Hypersensitive or Detrusor Overactivity: Which is Associated with Filling Symptoms in Female Bladder Outlet Obstructed Patients?

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Purpose: To investigate and compare detrusor overactivity (DO) and bladder filling sensation characteristics in female bladder outlet obstruction (FBOO) patients with or without overactive bladder (OAB) symptoms.

Materials and Methods: One hundred fifty-seven FBOO patients with urodynamic testing were recruited. Patients who showed urinary urgency (≥ 6 episodes/3 d), with or without urinary frequency (≥8 voids/24 h), and urge incontinence (≥ 3 episodes/3 d) were considered to have OAB. The detrusor overactivity (DO) and bladder filling sensation measures including first sensation (FSF), first desire to void (FDV) and strong desire to void (SDV) during filling cystometry were recorded. The associations between urodynamic variables and OAB symptoms were analysed.

Result: FBOO patients had a high incidence (79%) of OAB. FBOO patients with OAB symptoms had significantly younger age, higher incidence of DO (19.4% versus 6.1%) (P = .051) and lower bladder volumes of FSF (180.32 ± 83.48 versus 226.18 ± 100.90 mL), FDV (269.00 ± 109.78 versus 330.45 ± 123.95 mL) and SDV (345.56 ± 135.43 versus 422.33 ± 148.40 mL) (P < .05) compared to patients without OAB. In multivariate analyses, both DO (OR = 4.83, 95% CI: 1.02-22.85, P = .047) and lower bladder volumes at FDV(OR = 2.47, 95% CI: 1.03-5.95, P = .044) and SDV (OR = 3.07, 95% CI: 1.25-7.55, P < .014) were still independently associated with OAB, after adjustment for age and other confounding factors.

Conclusion: FBOO patients had a high incidence of OAB. Not only DO but also bladder hypersensitivity were independently associated with OAB symptoms in FBOO patients.

Keywords: hypersensitivity;urinary bladder neck obstruction; urinary bladder, overactive; urodynamics; urinary Incontinence, urge

INTRODUCTION

Female bladder outlet obstruction (FBOO) is a relative uncommon condition in clinical practice[1-4]. Overactive bladder (OAB) symptoms, including urgency, frequency and nocturia, are quite common among female patients, especially in patients with bladder outlet obstruction, which severely affect women's life quality[5-6]. The reported incidence of OAB among bladder outlet obstruction patients was around 50-75%[7]. OAB symptoms can be induced either by obstruction or the secondary effects of obstruction on the bladder[8]. Whereas, to date, the underlying mechanisms of OAB symptoms in FBOO patients remains the subject of debate and the anticholinergic drugs have many side effects[9]. A more thorough investigation of its pathophysiological mechanisms will be helpful in further investigations of therapeutic drugs.

Detrusor overactivity (DO), characterized by involuntary detrusor contractions during the filling phase in urodynamic test, is a known cause for OAB symptoms[10]. However, the antimuscarinic therapy based on this mechanism shows limited efficiency in clinical practice[11]. Urologist and clinical researchers have now placed a new focus on the effect of increasing bladder sensation on OAB symptoms. A few studies have found that OAB patients had lower micturition and decreased bladder volumes, which suggested that bladder hypersensitivity contributes to the development of OAB [12-13]. However, the association between bladder filling sensation and OAB symptoms was still not adequately investigated in FBOO patients. The objective of this study was to examine the urodynamic parameters associated with OAB symptoms in FBOO patients.

MATERIAL AND METHODS

Study design and participants

This study was an observational study approved by the Institutional Review Board of the First Affiliated Hospital of Sun Yat-Sen University. The study was conducted according to the principles expressed in the Declaration of Helsinki. We screened female patients who referred for evaluation of lower urinary tract symptoms (LUTS) and underwent urodynamic testing in the first affiliated hospital of Sun Yat-sen university from 2008 to 2016. Patients with clinical dysuria symptoms and having the maximum flow rate (Qmax) ≤ 15 ml/s and detrusor pressure at the maximum flow (Pdet. Qmax) ≥ 20 cmH_2O in urodynamic testing were eligible for

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Table 1. Comparisons of clinical and urodynamic parameters in FBOO patients with OAB and non-OAB symptoms.

Clincal&Urodynamic Parameters	All FBOO (N = 157)	OAB -FBOO (N= 124)	Non-OAB –FBOO (N = 33)	*p* value
Age, years	46.80 ± 14.45	45.44 ± 14.38	51.94 ± 13.71	.010
Free Qmax, mL/s	11.29 ± 4.91	11.11 ± 4.61	11.99 ± 5.91	.473
Qmax, mL/s	7.88 ± 3.43	8.15 ± 3.41	6.86 ± 3.37	.103
Pdet Qmax , cmH_2O	49.74 ± 80.32	51.46 ± 89.73	43.28 ± 21.15	.838
Pdetmax, cmH_2O	49.74 ± 23.02	49.50 ± 23.40	50.63 ± 21.86	.687
PVR, mL	87.04 ± 126.60	74.60 ± 109.19	133.42 ± 171.36	.064
DO	26(16.6%)	24 (19.4%)	2 (6.1%)	.051
FSF, mL	189.96 ± 89.07	180.32 ± 83.48	226.18 ± 100.90	.011
FDV, mL	281.92 ± 115.28	269.00 ± 109.78	330.45 ± 123.95	.009
SDV, mL	361.70 ± 141.29	345.56 ± 135.43	422.33 ± 148.40	.006
Blaivas-Groutz		1 (1-2)	1 (1-2)	.875

Abbreviations: FBOO, female bladder outlet obstruction; OAB, overactive bladder; Free Qmax, the maximum free-flow rate; Qmax, the maximum flow rate; Pdet Qmax, detrusor pressure at maximum flow; Pdetmax, maximum detrusor pressure; PVR, post-void residual urine; DO, detrusor overactivity; FSF, first sensation of bladder filling; FDV, first desire to void; SDV, strong desire to void.
Data were showed as means ± SD, numbers (%) or medians (interquartile range). P value for comparison between OAB-FBOO patients and Non-OAB-FBOO patients.

inclusion as FBOO[1]. Exclusion criteria were the presence of diabetes mellitus, bladder stone, bladder tumor, urine infection, nervous diseases, pelvic prolapse, and urological surgery history. The severity of obstruction was assessed using the Blaivas-Groutz Nomogram[3], and further categorized into severe obstruction (Pdet. max ≥ 107 cmH_2O), moderate obstruction (Pdet.max between 57 to 107 cmH_2O), and mild obstruction (Pdet. max ≤ 57 cmH_2O). According to the 3d-voiding diary, patients who showed urinary urgency (≥ 6 episodes/3 d) with or without urge incontinence (≥ 3 episodes/3 d) and urinary frequency (≥8 voids/24 h), were selected as OAB patients.[14]

Urodynamic testing

According to the suggested urodynamics practice standards of the International Continence Society[15], urodynamic testing was performed by a urotechnician using the Delphis 94-R01-BT UDS system (Laborie Medical Technologies, Canada). During the free-flow measurement, the maximum free-flow rate (Free Qmax) was recorded. Subsequently, post-void residual urine (PVR) was measured. The bladder was filled with saline solution at a temperature of around 37℃ at a speed of 50 ml/min during the filling cystometry. Bladder sensation variables were recorded when patients reported the first sensation of bladder filling (FSF), first desire to void (FDV), and strong desire to void (SDV) according to the International Continence Society definitions[15]. Lower bladder volumes at FSF, FDV, and SDV were considered as higher bladder sensitivity. DO was considered positive when involuntary detrusor contractions appeared during the filling phase[15]. Meanwhile, voiding variables including Qmax, Pdet. Qmax, maximum detrusor pressure (Pdet. max) were also recorded during the voiding cystometry.

Table 2. Results of logistic analyses on urodynamic factors to predict the occurrence of OAB symptoms in FBOO patients

Urodynamic Parameters	Occurrence of OAB OR (95 % CI)	*P* value
DO	4.83 (1.02-22.85)	.047
FSF < mean value	2.35 (0.99-5.59)	.053
FDV < mean value	2.47 (1.03-5.95)	.044
SDV < mean value	3.07 (1.25-7.55)	.014

Abbreviations: FBOO, female bladder outlet obstruction; OAB, overactive bladder; DO, detrusor overactivity; FSF, first sensation of bladder filling; FDV, first desire to void; SDV, strong desire to void. HR, hazard ratio; CI, confidence interval.
All urodynamic parameters were separately adjusted by age and PVR.

Statistical Analysis

Data are presented as the mean ± standard deviation (SD) or number (percentage). For comparisons between OAB-FBOO and non-OAB-FBOO patients, a Mann-Whitney test was used for numerical variables and a Chi square test for categorical variables. Multivariate logistic regression models were used to analyse DO and bladder volumes to predict the occurrence of OAB in FBOO patients separately, adjusting for age and other factors with p values < .1 in univariate analyses. All statistical analyses were pmerfored using SPSS for Windows (Version 13.0, IBM, USA). Two-tail *p* values < .05 were considered to be statistically significant.

RESULTS

Among 2600 female patients undergoing urodynamic studies, 157 patients were recruited as FBOO, suggesting the prevalence of BOO was approximately 6%. The mean age was 46 ± 14 years old. The incidence of DO among FBOO patients was around 16.6%. Detailed urodynamic characteristics of FBOO are listed in **Table 1**. According to Blaivas-Groutz Nomogram, 116 (73.9%) FBOO patients were mild obstruction, and 36 (22.9%) were moderate obstruction and 5 (3.2%) were severe obstruction. The severe/moderate obstruction group showed a higher incidence of DO (29.3%) compared with the mild obstruction group (12.1%). Nevertheless, all bladder volume measures were not significantly different between groups with severe/moderate obstruction and mild obstruction.
Among the FBOO patients, 124 (79.0%) had OAB. As shown in **Table 2**, patients with OAB had a higher incidence of DO than patients without OAB (19.4% versus 6.1%, $p = .051$). FBOO patients with OAB had significantly lower FSF, FDV and SDV than those without OAB (**Table 1**). Patients with OAB seems to be younger than those without OAB. After adjusting for age and PVR, DO, FDV and SDV were still independently associated with the occurrence of OAB, and FSF tended to independently associate with OAB symptoms (**Table**

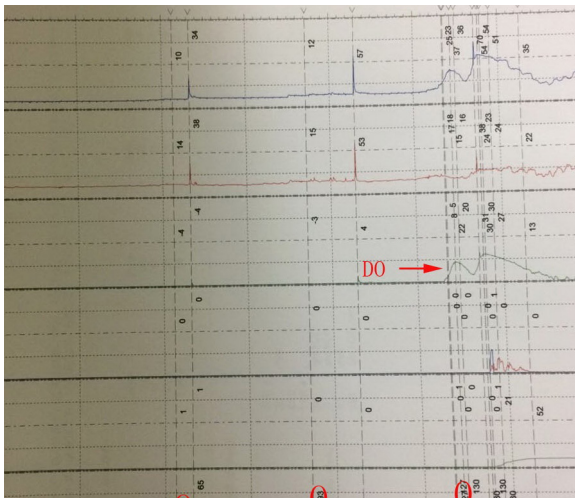

Figure 1. One typical urodynamic report of complicated FBOO show high Pdetmax and low Qmax with DO and hypersensitivity.

2). One typical urodynamic report of FBOO patients showing both DO and bladder hypersensitivity was showed in **Figure 1**.

DISCUSSION

In this cross-sectional study, we observe that both DO and low bladder volumes were correlated with OAB symptoms. Such results may indicate that not only DO but also increased bladder sensitivity could be the underlying pathophysiological mechanisms for OAB symptoms in FBOO patients.

Compared with male BOO, FBOO is a relative uncommon condition in clinical practice. The reported prevalence of BOO in female population varies widely from 2.7% to 23% in different studies because of various diagnostic criteria[1-4,16]. In our study, a combined criteria of Qmax ≤ 15 ml/s and Pdet Qmax ≥ 20 cm H_2O was used to define BOO, which had a sensitivity of 74.3% and a specificity of 91.1% to predict obstruction[1]. Such criteria is thought to have good concordance with clinically diagnosed obstructions.

The incidence of OAB in FBOO patients in our study was similar to the data in the male population (60-70%) [8]. After adjusting for age and other confounding factors, the higher DO rates was still independently associated with OAB symptoms in FBOO patients. The high incidence of OAB symptoms with low incidence of DO in FBOO patients was consistent with a previous study, which also demonstrated that only 54% of women with OAB had DO on urodynamic test, and 27% of the women with a diagnosis of DO on urodynamic test had OAB symptoms[17]. The inconsistence between OAB and DO rates suggests that other pathophysiological mechanisms might be responsible for OAB symptoms in FBOO patients.

Some researchers have placed focus on identifying the associations between bladder sensations and OAB[18-19]. Several studies reported that OAB patients not only had a higher incidence of DO but also revealed lower bladder volumes of FSF, FDV and SDV compared with non-OAB patients, suggesting hypersensitive bladder in OAB patients[12-13]. In our study, we adopted urodynamic variables during filling cystometry as an objective method to record bladder sensations, which has been demonstrated to have good correlations with sensory questionnaire scores in a prior study[13]. We found that the bladder volumes were lower in FBOO patients with OAB symptoms than those without OAB symptoms. Thus, this study suggested that FBOO could induce lower bladder volumes which may be related to OAB symptom in these patients.

The mechanisms of OAB symptoms in BOO patients remain a matter of debate, with neurogenic mechanism classified as one of the leading causes[20]. In the experimental studies, various neurochemical, such as nitric oxide synthase and NADPH-diaphorase, have been shown to change in afferent pathways of the animal model of bladder outlet obstruction[21-22]. Additionally, short latency micturition reflex was found in urethral obstructed rats[23]. These changes in reflex pathways were considered as neuronal plasticity, which indicated that the nerves were influenced by the pathological processes in target organs[24-25]. Recently, there are increasing interest in the investigation of afferent system (sensory) innervation as an important therapeutic target for lower urinary tract symptoms[26]. Our study might further support the neurogenic mechanisms and the importance of investigations on therapies directed at the afferent system in FBOO patients with OAB symptoms.

This study had several limitations. First, there was no general agreement on the urodynamic parameters for defining FBOO. We used the criteria of Qmax ≤ 15 ml/s and Pdet Qmax ≥ 20 cmH_2O in this study, which is thought to have high concordance with clinically diagnosed obstructions [27]. Second, this was a cross-sectional study, which could not support the cause and effect associations between DO, bladder hypersensitivity and OAB in FBOO patients. Further longitudinal, prospective, and large-scale studies are warranted to validate these findings.

CONCLUSIONS

FBOO patients had a high incidence of OAB symptoms. Both urodynamic DO and bladder volumes in filling cystometry tests were independently associated with the occurrence of OAB symptoms in FBOO patients, suggesting that not only DO but also increased bladder sensitivity may be pathophysiological mechanisms underlying this symptomatology.

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CONFLICT OF INTEREST

The authors declare that they have no competing interests.

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