



Clinical Correlates of Voiding Symptoms in Women Without Overt Urethral Obstruction

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Background: We hypothesized that voiding symptoms in women with normal free uroflow were not related to irritative symptoms and bladder storage dysfunction.

Purpose: This study was designed to explore the clinical associations between voiding symptoms in women without obvious anatomic urethral obstruction and dysfunctional voiding.

Methods: We retrospectively reviewed an urodynamic database and identified 335 women who had a positive response to the category of voiding symptoms in a questionnaire. All 335 women had undergone urodynamic studies and urethrocystoscopic examinations for voiding symptoms. None of the women had inappropriate sphincteric activity during voiding or anatomic evidence of urethral obstruction. In addition to categorization by menopausal status, the study subjects were further stratified based on the maximum flow rate on free uroflowmetry into two groups: the low flow group and the normal flow group. A further 125 women with lower urinary tract symptoms but without voiding symptoms and who had negative urodynamic findings were identified and served as controls.

Results: Of the 335 women, 137 (41%) belonged to the low flow group, including 73 premenopausal women and 64 postmenopausal women; 198 (59%) belonged to the normal flow group, including 127 premenopausal women and 71 postmenopausal women. Among premenopausal women, the frequency of irritative symptoms was significantly higher for those with voiding symptoms than for those without voiding symptoms. Urodynamic studies showed that lower flow rates, prolonged time to maximum flow, higher micturition resistance, and high postvoid residual urine volume were common characteristics of women with low uroflow. Irritative symptoms and bladder storage dysfunction (lower first desire to void volume and maximum cystometric capacity) were the common characteristics of premenopausal women with voiding symptoms.

Conclusion: Our study revealed the interesting finding that voiding symptoms in premenopausal women with normal uroflow are associated with irritative symptoms and that bladder storage dysfunction may cause voiding symptoms.

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1. Introduction

Lower urinary tract symptoms are a common health problem and cause considerable inconvenience for many women. A thorough evaluation, including urodynamic study and imaging of the lower urinary tract, is essential for the appropriate management of unpleasant symptoms. The management goals for lower urinary tract disorders are to identify the specific causes of the urinary symptoms and to tailor appropriate therapy, which may include medical, behavioral or surgical interventions. Subjective symptoms suggestive of voiding dysfunction are nonspecific and of limited value in diagnosis.^{1,2} Along with measurement of the residual urine volume, uroflowmetry is a simple urodynamic investigation that can be used as a preliminary screening test to identify patients who need more extensive follow-up studies. Abnormal flow rates require further investigation, such as urodynamic studies, videocystourethrography or cystourethroscopy, to assess any abnormalities that may originate in the bladder or urethra, or both. If the uroflow measures are normal in patients complaining of symptoms consistent with obstructive voiding, further investigation has been thought to be unnecessary. It has been suggested that these voiding symptoms in subjects with normal uroflow are due to habitual behaviors or psychogenic causes.³ In contrast, it has been reported that normal uroflow may coexist with a relative urethral obstruction.¹ We hypothesized that voiding symptoms in women with normal free uroflow were not associated with irritative symptoms or bladder storage dysfunction. This study was designed to explore the associations between voiding symptoms and clinical findings after exclusion of inappropriate sphincter activity during voiding and anatomic evidence of urethral obstruction, both of which are common causes of urethral obstruction.⁴

2. Methods

We retrospectively reviewed a urodynamic dataset compiled between August 1997 and June 2007 and identified 495 women who had a positive response to the category of voiding symptoms in an interviewer-directed symptom questionnaire. None of the women had urinary tract infections, diabetes, central or peripheral neuropathy, anti-incontinence or radical pelvic surgery. The symptom questionnaire addressed five categories of questions regarding urinary frequency, nocturia, urgency, incontinence, and voiding dysfunction. The questions regarding voiding dysfunction included descriptive statements about poor stream, straining to void, hesitancy in voiding, and incomplete emptying. The presence of any voiding symptom was regarded as a positive response to voiding dysfunction. Of the 495 women, pelvic examination identified 128 women with urethral

obstruction secondary to pelvic organ prolapse or an impacted pelvic mass; they were therefore excluded from this study. The remaining 367 women underwent further examination, including urodynamic study and cystourethroscopy. Urodynamic study consisted of free uroflowmetry, filling phase cystometry, pressure flow study, and urethral pressure profile.

Of the 367 women, 32 had either cystourethroscopic findings of urethral obstruction (e.g., urethral stricture, stenosis or narrowing) or inappropriate sphincter activity during voiding on pressure flow studies (dysfunctional voiding), or both, and they were therefore excluded from the study. The study group comprised the remaining 335 women, which included 200 premenopausal women (60%) and 135 postmenopausal women (40%). In addition to the categorization by menopausal status, the subjects were stratified based on the maximum flow rate on free uroflowmetry into two groups: the low flow group (< 15 mL/s for age < 60 years or < 10 mL/s for age \geq 60 years) and the normal flow group (\geq 15 mL/s for age < 60 years or \geq 10 mL/s for age \geq 60 years).^{4,5} A further 125 women, matched to the study group in terms of demographic characteristics, with a negative response to voiding dysfunction and negative urodynamic finding, were identified and served as controls, including 83 premenopausal women (66%) and 42 postmenopausal women (34%). Cystourethroscopy was not a prerequisite for the recruitment of controls.

Approval to carry out the study was obtained from the local ethics committee (MMH-I-S-199). Oral or written consent was obtained from the subjects for the investigations performed in this study. The methods, definitions and units conform to the standards recommended by the International Continence Society, unless specifically noted.⁶

Statistical analysis was performed using SPSS version 15.0 (SPSS Inc., Chicago, IL, USA). For parametric comparison, analysis of variance was used. When the statistical result was significant, multiple *post hoc* comparisons among the groups were performed with Scheffe's test. The χ^2 test was used for nonparametric comparisons. Values of $p < 0.05$ were considered significant.

3. Results

The mean age \pm standard deviation of the study group was 47.1 ± 13.5 years (range, 20–86 years), the mean gravidity was 3.6 ± 2.4 (range, 0–12), and the mean parity was 2.7 ± 2.0 (range, 0–9). Based on the maximum free flow rate, 198 (59%) of 335 study subjects belonged to the normal flow group and 137 (41%) to the low flow group. The low flow group comprised 73 (53%) premenopausal women and 64 (47%) postmenopausal women. Tables 1 and 2 summarize the demographic characteristics and distribution of lower urinary tract symptoms, respectively, in the control and study groups. Among

the premenopausal women, incidence of irritative symptoms (urinary frequency, nocturia, and urgency) was higher in women with voiding symptoms than in women without voiding symptoms. In contrast, among postmenopausal women, the incidence of irritative symptoms was significantly higher in women without voiding symptoms than in women with voiding symptoms. There was a significant difference in the distribution of urodynamic diagnoses between premenopausal women with low or normal uroflow ($p=0.001$). Among premenopausal women, the rate of urodynamic diagnosis of hypersensitive bladder was higher and the rate of negative finding on urodynamic studies was lower in women with normal uroflow than in women with low uroflow (Table 3). Nevertheless, this difference disappeared in postmenopausal women.

3.1. Premenopausal women

Urodynamic findings in the low flow group included prolonged time to maximum flow, higher micturition resistance, detrusor pressure at maximum flow, and postvoid residual urine volume, as well as lower uroflow rates, when compared with those in the control and normal flow groups (Table 4). Premenopausal women with either low or normal uroflow had significantly lower volume at first desire to void and maximum cystometric capacity compared to premenopausal controls ($p<0.05$).

3.2. Postmenopausal women

Urodynamic findings in the low flow group included prolonged time to maximum flow, higher micturition

Table 1 Demographic characteristics of the control and study groups according to menopausal status*

Variable	Premenopausal			Postmenopausal		
	Controls (n=83)	Normal flow (n=127)	Low flow (n=73)	Controls (n=42)	Normal flow (n=71)	Low flow (n=64)
Age (yr)	39.3±7.2	38.8±6.4	38.5±7.0	60.6±7.8	60.2±11.2	59.8±10.8
Gravidity	2.9±1.7	3.0±1.9	2.7±2.3	5.3±3.5	5.3±2.8	4.1±1.9
Parity	1.9±1.4	2.1±2.3	1.9±1.6	3.7±2.5	4.3±2.5	3.6±1.6
BMI (kg/m ²)	22.8±3.1	22.9±3.2	22.7±2.9	24.3±4.7	23.8±4.3	24.0±3.9

*Data presented as mean ± standard deviation; continuous variables were compared by analysis of variance. BMI = body mass index.

Table 2 Symptomatology in the control and study groups according to menopausal status*

Lower urinary tract symptoms	Premenopausal			Postmenopausal		
	Controls (n=83)	Normal flow (n=127)	Low flow (n=73)	Controls (n=42)	Normal flow (n=71)	Low flow (n=64)
Frequency	14 (16.8) [†]	77 (60.6)	52 (71.2)	34 (80.9) [†]	37 (52.1)	27 (42.2)
Nocturia	4 (4.8) [‡]	21 (16.5)	16 (21.9)	16 (38.1) [§]	13 (18.3)	12 (18.1)
Urgency	6 (7.2) [‡]	27 (21.3)	21 (28.8)	16 (38.1) [‡]	10 (14.1)	8 (12.5)
Urge incontinence	4 (4.8)	5 (3.9)	8 (11.0)	6 (14.3)	3 (4.2)	6 (9.4)
Stress incontinence	30 (36.1)	33 (25.9)	15 (20.5)	26 (61.9) [†]	18 (25.3)	15 (23.4)

*Data presented as n (%); [†] $p<0.001$, [‡] $p<0.01$ and [§] $p<0.05$ versus the other two subgroups (χ^2 test).

Table 3 Urodynamic diagnoses in the study groups*

Urodynamic diagnosis	Premenopausal [†]		Postmenopausal	
	Normal flow	Low flow	Normal flow	Low flow
Detrusor overactivity	7 (5.5)	5 (6.8)	12 (16.9)	8 (12.5)
Mixed incontinence	4 (3.1)	0	4 (5.6)	2 (3.1)
Hypersensitive bladder	33 (26.0)	8 (11.0)	4 (5.6)	5 (7.8)
Urodynamic stress incontinence	28 (22.0)	7 (9.6)	13 (18.3)	8 (12.5)
Negative findings	55 (43.3)	53 (72.6)	38 (42.3)	41 (64.0)

*Data presented as n (%); [†] $p=0.001$ for equality of distribution (χ^2 test).

Table 4 Urodynamic findings in the premenopausal control and study groups*

	Controls	Study group		<i>p</i> [†]
		Normal flow	Low flow	
Free uroflowmetry				
VV (mL/s)	314±107	309±124	248±134	<0.05 ^{‡§}
MFR (mL/s)	24±9	22±7	11±2	<0.05 ^{‡§}
AFR (mL/s)	11±4	9±4	5±2	<0.05 ^{‡§}
RU (mL)	18±31	28±63	85±130	<0.05 ^{‡§}
Filling phase cystometry				
FDV (mL)	161±49	126±48	135±59	<0.05
MCC (mL)	351±96	294±99	293±87	<0.05
Pressure-flow studies				
Qmax (mL/s)	22±7	20±6	13±4	<0.05 ^{‡§}
Time to Qmax (s)	28±35	43±72	56±92	<0.05 ^{‡§}
PdetQmax (cmH ₂ O)	29±12	30±14	39±17	<0.05 ^{‡§}
R [cmH ₂ O/(mL/s) ²]	0.18±0.31	0.21±0.25	0.59±0.60	<0.05 ^{‡§}
Pves.op (cmH ₂ O)	49±15	58±57	57±19	
Urethral pressure profile				
MUP (cmH ₂ O)	117±26	110±33	120±32	
FPL (cm)	3.1±0.6	3.1±0.6	3.4±0.7	
Length to MUP (cm)	2.0±2.8	2.0±1.8	1.7±2.4	
AUC _T (cmH ₂ O·cm)	219±68	220±68	219±66	
AUC _p (cmH ₂ O·cm)	117±40	121±48	126±37	

*Data presented as mean±standard deviation; [†]continuous variables were compared by analysis of variance followed by Scheffe's *post hoc* test if F was significant; [‡]control vs. low flow; [§]normal flow vs. low flow; ^{||}control vs. normal flow. VV=voided volume; MFR=maximum flow rate on free uroflowmetry; AFR=average flow rate on free uroflowmetry; RU=postvoid residual urine volume; FDV=first desire to void; MCC=maximum cystometric capacity; Qmax=maximum flow rate on pressure flow study; PdetQmax=detrusor pressure at maximum flow on pressure flow study; R=micturition resistance; Pves.op=intravesical opening pressure; MUP=maximum urethral pressure; FPL=functional profile length; AUC_T=total area under urethral pressure profile curve; AUC_p=proximal area under urethral pressure profile curve.

resistance, and postvoid residual urine volume, as well as lower uroflow rates, when compared with those in the control and normal flow groups (Table 5). In addition, the low flow group had significantly lower maximum cystometric capacity compared to the control and normal flow groups.

4. Discussion

The findings of this study rejected our null hypothesis in premenopausal women. Voiding symptoms in premenopausal women with normal uroflow was associated with irritative symptoms and bladder storage dysfunction, as demonstrated by the lower first desire to void volume and the maximum cystometric capacity on urodynamic studies. Our study also reconfirmed the use of free uroflowmetry as a screening test for women with voiding symptoms.

Among apparently normal women, 30–55% will describe at least one of the following voiding symptoms: hesitancy, poor stream, straining to void, incomplete emptying, or the need to revoid immediately.^{4,7} Furthermore, 70% of patients undergoing urodynamic

studies admit to having at least one symptom, and 53% to two or more symptoms.⁷ Incomplete emptying⁸ or poor stream are among the most common subjective complaints of voiding difficulty.⁴ Nevertheless, 29–33% of subjects meeting the urodynamic criteria for outlet obstruction only have irritative symptoms.^{3,9} However, the reason why subjects with outlet obstruction did not have voiding symptoms is beyond the scope of the present study.

The cause of voiding symptoms may be secondary to conditions of the bladder or urethra, or both.^{6,10} Bladder dysfunction includes detrusor underactivity or areflexia, while urethral dysfunction consists of functional or mechanical obstruction, which can further be categorized as compressive or constrictive.^{11,12} In this study, the pre- and postmenopausal low flow groups had a prolonged time to maximum flow, higher micturition resistance, and lower flow rates than did the control and normal flow groups. These urodynamic findings indicate poor urethral distensibility or compliance, a sign of constrictive urethral obstruction.^{11,13} The other common feature was a significantly higher postvoid residual urine volume, suggesting poorer detrusor sustainability.^{11,13} The premenopausal and postmenopausal normal flow

Table 5 Urodynamic findings in the postmenopausal control and study groups*

	Controls	Study group		<i>p</i> [†]
		Normal flow	Low flow	
Free uroflowmetry				
VV (mL/s)	271±100	298±119	192±107	<0.05 ^{‡§}
MFR (mL/s)	20±7	21±8	10±3	<0.05 ^{‡§}
AFR (mL/s)	8±3	9±4	4±2	<0.05 ^{‡§}
RU (mL)	31±40	48±87	96±133	<0.05 ^{‡§}
Filling phase cystometry				
FDV (mL)	175±57	154±55	150±59	
MCC (mL)	348±104	312±94	282±90	<0.05 ^{‡§}
Pressure-flow studies				
Qmax (mL/s)	18±6	20±11	11±5	<0.05 ^{‡§}
Time to Qmax (s)	26.5±40.3	32.2±52.1	56.8±96.5	<0.05 ^{‡§}
PdetQmax (cmH ₂ O)	27±13	28±18	30±16	
R [cmH ₂ O/(mL/s) ²]	0.24±0.22	0.45±0.81	1.11±1.54	<0.05 ^{‡§}
Pves.op (cmH ₂ O)	52±21	61±23	53±16	
Urethral pressure profile				
MUP (cmH ₂ O)	96±22	89±30	93±31	
FPL (cm)	2.9±0.6	3.0±0.6	3.2±0.8	
Length to MUP (cm)	1.7±0.6	1.7±0.5	2.4±3.1	
AUC _T (cmH ₂ O·cm)	178±51	181±67	188±56	
AUC _P (cmH ₂ O·cm)	105±39	101±44	102±49	

*Data presented as mean ± standard deviation; [†]continuous variables were compared by analysis of variance followed by Scheffe's *post hoc* test if F was significant; [‡]control vs. low flow; [§]normal flow vs. low flow. VV=voided volume; MFR=maximum flow rate on free uroflowmetry; AFR=average flow rate on free uroflowmetry; RU=postvoid residual urine volume; FDV=first desire to void; MCC=maximum cystometric capacity; Qmax=maximum flow rate on pressure flow study; PdetQmax=detrusor pressure at maximum flow on pressure flow study; R=micturition resistance; Pves.op=intravesical opening pressure; MUP=maximum urethral pressure; FPL=functional profile length; AUC_T=total area under urethral pressure profile curve; AUC_P=proximal area under urethral pressure profile curve.

groups had comparable urodynamic findings to those of the corresponding controls. Our findings were also consistent with those of another study, that voiding symptoms were not associated with the urethral pressure profile.¹

Interestingly, our study demonstrated that irritative symptoms were more common and bladder volume was lower among premenopausal women with voiding symptoms compared with premenopausal women without voiding symptoms. The irritative symptoms and reduced bladder volume seemed to be partly responsible for the misinterpretation of incomplete emptying and the subjective sensation of a poor stream, respectively, in premenopausal women. Nevertheless, this relationship disappeared in postmenopausal women.

Although the main goal of this study was to explore the associations with voiding symptoms in women without overt causes of urethral obstruction, the inability to recruit female subjects with isolated voiding symptom is a limitation of this study. Another limitation is that we did not conduct analyses to identify the specific voiding symptom that was primarily responsible for voiding dysfunction. Nevertheless, it has been reported that there is no correlation between any particular

voiding symptom and the objective diagnosis of voiding difficulty.^{2,8} The controls were selected to match the demographic characteristics of the study subjects, except for a negative response to voiding dysfunction and a negative finding on urodynamic studies. It is well known that the absence of voiding symptoms does not exclude the possibility of bladder outlet obstruction.^{3,9} Although the incidence of bladder outlet obstruction is low in females,^{9,10} the absence of cystourethroscopic examination to exclude the possibility of intraluminal lesion in the controls is also a limitation of this study. Despite these limitations, our study highlighted a significant relationship between voiding symptoms with irritative symptoms and bladder storage dysfunction. Therefore, voiding symptoms may improve after alleviating the irritative symptoms or improving bladder storage function in premenopausal women.

In the absence of inappropriate sphincteric activity during voiding and overt causes of urethral obstruction, our study demonstrated that voiding symptoms in premenopausal women may be partly explained by the misapprehension resulting from restricted bladder volume or irritative symptoms. However, this association was not present in postmenopausal women.

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