (314)	
• Bladder neck dysfunction	27 (1.7)
• Dysfunctional voiding	168 (10.5)
• Urethral stricture	17 (1.1)
• Poor relaxation of pelvic floor muscles	102 (6.4)

Data are presented as *n* (%).

Patients with sacral neuropathy had a lower bulbocavernous reflex positive rate ($p = 0.001$), a non-significant but higher denervation rate ($p = 0.059$) in electrometrography studies, and a higher rate of decreased amplitude in NCV studies ($p = 0.011$) than those without sacral neuropathy. DU patients had a high percentage of neurological deficits in EP studies. Reinnervation and reduced recruitment of the EUS indicated that the lower urinary tract experienced an incomplete or inadequate recovery from potential neurological insults. Decreased amplitude in NCV studies also suggested the presence of internal pudendal neuropathy. Potential neurological insults explored in EP studies could play an important role in the pathophysiology of DU, and EP studies may aid in the treatment strategy of nonobstructive voiding dysfunction (including DU) in the future.

4.2. UAB/DU due to detrusor failure or BOO

Diabetic cystopathy can occur silently early or late in the course of DM. DM induces a decrease in detrusor contractility and increases oxidative stress factors, resulting in urothelial dysfunction or causing an alteration of the pathophysiology of detrusor muscle cells, resulting in impaired bladder sensation or impaired detrusor contractility [28]. BOO can result in structural and functional changes in the bladder wall. Detrusor contractility may be reduced in patients with chronic urinary retention or a large PVR due to benign prostatic hyperplasia with BOO [29]. It is difficult, however, to differentiate idiopathic UAB/DU from chronic urinary retention secondary to BOO. Patients with chronic BOO might also have a low detrusor pressure and a large PVR. In a minimum 10-year urodynamic follow-up in men with BOO, there was no evidence to suggest that detrusor contractility declined with long-term BOO. Relieving the obstruction surgically did not improve detrusor contractility. An underactive detrusor remained underactive, but did not get worse with time [30].

In adult male patients with LUTS, detrusor contraction power parameters, the bladder contractility index and the maximum work (W_{max}) continuously increase with an increasing grade of BOO. We were unable to determine a single threshold value for detrusor contraction power to diagnose idiopathic DU (non-BOO DU) in a group of LUTS patients with different grades of BOO [31]. The ultrastructural changes seen on electromicroscopic examination of detrusor biopsies from DU bladders revealed approximately four times more disruptive cells than in controls, which might interrupt the electrical transmission between muscle cells and result in low detrusor contractility on stimulation [32]. Passive bladder wall stiffness in rats with spinal cord transection was significantly reduced compared with that in the sham-operated control group, and spinal cord transection bladder strips relaxed more quickly than those sham-operated rats. The reduced passive bladder wall stiffness and enhanced rate of stress relaxation revealed that increased compliance is marked by altered matrix properties that dissipate muscle force, thereby generating low pressures [33]. Whether UAB/DU is a progressive change from DHIC remains unknown, but the impairment of detrusor contractility with and without altered bladder sensation might be the cause of UAB/DU and DHIC in aging patients, respectively [5,34].

4.3. Impaired bladder sensation and UAB/DU

Normal bladder sensation and transduction of stretch (urothelial pathway) are essential for normal micturition. Normal afferent nerves convey the bladder sensations of filling, urgency, and nociception via C-fibers within the urothelium and suburothelium or A-delta fibers within the detrusor muscles. The sensory activation of the micturition reflex is essential for normal detrusor contractility on stimulation [6]. In patients with acute or chronic sensory afferent nerve lesions (such as herpes zoster infection or syphilis-induced tabes dorsalis), detrusor contractility is greatly impaired and urinary retention may ensue.

The inhibitory effects of detrusor contraction by the striated urethral sphincter and the bladder neck via alpha-adrenergic activity may also play a role in the development of UAB/DU. Furthermore, normal perception of bladder fullness and an urge sensation are the fundamental bases for a normal micturition process. Patients with severe cortical degenerative disease may lack bladder perception and be unable to initiate voiding. Ageing can cause structural and functional changes in the bladder afferent nerves and detrusor power, and reflex activity might also be impaired [5]. In addition, chronic BOO and latent cortical degeneration might also occur in elderly patients, especially when they experience severe illness or major surgery, resulting in UAB/DU.

4.4. Urothelial dysfunction and UAB/DU

It is possible that bladder urothelial dysfunction, sensory nerve dysfunction, and detrusor myogenic dysfunction – as well as impaired central nervous system control – are involved, in part or totally, in the development of UAB/DU. Understanding the pathophysiology of UAB/DU in individual patients is the mainstay of appropriate management.

The urothelium is not only a barrier to urine solutes but also expresses various receptors and ion channels that are responsible for mechanical or thermal changes in the bladder, such as receptors to bradykinin, trkA, p75, purine (P2X and P2Y), noradrenaline (alpha and beta adrenaline), and acetylcholine (muscarinic or nicotinic) [35–43]. The urothelium also expresses several vanilloid receptors, called transient receptor potential channels (TRPV1, TRPV 2, TRPV4, TRPM8, and TRPA1), suggesting that urothelial cells also exert a sensory function in bladder filling and noxious stimuli [44–48]. Stimulation of these sensory receptors by mechanical trauma, hydrostatic pressure changes, and chronic inflammation can release chemicals such as adenosine triphosphate (ATP), prostaglandins, nerve growth factors (NGF), acetylcholine, and nitric oxide (NO), which may have excitatory or inhibitory effects on the afferent nerves or detrusor contractility [49–53]. Recent study suggests that TRPV4 senses bladder urothelial cultured cell stretching, which is converted to ATP signals in the micturition reflex pathway during the storage phase [54]. Downregulation of TRPV4 might lead to a decreased sensation of bladder fullness and detrusor underactivity.

The urothelium might influence the contractile state of detrusor smooth muscles, through modifying its contractility and the extent of spontaneous activity [2]. In one study, the ratio of ATP to NO, representing sensory transmission in the bladder, was high in a bladder model of overactive bladder and low in a bladder model of UAB/DU. ATP release had a positive correlation whereas NO release had a negative correlation with the bladder contraction frequency. The urinary ATP/NO ratio may be a clinically relevant biomarker that characterizes the extent of bladder dysfunction [55]. In addition, bladder ischemia and repeated ischemia/reperfusion during a micturition cycle may produce oxidative stress, leading to denervation and further tissue damage in the bladder wall [56]. This ischemic effect on the bladder wall might be the cause of transient urinary retention in patients after major surgery or acute illness.

An intact bladder mucosa has been associated with an increase in spontaneous contractile activity in whole-bladder preparations [57]. The urothelium exerts an excitatory effect on the underlying muscle whereas suburothelial tissue causes an inhibitory effect. It was proposed that mucosal M3 receptors induce the release of a

contractile agonist or suppress the release of an agent that inhibits detrusor contractility [58]. A group of interstitial cells that have a contractile phenotype and contain smooth muscle actin have been found between the bladder mucosa and detrusor [59]. Interstitial cells are the major site for the gap junction protein connexin 43 (Cx43), and allow propagation of electrical and calcium signals across a functional syncytium [60]. Currently, interstitial cells are believed to transmit signals from the urothelium or detrusor. Impaired function of interstitial cells might cause impaired detrusor contractility through impaired bladder urothelial sensory input. The number of interstitial cells and the density of Cx43 were found to increase in an overactive bladder [61]. Whether the density of Cx43 is decreased in the bladders of patients with UAB/DU has not been elucidated. The density of interstitial cells in UAB/DU bladders has also not been reported.

We investigated urothelial dysfunction in 37 patients with DU and 20 healthy controls. In patients with DU, junction protein E-cadherin was significantly lower and suburothelial inflammation determined by mast cell count and urothelial cell apoptosis were significantly higher than in controls. However, there was no significant difference in barrier protein zonula occludens-1 expression between DU and controls (Table 2). These results indicate that chronic inflammation and urothelial dysfunction are present in DU bladders. These immunohistochemistry findings can only explain that urothelial dysfunction is evident in patients with DU. We need further molecular studies of functional receptors such as TRPV4 and P2X3 to explore the possible pathomechanisms of UAB/DU. TRPV4 is a nonselective cation channel involved in different sensory functions and was recently implicated in bladder mechanosensation. Immunoprecipitation experiments established a molecular connection between TRPV4 and the adherence junctions of the bladder mucosa [62]. The lower expression of E-cadherin may be associated with decreased bladder sensation during mucosal stretching.

Investigation of the expressions of urothelial sensory receptors (P2X3, TRPV1, TRPV4, etc.), urothelial junction proteins (E-cadherin), chronic inflammation of the urothelium (tryptase, inducible NO synthase, cyclooxygenase-2 etc), sensory nerve functional proteins (NGF, prostaglandin E2 and NO), detrusor muscarinic M2 and M3 receptors, muscular junction protein (Cx43), and analysis of apoptotic cell activities (terminal deoxynucleotidyl transferase dUTP nick end labeling), might provide valuable information on the pathophysiology of UAB/DU. In addition, using urine and serum biomarkers to measure neuronal regeneration activity, such as NGF, brain-derived neurotrophic factor and prostaglandin E2 will also be helpful. Investigation of serum inflammatory proteins and cytokines such as NGF, C-reactive protein, interleukin (IL)-1beta, IL-6, IL-8, and IL-10 will also benefit the understanding of the pathophysiology of UAB/DU. Finally, study of urethral mucosal dysfunction including alpha-1 adrenoceptors and muscarinic receptor density might also provide evidence of the underlying causes of UAB/DU.

Table 2
The differences in E-cadherin, mast cell count, urothelial cell apoptosis, and zonula occludens-1 expression in detrusor underactivity and normal controls.

	Normal	Detrusor underactivity	*p*
E-cadherin	38.41 ± 19.21	28.82 ± 18.12	0.001
Mast-cell	3.0 ± 2.83	10.81 ± 5.53	< 0.001
Terminal deoxynucleotidyl transferase dUTP nick end labeling	0.49 ± 0.99	6 ± 3.23	< 0.001
Zonula occludens-1	8.23 ± 4.99	7.74 ± 3.37	0.693

4.5. Role of the bladder neck and urethral sphincter hyperactivity in UAB/DU

Detrusor, bladder neck, and urethral sphincter dysfunction are usually characterized as motor neuron diseases because their features correspond to damage to the spinal cord or cauda equina, which involves the somatic and parasympathetic pathways [63]. Afferent nerves of the pudendal nerve are postulated to have a potential modulatory effect on sympathetic neuronal control in various neuropathic and non-neuropathic bladder dysfunctions, but the mechanisms and pathways remain unknown [64]. Bladder neck dysfunction seems to represent sympathetic hyperactivity or dysfunction and poor accommodation, which are considered to be secondary to abnormal adrenergic detrusor innervation [65]. Clinically, transurethral incision of the bladder neck (TUI-BN) not only disrupts the continuity of a tight bladder neck but might also abolish the inhibitory effect on detrusor contractility [66]. Patients with idiopathic DU may regain adequate detrusor contractility and resume spontaneous voiding [67,68]. Decreased urethral pressure by preganglionic pelvic nerve stimulation and the administration of alpha- and beta-methylene ATP in female pigs also resulted in bladder detrusor contractions [69]. A poorly relaxed urethral sphincter is thought to cause increased urethral afferent activity, which inhibits bladder afferent signaling leading to poor bladder sensation and UAB/DU. The application of sacral neuromodulation in patients with Fowler's syndrome can therefore restore normal voiding [70]. Patients with stroke and incomplete bladder emptying might also develop UAB/DU due to spasticity of the external sphincter [71]. Bladder neck dysfunction, dysfunctional voiding, and DU are the main urodynamic abnormalities in young men with LUTS [72,73]. Treatment targeting bladder or urethral sphincter hyperactivity might restore normal detrusor contractility and improve voiding efficiency in patients without BOO who have incomplete bladder emptying.

5. Clinical investigations of UAB/DU

Clinical investigation of patients with UAB/DU or DHIC should be very comprehensive. A history and detailed physical examination including neurological examination should be carried out. There should be a careful search for medical diseases that waste body energy or local diseases that cause poor relaxation of the pelvic floor muscles. Other examinations should include: urodynamic pressure flow study to test bladder sensory function, bladder compliance, and detrusor contractility, as well as external sphincter electrometrography coordination; VUDS to exclude possible bladder outlet obstruction; and electrophysiology study to test for a normal micturition reflex circuit, normal pudendal nerve conduction, and normal urethral sphincter electrometrography activity.

6. Treatment of UAB/DU

The treatment goal for UAB/DU is focused on reducing the PVR and preventing UTI. Treatment of UAB/DU may include increasing detrusor contractility, decreasing bladder outlet resistance, or increasing the cortical perception of bladder sensation. However, medical treatment for UAB/DU is usually disappointing. Parasympathomimetic agents and acetylcholinesterase inhibitors, with or without alpha-blockers, might benefit patients with DU [74–76]. Cholinesterase inhibitors might inhibit the degradation of acetylcholine and provide beneficial effects in patients with UAB/DU. These pharmacological treatments might not be suitable for patients with DHIC, however, as pharmacological treatment can exacerbate overactive symptoms. Decreasing bladder outlet resistance has been considered effective in reducing the PVR and

improving voiding efficiency. However, randomized control trials are lacking to prove its efficacy. In addition to pharmacological treatment, percutaneous tibial nerve stimulation and intravesical electrical stimulation have been effective for non-neurogenic, refractory lower urinary tract dysfunction in children [77,78].

We performed TUI-BN to decrease bladder outlet resistance in patients with UAB/DU [67]. A total of 46 patients with bladder neck dysfunction underwent TUI-BN to relieve LUTS. Compared with baseline data, postoperative VUDS revealed that the detrusor pressure at the maximum flow rate ($P_{det\cdot Qmax}$) decreased in 28 patients and increased in 12 patients, with persistent DU in six individuals. The $P_{det\cdot Qmax}$ increased significantly from 8.7 ± 9.8 cmH_2O to 28.3 ± 13.8 cmH_2O ($p = 0.021$) in patients with low detrusor contractility or DU before the operation. Four (67%) of the six patients with DU could void with the aid of abdominal pressure after TUI-BN. Interestingly, some patients recovered detrusor contractility after the surgical procedure. This phenomenon has been observed not only in neurogenic bladders but also in non-neurogenic DU [66,68], suggesting a micturition facilitating reflex might be triggered after TUI-BN. A total of 31 women with DU and failed medical treatment underwent TUI-BN and were retrospectively studied. The patients with a postoperative voiding efficiency of >67% had excellent outcomes, those with 33–66% efficiency had moderate results, and those with <33% efficiency had poor surgical outcomes. The PVR, voiding efficiency, and Q_{max} significantly improved after TUI-BN. The PVR decreased by 56.3% overall. Intermittent catheterization was needed in 27 patients before surgery and in only seven patients after TUI-BN. Among the 17 patients with urodynamic DU prior to TUI-BN, six (35.3%) regained detrusor contractility after the operation. There were 14 (45.2%) patients, 11 (35.5%) patients, and six (19.3%) patients with excellent, moderate, and poor surgical outcomes, respectively [68]. The study suggested that TUI-BN is an effective procedure to improve the PVR, Q_{max}, and voiding efficiency in women with DU and urine retention.

It is also possible that the inhibitory effect of adrenergic hyperactivity on detrusor contractility can be modulated after TUI-BN, resulting in a recovery of detrusor function that has been inhibited through unknown mechanisms. A recent clinical study showed that 78.9% of patients with an acontractile bladder had significant return of detrusor contractility after laser enucleation of the prostate [79]. Because the prostatic urethra is innervated mainly by the sympathetic adrenergic nerves, ablation of the prostatic urethra might abolish the sympathetic hyperactivity that inhibits detrusor contractility.

References

[1] Andersson KE. The many faces of impaired bladder emptying. Curr Opin Urol 2014;24:363–9.
[2] Birder LA, Ruggieri M, Takeda M, van Koeveringe G, Veltkamp S, Korstanje C, et al. How does the urothelium affect bladder function in health and diseases? ICI-RS 2011. Neurourol Urodyn 2012;31:293–9.
[3] Abrams P, Cardozo L, Fall M, Griffiths D, Rosier P, Ulmsten U, et al. The standardisation of terminology of lower urinary tract function: report from the Standardisation Subcommittee of the International Continence Society. Neurourol Urodyn 2002;21:167–78.
[4] Thomas AW, Cannon A, Bartlett E, Ellis-Jones J, Abrams P. The natural history of lower urinary tract dysfunction in men: the influence of detrusor underactivity on the outcome after transurethral resection of the prostate with a minimum 10-year urodynamic follow-up. BJU Int 2004;93:745–50.
[5] Smith PP. Aging and the underactive detrusor: a failure of activity or activation? Neurourol Urodyn 2010;29:408–12.
[6] Kanai A, Andersson KE. Bladder afferent signaling: recent findings. J Urol 2010;183:1288–95.
[7] Cucchi A, Quaglini S, Rovereto B. Proposal for a urodynamic redefinition of detrusor underactivity. J Urol 2009;181:225–9.
[8] Cucchi A, Quaglini S, Rovereto B. Development of idiopathic detrusor underactivity in women: from isolated decrease in contraction velocity to obvious impairment of voiding function. Urology 2008;71:844–8.
[9] Resnick NM, Yalla SV, Laurino E. The pathophysiology of urinary incontinence among institutionalized elderly persons. N Engl J Med 1989;320:1–7.
[10] Jeong SJ, Kim HJ, Lee YJ, Lee BK, Choo YM, Oh JJ, et al. Prevalence and clinical features of detrusor underactivity among elderly with lower urinary tract symptoms: A comparison between men and women. Korean J Urol 2012;53:342–8.
[11] Osman NI, Chapple CR, Abrams P, Dmochowski R, Haab F, Koelbl H, et al. Detrusor underactivity and the underactive bladder: a new clinical entity? A review of current terminology, definitions, epidemiology, aetiology, and diagnosis. Eur Urol 2014;65:389–98.
[12] Diokno AC, Brown MB, Goldstein NG, Herzog AR. Urinary flow rates and voiding pressures in elderly men living in a community. J Urol 1994;151:1550–3.
[13] Chi YS, Kim JC, Lee KS, Seo JT, Kim HJ, Yoo TK, et al. Analysis of female voiding dysfunction: a prospective, multi-center study. Int Urol Nephrol 2013;45:989–94.
[14] Gotoh M, Yoshikawa Y, Ohshima S. Pathophysiology and subjective symptoms in women with impaired bladder emptying. Int J Urol 2006;13:1053–7.
[15] Sakakibara R, Yamamoto T, Uchiyama T, Liu Z, Ito T, Yamazaku T, et al. Is lumbar spondylosis a cause of urinary retention in elderly women? J Neurol 2005;252:953–7.
[16] Ueda T, Yoshimura N, Yoshida O. Diabetic cystopathy: relationship to autonomic neuropathy detected by sympathetic skin response. J Urol 1997;157:590–4.
[17] Lin TL, Chen GD, Chen YC, Huang CN, Ng SC. Aging and recurrent urinary tract infections are associated with bladder dysfunction in type 2 diabetes. Taiwan J Obstet Gynecol 2012;51:381–6.
[18] Bansal R, Agarwal MM, Modi M, Mandal AK, Singh SK. Urodynamic profile of diabetic patients with lower urinary tract symptoms: association of diabetic cystopathy with autonomic and peripheral neuropathy. Urology 2011;77:699–705.
[19] Lee WC, Wu HP, Tai TY, Yu HJ, Chiang PH. investigation of urodynamic characteristics and bladder sensory function in the early stages of diabetic bladder dysfunction in women with type 2 diabetes. J Urol 2009;181:198–203.
[20] Pizzi A, Falsini C, Martini M, Rossetti MA, Verdesca S, Tosto A. Urinary incontinence after ischemic stroke: clinical and urodynamic studies. Neurourol Urodyn 2014;33:420–5.
[21] Chung DE, Dillon B, Kurta J, Maschino A, Cronin A, Sandhu JS. Detrusor underactivity is prevalent after radical prostatectomy: a urodynamic study including risk factors. Can Urol Assoc J 2012 Jan;24:1–5.
[22] Andersson KE. Detrusor underactivity/underactive bladder: new research initiatives needed. J Urol 2010;184:1829–30.
[23] Chen YC, Kuo HC. Clinical and video urodynamic characteristics of adult women with dysfunctional voiding. J Formos Med Assoc 2014;113:161–5.
[24] Van Koeveringe GA, Vahabi B, Andersson KE, Kirschner-Herrmans R, Oelke M. Detrusor underactivity: a plea for new approaches to a common bladder dysfunction. Neurourol Urodyn 2011;30:723–8.
[25] Miyazato M, Yoshimura N, Chancellor MB. The other bladder syndrome: underactive bladder. Rev Urol 2013;15:11–22.
[26] Chancellor MB, Blaivas JG. Classification of neurogenic bladder disease. In: Chancellor MB, editor. Practical neurology. Boston: Butterworth; Heinemann; 1995. p. 25–32.
[27] VaKoeveringe GA, Rademakers KL, Birder LA, Korstanje C, Daneshgari F, Ruggieri MR, et al. Detrusor underactivity: pathophysiological considerations, models and proposals for future research. ICI-RS 2013. Neurourol Urodyn 2014;33:591–6.
[28] Yoshimura N, Chancellor MB, Andersson KE, Christ GJ. Recent advances in understanding the biology of diabetes-associated bladder complications and novel therapy. BJU Int 2005;95:733–8.
[29] Taylor 3rd JA, Kuchel GA. Detrusor underactivity: clinical features and pathogenesis of an underdiagnosed geriatric condition. J Am Geriatr Soc 2006;54:1920–32.
[30] Al-Hayek S, Thomas A, Abrams P. Natural history of detrusor contractility–minimum ten-year urodynamic follow-up in men with bladder outlet obstruction and those with detrusor. Scand J Urol Nephrol Suppl 2004;215:101–8.
[31] Oelke M, Rademakers KL, van Koeveringe GA. Detrusor contraction power parameters (BCI and W max) rise with increasing bladder outlet obstruction grade in men with lower urinary tract symptoms: results from a urodynamic database analysis. World J Urol 2014;32:1177–83.
[32] Brierly RD, Hindley RG, McLarty E, Harding DM, Thomas PJ. A prospective controlled quantitative study of ultrastructural changes in the underactive detrusor. J Urol 2003;169:1374–8.
[33] Young JS, Johnston L, Soubrane C. The passive and active contractile properties of the neurogenic, underactive bladder. BJU Int 2013;111:355–61.
[34] Cucchi A, Quaglini S, Rovereto B. Different evolution of voiding function in underactive bladders with and without detrusor overactivity. J Urol 2010;183:229–33.
[35] Chopra B, Barrick S, Meyers S, Beckel JM, Zeidel ML, Ford AP, et al. Expression and function of bradykininB1 and B2 receptors in normal and inflamed rat urinary bladder urothelium. J Physiol 2005;562:859–71.
[36] Murray E, Malley S, Qiao LY, Hu YY, Vizzard MA. Cyclophosphamide induced cystitis alters neurotrophin and receptor tyrosine kinase expression in pelvic ganglia and bladder. J Urol 2004;172:2434–9.

[37] Birder LA, Ruan H, Chopra B, Xiang Z, Barrick S, Buffington CA, et al. Alterations in P2X and P2Y purinergic receptor expression in urinary bladder from normal cats and cats with interstitial cystitis. Am J Physiol 2004;287:F1084–91.
[38] Lee HY, Bardini M, Burnstock G. Distribution of P2X receptors in the urinary bladder and the ureter of the rat. J Urol 2000;163:2002–7.
[39] Tempest HV, Dixon A, Turner WH, Elneil S, Sellers LA, Ferguson DR. P2X receptor expression in human bladder urothelium and changes in interstitial cystitis. BJU Int 2004;93:1344–8.
[40] Birder LA, Apodaca G, de Groat WC, Kanai A. Adrenergic- and capsaicin-evoked nitric oxide release from urothelium and afferent nerves in urinary bladder. Am J Physiol 1998;275:F226–9.
[41] Birder LA, Nealen M, Kiss S, de Groat WC, Caterina MJ, Wang E, et al. Beta-adrenoceptor agonists stimulate endothelial nitric oxide synthase in rat urinary bladder urothelial cells. J Neurosci 2002;22:8063–70.
[42] Beckel JM, Kanai A, Lee SJ, de Groat WC. Birder LAl. Expression of functional nicotinic acetylcholine receptors in rat urinary bladder epithelial cells. Am J Physiol 2006;290:F103–10.
[43] Chess-Williams R. Muscarinic receptors of the urinary bladder: detrusor urothelial and prejunctional. Auton Autacoid Pharmacol 2002;22:133–45.
[44] Birder LA, Kanai A, de Groat WC, Kiss S, Nealen ML, Burke NE, et al. Vanilloid receptor expression suggests a sensory role for urinary bladder epithelial cells. Proc Natl Acad Sci USA 2001;98:13396–401.
[45] Birder LA, Nakamura Y, Kiss S, Nealen ML, Barrick S, Kanai AJ, et al. Altered urinary bladder function in mice lacking the vanilloid receptor TRPV1. Nat Neurosci 2002;5:856–60.
[46] Birder L, Kullmann FA, Lee H, Barrick S, de Groat W, Kanai A, et al. Activation of urothelial transient receptor potential vanilloid 4 by 4-alpha-phorbol 12,13-didecanote contributes to altered bladder reflexes in the rat. J Pharmacol Exp Ther 2007;323:227–335.
[47] Stein RJ, Nagatomi J, Nagatomi J, Hayashi Y, Minnery BS, Xavier M, et al. Cool (TRPM8) and hot (TRPV1) receptors in the bladder and male genital tract. J Urol 2004;172:1175–8.
[48] Streng T, Axelsson HE, Hedlund P, Andersson DA, Jordt SE, Bevan S, et al. Distribution and function of the hydrogen sulfide-sensitive TRPA1 ion channel in rat urinary bladder. Eur Urol 2008;53:391–9.
[49] Downie JW, Karmazny M. Mechanical trauma to bladder epithelium liberates prostanoids which modulate neurotransmission in rabbit detrusor muscle. J Pharmacol Exp Ther 1984;230:445–9.
[50] Ferguson DR, Kennedy I, Burton TJ. ATP is released from rabbit urinary bladder epithelial cells by hydrostatic pressure changes—A possible sensory mechanism? J Physiol 1997;505:503–11.
[51] Wang EC, Lee J, Ruiz WG, Balestreire EM, von Bodungen M, Barrick S, et al. ATP and purinergic receptor-dependent membrane traffic in bladder umbrella cells. J Clin Invest 2005;115:2412–22.
[52] Yoshida M, Inadome A, Maeda Y, Satoji Y, Masunaga K, Sugiyama Y, et al. Non-neuronal cholinergic system inhuman bladder urothelium. Urology 2006;67:425–30.
[53] Andersson KE. Bladder activation: afferent mechanisms. Urology 2002;59:43–50.
[54] Mochizuki T, Sokabe T, Araki I, Fujishita K, Shibassaki K, Uchida K, et al. The TRPV4 cation channel mediates stretch-evoked Ca2+ influx and ATP release in primary urothelial cell cultures. J Biol Chem 2009;284:21257–64.
[55] Munoz A, Smith CP, Boone TB, Somogyi GT. Overactive and underactive bladder dysfunction is reflected by alterations in urothelial ATP and NO release. Neurochem Int 2011;58:295–300.
[56] Yamaguchi O, Nomiya M, Andersson KE. Functional consequences of chronic bladder ischemia. Neurourol Urodyn 2014;33:54–8.
[57] Sui GP, Wu C, Roosen A, Ikeda Y, Kanai AJ, Fry CH. Modulation of bladder myofibroblast activity: implications for bladder function. Am J Physiol 2008;295:F688–97.
[58] Braverman AS, Lebed B, Linder M, Ruggieri MR. M2 mediated contractions of human bladder from organ donors is associated with an increase in urothelial muscarinic receptors. Neurourol Urodyn 2007;26:63–70.
[59] Thompson SA, Copeland CR, Reich DH, Tung L. Mechanical coupling between myofibroblasts and cardiomyocytes slows electric conduction in fibrotic cell monolayers. Circulation 2011;123:2083–93.
[60] Sui GP, Rothery S, Dupont E, Fry CH, Severs NJ. Gap junctions and connexin expression in human suburothelial interstitial cells. BJU Int 2002;90:118–29.
[61] Ikeda Y, Fry CH, Hayashi F, Stolz D, Friffiths D, Kanai A. Role of gap junctions in spontaneous activity of the rat bladder. Am J Physiol 2007;293:F1018–25.
[62] Janssen DA, Hoenderop JG, Jansen KC, Kemp AW, Heesakkers JP, Schalken JA. The mechanoreceptor TRPV4 is localized in adherence junctions of the human bladder urothelium: a morphological study. J Urol 2011;186:1121–7.
[63] Fam BA, Sarkarati M, Yalla SV, et al. Spinal cord injury. In: Yalla SV, McGuire EJ, Elbadawi A, Blaivas JG, editors. Neurology and urodynamics. New York: Macmillan Publishing Company; 1988. p. 291–302.
[64] Reitz A, Schmid DM, Curt A, Knapp PA, Schurch B. Afferent fibers of the pudendal nerve modulate sympathetic neurons controlling the bladder neck. Neurourol Urodyn 2003;22:597–601.
[65] Krongrad A, Sotolongo Jr JR. Blasdder neck dyssynergia in spinal cord injury. Am J Phys Med Rehabil 1996;75:204–7.
[66] Ke QS, Kuo HC. Transurethral incision of the bladder neck to treat bladder neck dysfunction and voiding dysfunction in patients with high-level spinal cord injuries. Neurourol Urodyn 2010;29:748–52.
[67] Peng CH, Kuo HC. Transurethral incision of bladder neck in treatment of bladder neck obstruction in women. Urology 2005;65:275–8.
[68] Jhang JF, Jiang YH, Kuo HC. Transurethral incision of the bladder neck improves voiding efficiency in female patients with detrusor underactivity. Int Urogynecol J 2014;25:671–6.
[69] Dalmose AL, Rijkhoff NJ, Andersen IS, Stefania D, Jørgensen TM, Djurhuus JC. Bladder and urethral responses to pelvic nerve stimulation in the pig. Scand J Urol Nephrol 2002;210:34–45.
[70] Osman NI, Chapple CR. Fowler's syndrome – a cause of unexplained urinary retention in young women? Nat Rev Urol 2014;11:87–98.
[71] Meng NH, Lo SF, Chou LW, Yang PY, Chang CH, Chou EC. Incomplete bladder emptying in patients with stroke: is detrusor external sphincter dyssynergia a potential cause? Arch Phys Med Rehabil 2010;91:1105–9.
[72] Karami H, Valipour R, Lotfi B, Mokhtarpour H, Razi A. Urodynamic findings in young men with chronic lower urinary tract symptoms. Neurourol Urodyn 2011;30:1580–5.
[73] Jamzadeh AE, Xie D, Laudano M, Seklehner S, Elterman DS, Shtromvaser L. Urodynamic characterization of lower urinary tract symptoms in men less than 40 years of age. World J Urol 2014;32:469–73.
[74] Barendrecht MM, Oelke M, Maria P. Is the use of parasympathomimetics for treating an underactive urinary bladder evidence-based? BJU Int 2007;99:749–52.
[75] Chang SJ, Chiang IN, Yu HJ. The effectiveness of tamsulosin in treating women with voiding difficulty. Int J Urol 2008;15:981–5.
[76] Yamanishi T, Yasuda K, Kamai T, Tsujii T, Sakakibara R, Uchiyama T, et al. Combination of a cholinergic drug and an alpha-blocker is more effective than monotherapy for the treatment of voiding difficulty in patients with underactive detrusor. Int J Urol 2004;11:88–96.
[77] Capitanucci ML, Camanni D, Demelas F, Mosiello G, Zaccara A, De Gennaro M. Long-term efficacy of percutaneous tibial nerve stimulation for different types of lower urinary tract dysfunction in children. J Urol 2009;182:2056–61.
[78] Gladh G, Mattsson S, Lindström S. Intravesical electrical stimulation in the treatment of micturition dysfunction in children. Neurourol Urodyn 2003;22:233–42.
[79] Mitchell CR, Mynderse LA, Lightner DJ, Husmann DA, Krambeck AE. Efficacy of holmium laser enucleation of the prostate in patients with non-neurogenic impaired bladder contractility: results of a prospective trial. Urology 2014;83:428–32.