# The Role of Urodynamic Study in the Evaluation and Management of Overactive Bladder

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## ABSTRACT

Overactive bladder (OAB) is a condition of urinary urgency with or without urgency incontinence, and is usually accompanied by frequency and nocturia. Urgency is the core symptom for OAB. The actual pathophysiology of OAB has not been well elucidated. OAB could be caused by sensory urgency from urothelial dysfunction or detrusor overactivity (DO). OAB is a symptom syndrome which includes either sensory dysfunction or a combination of sensory and motor disorders of the urinary bladder. Symptomatic diagnosis of OAB does not correlate with a urodynamic diagnosis of DO. In the differential diagnosis of OAB, urodynamic study is essential and important, especially in determining the therapeutic strategy. Urodynamic testing should serve as an essential part of therapy and it should guide the diagnosis and management of OAB. *Key words:* overactive bladder, detrusor overactivity, urodynamics

## OVERACTIVE BLADDER AND DETRUSOR OVERACTIVITY

Overactive bladder (OAB) is a condition of urgency with or without urge incontinence and is usually accompanied by frequency and nocturia [1]. Individuals with an OAB have a lower quality of life in the social and functional domains than those with diabetes [2]. Patients with an OAB might also have major depression and other diseases associated with urinary incontinence and nocturia [3]. Urgency is the core symptom of OAB. It has been estimated that 10%-16% of the world population has an OAB condition [4]. However, although use of an urgency severity scale has been advised, the grade of urgency is reported subjectively by the patients, and therefore, there could be a wide variation among different grades in the reported urgency severity [5]. Urgency frequency symptoms could be due to psychological factors, increased urine production, and uninhibited urge due to central nervous lesions or detrusor overactivity (DO).

Urgency symptoms can be caused by sensory dysfunction (hypersensitive bladder) or DO. Sensory urgency might be due to micro-motion of the detrusor during bladder filling (increased excitability), rapid bladder filling or diuresis, urothelial dysfunction, or a high sensory perception due to anxiety, depression or emotional stress. OAB is a symptom syndrome which includes either sensory dysfunction or a combination of sensory and motor disorders of the urinary bladder.

Urodynamic study is an established tool to prove DO. Although patients with urgency frequency symptoms may have DO, patients with OAB symptoms might not have DO or incontinence [6]. In clinical practice, treatment of OAB is based on the subjective symptoms of urgency and frequency. The most widely used medicine is antimuscarinics. Because antimuscarinics target abnormal detrusor contractility, treatment in OAB patients without DO might fail.

Urothelial dysfunction in pathological conditions such as bladder outlet obstruction (BOO) or neurogenic lesions may cause increased acetylcholine or adenosine triphosphate (ATP) release, and increased sensitivity of the suburothelial sensory fibers. Increased excitability of the detrusor muscles or the interstitial cells may result in DO during bladder filling. Therefore, not all patients with OAB have uninhibited detrusor contractions during bladder filling. In one report, urodynamic study detected detrusor instability in only about 50% of patients with OAB symptoms [7]. Because of this, urodynamic study has been considered useless in the diagnosis of OAB. However, urodynamic study is essential in the differential diagnosis of etiologies of OAB such as bladder outlet obstruction (BOO), detrusor hyperactivity with impaired contractility (DHIC), dysfunctional voiding and mixed urinary incontinence [8].

## PATHOPHYSIOLOGY OF OVERACTIVE BLADDER

### *Role of the urothelium in bladder function*

The urinary bladder urothelium has been viewed as a passive barrier, however, recent evidence has demonstrated that the urothelium is a responsive structure which exhibits both sensor (ability to respond to thermal, mechanical and chemical stimuli) and transducer (ability to release chemicals) functions. Studies have also revealed that afferent nerves and urothelial cells in the bladder exhibit a number of common properties, including the expression of certain receptors and ion channels (such as transient receptor potential vanilloid 1. In addition, localization of afferent nerves adjacent to the urothelium suggests that these cells may be targets for transmitter release from bladder nerves or that chemicals released by urothelial cells may alter afferent excitability. The alteration in afferents or urothelial cells in the pelvic viscera may contribute to sensory abnormalities in the urinary bladder [9].

### *Sensory afferents in OAB*

The actual pathophysiology of DO after neurogenic lesions, BOO or ageing, has not been well elucidated. Recently, the urothelium and suburothelial space have received renewed interest because of their possible roles not only in mediating solute transport but also in sensing bladder fullness [10]. An abundance of suburothelial sensory nerves and acetylcholine and ATP-containing vesicles in nerve fiber terminals have been found in the human bladder wall, suggesting the lamina propria of the bladder plays an important role in transmitting the sen-

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sation of bladder fullness and in the response of the bladder to stretch [11-13]. These stretch-sensing apparatus may transmit sensory signals as well as mediate the detrusor reflex [14]. A change in hydrostatic pressure on the apical face of the urothelium results in ATP generation that is postulated to activate purinergic receptors $P2X_3$ on sensory nerves [15]. The $P2X_3$ receptors are co-localized with vanilloid type 1 receptors and are believed to be involved in afferent pathways that control urinary bladder volume reflexes [16]. Increased stretch activated ATP release has been reported from human urothelial cells cultured from the bladders of patients with interstitial cystitis and spinal cord injury.

*Abnormal sensory nerve- mediated DO*

Under some pathological conditions in the urinary bladder such as infection or trauma, the production of transmitters such as ATP, substance P, and calcitonin gene-related peptide (CGRP) can act on nearby tissues and on afferent nerve terminals in an autocrine fashion to increase afferent nerve activity [17]. The production and release of these neurotransmitters increase during conditions of inflammation and pain [18,19]. The suburothelial interstitial cells may be affected and sensory transmission occurs earlier, resulting in a sensation of increased bladder fullness or mediation of detrusor overactivity through gap junctions extending into the detrusor muscles [20,21]. Moreover, many C fibers in the bladder mucosa contain sensory neuropeptides (such as substance P, neurokinin A, CGRP) which on release, can modulate the micturition reflex and might cause detrusor overactivity [22]. A local inflammatory process might be induced through the afferent and efferent nerves in these interstitial cellular networks which integrate signal transmissions from the urothelium to detrusor muscles in the bladder wall.

## URODYNAMIC STUDY IN OAB AND DO

OAB is either a sensory disorder or a combined sensory and motor dysfunction. Patients with OAB might have pure sensory urgency without urinary incontinence or have motor urgency that usually elicits detrusor contractions during bladder filling, causing urinary incontinence. Therefore, about 50% of patients with OAB might have DO but the other half of patients might not. A symptomatic diagnosis of OAB does not correlate with a urodynamic diagnosis of DO.

*Urodynamic findings of sensory urgency in OAB*

Urodynamic study in sensory urgency does not elicit detrusor contractions during bladder filling. Patients usually have a reduced bladder sensation at first filling (<100 mL) or fullness (<300 mL). Some patients present with low bladder compliance (<30 mL/cm $H_2O$). This urodynamic finding should be compatible with the results of a voiding diary, in which a functional bladder capacity of <350 mL is recorded. For patients with sensory urgency, interstitial cystitis should be carefully ruled out. A potassium chloride (KCl) test uses a 0.4 M KCl solution to provoke urothelial dysfunction. If patients have a positive KCl test, cystoscopic hydrodistention under general anesthesia might be used to diagnose interstitial cystitis.

*Urodynamic findings of detrusor overactivity in OAB*

According to the terminology recommended by the International Continence Society, DO is defined as uninhibited contractions during bladder filling [23]. Urodynamic DO can be either phasic DO during the filling phase that does not induce urinary incontinence, or terminal DO that usually induces urgency incontinence. The former can be classified as OAB dry and the latter OAB wet. The presence of uninhibited detrusor contractions is the key to diagnosis of DO, however, a certain percentage of patients with OAB wet may not have this urodynamic finding, possibly due to inhibition through the guarding reflex. Elderly patients may present with DHIC which results in incomplete bladder emptying and a large postvoid residual (PVR). Patients with DHIC should be carefully monitored for PVR if antimuscarinics are used to treat their OAB symptoms.

*Clinical observations of DO in OAB*

In a urodynamic study in women with OAB, Digesu et al found 18.7% of 4,500 women with LUTS could be classified as having OAB. Of these women with OAB, 54.2% had urodynamically proven DO. Among the 4,500 women undergoing urodynamic study, 36.5% were found to have urodynamic DO, but only 27.5% of patients with DO had OAB symptoms [7]. However, the symptom of urge incontinence is strongly correlated with DO in men. Hyman et al found that a higher incidence of DO was associated with urge incontinence than with other lower urinary tract symptoms in men. Of the men with LUTS, 68% had BOO, including 46% of men with DO [24]. Hashim and Abrams found the correlation between OAB symptoms and urodynamic DO was better in men than in women. Sixty-nine percent of men and 44% of women with urgency (OAB dry) had DO, while 90% of men and 58% of women with urgency and urgency incontinence (OAB wet) had DO. They concluded that the bladder is a better and more reliable witness in men than in women [25].

In a study investigating men with LUTS, OAB symptoms were found in 31%-74% of patients with various lower urinary tract dysfunctions including BOO, bladder neck dysfunction, hypersensitive bladder, DHIC, detrusor sphincter dyssynergia and detrusor underactivity. However, the incidence of urodynamic DO was more commonly seen in patients with BOO such as benign prostatic hypertrophy, bladder neck dysfunction, and detrusor sphincter dyssynergia, but not in those with bladder sensory disorder and underactive bladder. Urodynamic study is necessary if clinical presentations favor pathological causes other than hypersensitive bladder [26]. In the differential diagnosis of OAB symptoms, urodynamic study is essential and important, especially in determining the therapeutic strategy [8].

*Indications for urodynamic study in OAB*

Since OAB is a symptom syndrome, a diagnosis of OAB does not need urodynamic study. Treatment with antimuscarinics can be started once patients have been verified to have urgency with or without urgency incontinence. However, if the initial treatment has failed to resolve the OAB symptoms, or patients have suspected bladder outlet obstruction, or occult neurogenic bladder, a urodynamic study is mandatory to find out the underlying pathology. In elderly patients with OAB symptoms and a large PVR, urodynamic study should be performed before treating with antimuscarinics.

## CONCLUSIONS

OAB is a symptom syndrome which comprises sensory (hypersensitive bladder) and motor urgency syndrome (DO). DO is a blad-

der disorder, which may result from idiopathic causes, BOO, neurogenic lesions, bladder lesions or urethral conditions. A diagnosis of OAB symptoms based on the symptom of urgency might be inadequate. A diagnosis of DO and associated lower urinary tract disorder is best done by urodynamic study. Urodynamic testing should serve as an essential part of therapy and guide the diagnosis and management of OAB. We suggest a trial with antimuscarinics in patients with OAB symptoms. If the treatment results are not as good as expected, a urodynamic study, especially a pressure flow study or videourodynamic study, is recommended.

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