REFINING DIAGNOSIS OF ANATOMIC FEMALE BLADDER OUTLET OBSTRUCTION: COMPARISON OF PRESSURE-FLOW STUDY PARAMETERS IN CLINICALLY OBSTRUCTED WOMEN WITH THOSE OF NORMAL CONTROLS

GINA A. DEFREITAS, PHILIPPE E. ZIMMERN, GARY E. LEMACK, AND SHAROKH F. SHARIAT

ABSTRACT

Objectives. To improve the definition of pressure-flow study cutoff values for anatomic female bladder outlet obstruction (BOO) by comparing these parameters in women with clinical obstruction with those of normal controls.

Methods. In the past 3 years, 82 consecutive women with clinical anatomic BOO were investigated according to an institutional review board-approved protocol that included imaging and urodynamic studies. The data from these women were then added to those of our previously published cohort of 87 patients. The controls were 20 female volunteers without any urologic complaints and without a history of bladder or urethral surgery who had undergone a urodynamic study. Three groups of women with BOO were identified in the most recent cohort: 20 with Stage III-IV cystocele, 23 who had undergone previous anti-incontinence surgery, and 39 with distal periurethral fibrosis or stricture. The optimal combination of the maximal flow rate (Qmax) and detrusor pressure at maximal flow rate (PdetQmax) for determining BOO was calculated using nonparametric receiver operating characteristic curves for the entire cohort of 169 women with obstruction.

Results. Age, Qmax, and PdetQmax were similar among the three BOO groups. The area under the receiver operating characteristic curve for BOO was 0.762 for Qmax (95% confidence interval 0.661 to 0.864, $P < 0.001$) and 0.721 for PdetQmax (95% confidence interval 0.617 to 0.824, $P < 0.001$). After adjusting for the effect of age, PdetQmax ($P < 0.001$) and Qmax ($P < 0.011$) were independently associated with BOO.

Conclusions. After adjusting for age and using normal controls rather than an incontinent control population, we present pressure-flow study cutoff values to aid in the urodynamic study diagnosis of women with anatomic BOO. UROLOGY **64:** 675–681, 2004. © 2004 Elsevier Inc.

Despite the attention it has recently received in urologic published reports, female bladder outlet obstruction (BOO) continues to be an elusive and controversial entity. Opinions vary as to the best way to diagnose this condition, and, if urodynamic studies (UDSs) are considered, what pressure-flow values are most suggestive of obstruction. One of the reasons underlying this dilemma is that normal pressure-flow study (PFS) parameters for women have not been well defined. To our knowledge, no study has yet compared flow rates and voiding pressures in women who are clinically obstructed with those of strictly defined normal controls.

In 1998 and 2000, our institution published studies in which receiver operating characteristic (ROC) curves were used to calculate the optimal combination of the maximal urinary flow rate (Qmax) and detrusor pressure at maximal urinary flow rate (PdetQmax) for women who had a clinical diagnosis of BOO.[1,2] These studies included women with lower urinary tract symptoms (LUTS) who were not thought to be clinically obstructed or women with stress urinary incontinence (SUI) who had no history of bladder or urethral surgery as the control population. Recent data, however,

S. F. Shariat was supported by the Austrian Program for Advanced Research and Technology.

From the Department of Urology, University of Texas Southwestern Medical Center, Dallas, Texas

Reprint requests: Philippe Zimmern, M.D., Department of Urology, University of Texas Southwestern Medical Center, 5323 Harry Hines Boulevard, Dallas, TX 75390-9110

Submitted: February 26, 2004, accepted (with revisions): April 21, 2004

0090-4295/04/$30.00
doi:10.1016/j.urology.2004.04.089

have suggested that the pressure-flow parameters differ significantly between asymptomatic, urologically normal women and those with SUI.[3] To confirm this, and to identify the optimal cutoff point of Qmax and PdetQmax for detecting women with clinical BOO, we performed ROC curve calculations using an updated cohort of 169 clinically obstructed women with 20 normal female volunteers as the controls. The urodynamic parameters were compared among women with BOO, women with SUI, and normal female controls to determine whether any of these findings were predictive of anatomic BOO.

MATERIAL AND METHODS

The institutional review board approved this open-label prospective study, and all women provided informed consent before the study. Our analysis included 169 consecutive women with clinically diagnosed obstruction who were seen in the urology clinic for LUTS and who had undergone multichannel UDSs at our institution between March 2000 and February 2003. Of these 169 women, 87 had been a part of a previous study.[2] All women had BOO as determined by the presence of obstructive and/or irritative LUTS; a history of urethral or bladder neck surgery; a pelvic examination revealing urethral hyper-elevation or Stage 3 or 4 anterior vaginal wall prolapse; standing voiding cystourethrography showing deviation of the urethra or urethrovesical angle from its normal course (urethral kinking) or a narrow-caliber distal urethra with proximal widening or distension (urethral narrowing) on lateral voiding films; and/or endorectal coil magnetic resonance imaging demonstrating periurethral fibrosis and/or an obstructing urethral diverticulum.[4] We excluded women with a neurologic condition that could affect bladder function, women who had a bladder capacity of less than 100 mL, women who voided with abdominal straining greater than 10 cm H_2O, women who failed to relax the pelvic floor or urethral sphincter during voiding as determined by patch electrode electromyographic testing, and women who were unable to void for the PFS.

All patients underwent UDS testing according to a "two fill and void" protocol using the Laborie Aquarius XLT system (Laborie Medical Technologies, Toronto, Canada) in which the filling and voiding phases were repeated after the initial study during the same UDS session, and which has been previously described.[2] A 6F double-lumen catheter was used for filling and bladder pressure measurement. Because women with prolapse underwent UDS testing with and without the prolapse reduced, the PFS obtained without prolapse reduction was used in our calculations. When two PFSs were obtained under identical conditions, the study with the greatest Qmax was used for analysis. The data were extracted manually from the UDS tracing rather than relying on computer readings. All UDS definitions were in accordance with the International Incontinence Society guidelines.[5]

We also studied 124 patients with SUI and 20 healthy female volunteers. The volunteers were recruited from the community.[3] None of them had LUTS, as assessed by the UDI-6 questionnaire,[6] or a history of bladder or urethral surgery. These normal women underwent a "two fill and void" UDS conducted in exactly the same manner as for the BOO cohort. The SUI cohort consisted of 124 consecutive women who presented to the clinic with incontinence as their primary complaint and who underwent a UDS identical to that of the BOO and control groups. The patients with SUI were excluded from analysis if they had a history of anti-incontinence surgery, obstructive voiding symptoms, cystocele, or urethral pathologic findings on physical examination or standing lateral voiding cystourethrography.

Statistical Analysis

Differences in the continuous variables across the categorical variables were assessed using the Mann-Whitney *U* test or the Kruskal-Wallis nonparametric analysis of variance. The correlation among the continuous variables was examined using the Spearman correlation coefficient. Discordances between two related dichotomous variables were tested using the nonparametric McNemar test. Nonparametric ROC curves in which sensitivity is plotted against the false-positive rate (1 − specificity) were generated. Areas under the curve (AUCs) were compared using nonparametric Mann-Whitney *U* tests. Logistic multivariate regression analysis was used to calculate the odds ratios with 95% confidence intervals (CIs) to account for any dependency that might exist among Qmax, PdetQmax, and age. Qmax and PdetQmax had a skewed distribution and, therefore, were modeled with natural (base e) logarithmic transformation of series values. Statistical significance was set at $P < 0.05$, and all reported *P* values were two-sided. All analyses were performed with Statistical Package for Social Sciences, version 11.0.

RESULTS

Comparison of Patients with BOO, SUI, and Controls

Table I shows the characteristics of all three groups. Of the 169 clinically obstructed women, 53 had high-stage anterior vaginal wall prolapse, 48 had a history of anti-incontinence surgery, and 68 had distal urethral obstruction/periurethral fibrosis documented on standing lateral voiding cystourethrography and endorectal coil urethral magnetic resonance imaging.[3] The patients with BOO were significantly older, had a significantly lower Qmax, and had a significantly greater PdetQmax than did controls ($P < 0.001$, $P < 0.001$, and $P < 0.001$, respectively), regardless of the etiology of the obstruction. Similarly, obstructed patients had a lower Qmax and greater PdetQmax than did the patients with SUI ($P < 0.001$ and $P < 0.001$, respectively). The voided volume was lower in the whole BOO cohort compared with that of controls and in women with prolapse ($P < 0.02$ and $P < 0.001$, respectively). Although the Qmax was lower in the control subjects than in the patients with SUI ($P < 0.017$), the PdetQmax was not significantly different statistically. Figure 1 shows the distribution of Qmax and PdetQmax according to the clinical diagnosis.

Overall Diagnostic Performance of Qmax and PdetQmax for the Detection of BOO

The ability of Qmax and PdetQmax to detect BOO was analyzed using nonparametric ROC curves. Qmax (AUC = 0.762, 95% CI 0.661 to 0.864, $P < 0.001$) and PdetQmax (AUC = 0.721, 95% CI 0.617 to 0.824, $P < 0.001$) were more ac-

TABLE I. *Population characteristics*

Characteristic	Patients (n)	Age* (yr)	Median Qmax† (mL/s)	Median PdetQmax† (cm H_2O)	Volume Voided (mL)
Asymptomatic controls	20	42 ± 7	16 (8–31)	24 (6–38)	330 ± 110
Obstructed patients	169	60 ± 15	10 (1–34)	34 (5–116)	259 ± 142
Prolapse	53	68 ± 11	9 (1–28)	32 (7–76)	197 ± 108
Previous surgery	48	60 ± 12	10 (2–29)	33 (5–80)	273 ± 174
Urethral stricture	68	49 ± 15	12 (2–34)	37 (10–116)	283 ± 131
SUI	124	NA	21 (3–50)	20 (7–60)	NA
P values					
Controls vs. obstructed	—	<0.001‡	<0.001§	<0.001§	0.020‡
Controls vs. prolapse	—	<0.001‡	<0.001§	0.021§	<0.001‡
Controls vs. previous surgery	—	<0.001‡	<0.001§	0.007§	0.203‡
Controls vs. urethral stricture	—	0.034‡	0.002§	<0.001§	0.153‡
Controls vs. SUI	—	NA	0.017§	0.245§	NA
Obstructed vs. SUI	—	NA	<0.001§	<0.001§	NA

Key: Qmax = maximal urinary flow rate; PdetQmax = detrusor pressure at Qmax; SUI = stress urinary incontinence; NA = not available.
Data presented as mean ± SD, unless otherwise noted; data in parentheses are ranges.
* *Age unavailable in 22 obstructed patients.*
† *Median values reported because parameter did not have normal distribution.*
‡ *Independent t test.*
§ *Mann-Whitney U test.*

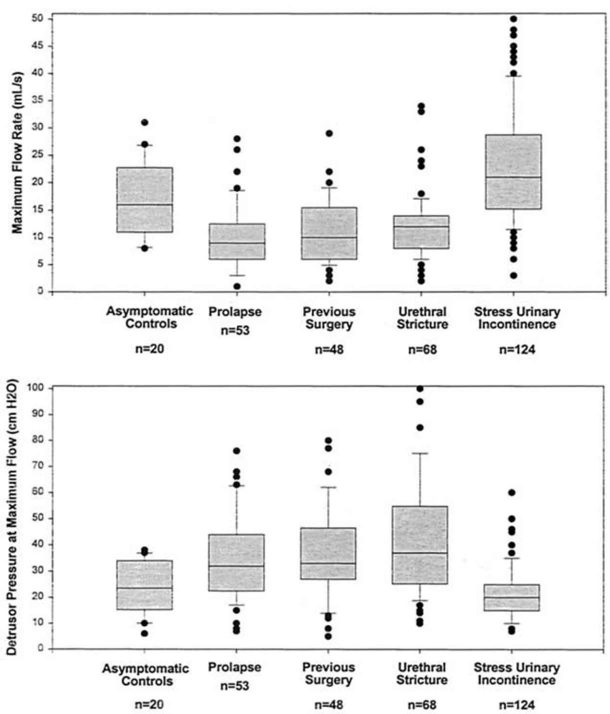

FIGURE 1. *Box plot distribution of Qmax and PdetQmax according to clinical diagnosis (median, quartiles, and outliers).*

curate than flipping a coin (null hypothesis AUC = 0.5) for the detection of BOO. In a multivariate logistic regression analysis, greater PdetQmax (odds ratio [OR] 5.526, 95% CI 2.046 to 14.926, *P* <0.001) and lower Qmax (OR 0.157, 95% CI 0.038 to 0.649, *P* <0.001) were associated with an increased risk of BOO after adjusting for the effects of age (OR 1.104, 95% CI 1.049 to 1.162, *P* <0.001).

Selection of Qmax and PdetQmax Cutoff Points for Detection of BOO

The sensitivity, specificity, and positive and negative predictive values for the detection of BOO were calculated for the Qmax and PdetQmax cutoff values. The resulting matrix of cutoff values and the corresponding percentages of sensitivity, specificity, and accuracy were plotted to represent the three observed parameters within a specific range of PdetQmax and Qmax cutoff intervals. The PdetQmax level with a specificity of at least 60% and the greatest sensitivity for the detection of BOO was 25 cm H_2O. This value was close to the point of equivalence (intersection of sensitivity and specificity curves) for detection of BOO. The Qmax cutoff point resulting in equal sensitivity, specificity, and accuracy (68%) for predicting BOO was close to 12 mL/s (Fig. 2). The PFS test results were combined into two categories: both Qmax and PdetQmax normal and either Qmax or PdetQmax abnormal.

Association of Combined PdetQmax and Qmax Variables with BOO

$PdetQmax_{25}/Qmax_{10}$ and $PdetQmax_{25}/Qmax_{12}$ were combined into three categories: both abnormal, one abnormal, and both normal. Multivariate analyses demonstrated that the combined variables were statistically significantly associated with BOO after adjusting for age (Table II). Patients could be

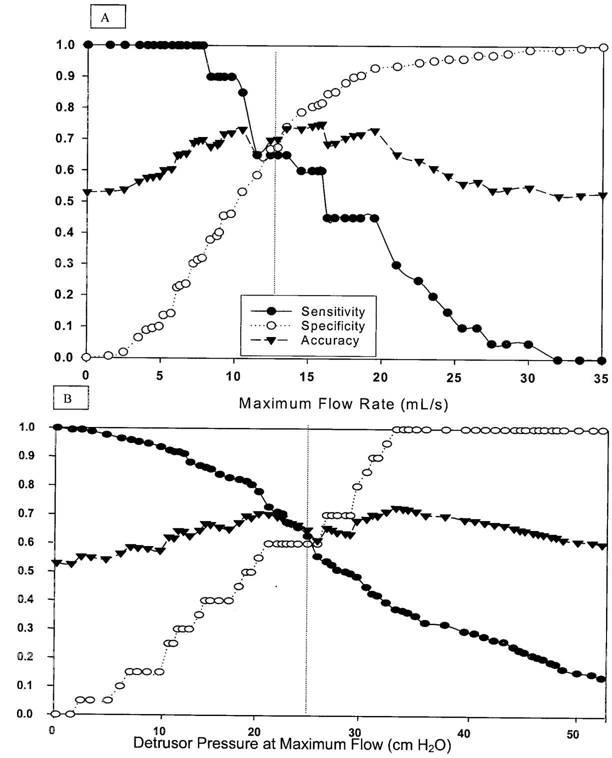

FIGURE 2. *ROC curves of relative diagnostic sensitivity, specificity, and accuracy for detection of BOO according to different (A) PdetQmax and (B) Qmax cutpoint levels. Point of equivalence for detection of BOO (intersection of sensitivity and specificity curves) indicated by broken line.*

stratified into low, intermediate, and high-risk groups for having BOO on the basis of the combined status of the PFS parameters for both $PdetQmax_{25}/Qmax_{10}$ and $PdetQmax_{25}/Qmax_{12}$.

COMMENT

BOO is rarer in women than it is in men, with an estimated incidence of 2.7% to 8% in women with LUTS who are referred to urologists or urogynecologists.[7–9] Although a number of validated PFS nomograms exist to aid in the diagnosis of BOO in men, reliable urodynamic data for women is lacking. Groutz and Blaivas[9] published a nomogram for obstructed women in 2000, but they studied a cohort of only 50 women and used women with LUTS as controls. Furthermore, they used Qmax values taken from noninvasive uroflow tests that had been performed separately from the PFSs. In this study, we attempted to improve our ability to make a urodynamic diagnosis of female BOO by calculating cutoff values for Qmax and PdetQmax that had been obtained during the same PFS. We calculated these cutoff values by constructing ROC curves using a large sample of women who had been diagnosed with BOO on the basis of clinical and radiographic criteria and comparing the values with those from normal, asymptomatic controls who were selected using strict exclusion criteria.

The PFS cutoff values proposed by these most recent ROC curve analyses differ somewhat from the values proposed in our previous studies. The PdetQmax cutoff of 25 cm H_2O is slightly greater than the 21 cm H_2O obtained when we used women with SUI as the control group. This discrepancy may have occurred because women with SUI, owing to their lower outlet resistance, void with significantly lower detrusor pressures than normal asymptomatic women.[3] The greater voiding pressures exhibited by normal women have likely resulted in a greater PdetQmax cutoff point to discriminate between obstructed and normal voiding. Although a PFS in which both the Qmax and PdetQmax are abnormal, as defined by our ROC curve analysis, was highly associated with the presence of BOO (OR greater than 10 for both $PdetQmax_{25}/Qmax$ combinations), the presence of just one abnormal PFS parameter may also indicate obstruction (OR 5.504 and 5.302 for $Qmax_{10}$ and $Qmax_{12}$, respectively). These findings suggest that a low Qmax alone may serve as a marker for BOO in the female population, as has already been found to be the case for men.

One of the shortcomings of this study is that these cutoff values can only be applied to women with anatomic BOO who are able to void during the UDS assessment or who void without a substantial increase in abdominal pressure, because patients who could not urinate or who exhibited Valsalva voiding or a lack of pelvic floor relaxation during urination (which may be indicative of functional BOO) were excluded from our analysis. The small number of control subjects and the lower age of the normal women compared with that of the obstructed group were also relative deficiencies of this study. Even though the effect of age was taken into account in the multivariate analysis, it is likely that the dissimilar ages between the obstructed and control groups could have influenced the Qmax and PdetQmax cutoff values. The collection of UDS parameters from a larger number of asymptomatic women in the sixth to eighth decades will enable us to compile a control group more comparable in terms of age to obstructed women, but will not be easy to obtain given the high prevalence of LUTS and voiding pathologic features in the aging population.

The next step in our investigation of female BOO will be to construct a PFS nomogram for women with obstruction after incontinence surgery using age-matched normal women as controls. Such a nomogram, once validated, would be useful in guiding the treatment of those women who have voiding dysfunction with a history of previous in-

TABLE II. ***Multivariate logistic regression analyses of age and combined variable $PdetQmax_{25}/Qmax_{10}$ or $PdetQmax_{25}/Qmax_{12}$ for detection of bladder outlet obstruction***

	Patients (n)	Odds Ratio	95% CI	*P* Value
$PdetQmax_{25}/Qmax_{10}$				
Both normal	28 (15)	1.000	Referent	
One abnormal	88 (47)	5.504	1.604–18.844	0.007
Both abnormal	73 (39)	28.632	3.155–159.823	0.003
Test for trend				0.002
Age*	—	1.092	1.042–1.145	<0.001
$PdetQmax_{25}/Qmax_{12}$				
Both normal	21 (11)	1.000	Referent	
One abnormal	75 (40)	5.302	1.350–20.810	0.017
Both abnormal	93 (49)	15.148	3.074–74.633	0.001
Test for trend				
Age*	—	1.094	1.044–1.147	<0.001

Key: $PdetQmax_{25}$ = PdetQmax using 25 cm H_2O as cutpoint; $Qmax_{10}$ = Qmax using 10 mL/s as cutpoint; $Qmax_{12}$ = Qmax using 12 mL/s as cutpoint; CI = confidence interval; other abbreviations as in Table I.
Data in parentheses are percentages.
** Age analyzed as continuous variable.*

continence surgery, since a clear-cut temporal sequence of voiding difficulties occurring immediately after such procedures is not always present. In such ambiguous cases, the decision as to whether to perform sling takedown or urethrolysis, which may result in recurrent SUI, is partially dependent on the ability to distinguish bladder atony or hypocontractility from BOO. Because no universally agreed on urodynamic definition of female BOO is available, it is not known whether PFS results are predictive of urethrolysis outcome. Women with BOO may have a greater likelihood of benefiting from urethrolysis, and those with a weak detrusor might be better treated with intermittent catheterization.

CONCLUSIONS

In this study, we proposed cutoff values to aid in the diagnosis of women with outlet obstruction. These cutoff values were derived from ROC curve analysis using normal controls. The PdetQmax value with a specificity of at least 60% and the greatest sensitivity for the detection of BOO was 25 cm H_2O, and the Qmax value resulting in equal sensitivity, specificity, and accuracy (68%) for predicting BOO was close to 12 mL/s.

REFERENCES

1. Chassagne S, Bernier PA, Haab F, *et al:* Proposed cutoff values to define bladder outlet obstruction in women. Urology **51:** 408–411, 1998.
2. Lemack GE, and Zimmern PE: Pressure flow analysis may aid in identifying women with outflow obstruction. J Urol **163:** 1823–1828, 2000.
3. Lemack GE, Baseman AG, and Zimmern PE: Voiding dynamics in women: a comparison of pressure-flow studies between asymptomatic and incontinent women. Urology **59:** 42–46, 2002.
4. Lorenzo AJ, Zimmern PE, Lemack GE, *et al:* Endorectal coil magnetic resonance imaging for diagnosis of urethral and periurethral pathologic findings in women. Urology **61:** 1129–1134, 2003.
5. Abrams P, Cardozo L, Fall M, *et al:* The standardization of terminology of lower urinary tract function: report from the Standardization Sub-Committee of the International Continence Society. Neurourol Urodyn **21:** 167–178, 2002.
6. Ubersax JS, Wyman JF, Shumaker SA, *et al,* for the Continence Program for Women Research Group: Short forms to assess life quality and symptom distress for urinary incontinence in women: the Incontinence Impact Questionnaire and the Urogenital Distress Inventory. Neurourol Urodyn **14:** 131–139, 1995.
7. Massey JA, and Abrams PH: Obstructed voiding in the female. BJU Int **61:** 36–39, 1988.
8. Carr LK, and Webster GD: Bladder outlet obstruction in women. Urol Clin North Am **23:** 385–391, 1996.
9. Groutz A, and Blaivas JG: Bladder outlet obstruction nomogram for women with lower urinary tract symptomatology. Neurourol Urodyn **19:** 553–564, 2000.

EDITORIAL COMMENT

The authors have written their third report regarding the diagnosis of BOO in women using similar diagnostic criteria but a different control group. They should be commended for including a control group of normal asymptomatic women (not an easy task) to eliminate the effects of SUI and low outlet resistance on the control group. As such, the PdetQmax parameter that best diagnoses obstruction has been raised by several centimeters of water.

As in the other studies used to define obstruction by these authors, three distinct types of anatomic obstruction were included. Postincontinence surgery obstruction, prolapse, and periurethral fibrosis/distal urethral stricture. The largest per-