IN SEARCH OF BEST PRESSURE FLOW CRITERIA TO DEFINE BLADDER OUTLET OBSTRUCTION IN INDIAN FEMALES

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ABSTRACT

BACKGROUND
Bladder outlet obstruction in females is increasingly being understood. However, caveats remain in defining clinical and urodynamic parameters to suggest BOO precisely. We compared urodynamic parameters of women with obstructive voiding to control, to better characterise BOO.

MATERIALS AND METHODS
Prospective observational study included 80 females with LUTS and 20 others, admitted for nephrolithiasis without LUTS, as control. Patients were divided into three groups based on symptomology. Group A had obstructive symptoms; Group B had irritative symptoms; while C was control. Clinical evaluation, Qmax, PVR, cystourethroscopy and urodynamic study were performed. ANOVA, Chi-square and ROC curve were used. Fixed combinations [set1 (Qmax<12, PdetQmax>20), set2 (Qmax<15, PdetQmax>30)] were tested to define BOO.

RESULT
Mean age in group A (n=27), B (n=53) and C (n=20) was 43 ± 17, 40 ± 14 and 37 ± 12 years respectively. Group A had lower Qmax [MD_{A-B}=-5.94, p=.0005 & MD_{A-C}=-15.5, p=.0005] and higher PVR [MD_{A-B}=120, p=.005 & MD_{A-C}=187, p=.0005,]. PdetQmax did not differ significantly (p=.061). BOO was found in 16/27 and 9/53 cases in group A and B respectively [Pearson value=25.38, p=.0005]. AUC for BOOI, Qmax, PdetQmax, PVR and MVV was 0.956, 0.939, 0.866, 0.810 and 0.809, respectively. Predicted cut-off values of above parameters were 4.7, 13.15, 28.5, 68.5 and 290.5. Set1 had lower sensitivity than set2 (80% v/s 84%), but higher specificity (94.5% v/s 87.3%).

CONCLUSION
We suggest Qmax<13.1 mL/s, PdetQmax> = 28.5 cm H_2O, BOOI of> = 4.7 and PVR of > = 68.5 mL, as cut-off limit to define BOO. Relation with symptomology is modest. Fixed combination may give variable result; correlation with all parameters helps indeed.

KEYWORDS
Bladder Outlet Obstruction, Female Urology, Female Voiding Dysfunction, Urodynamic Study, Pressure Flow Study.

HOW TO CITE THIS ARTICLE: Majee P, Das RK, Chowdhury A, et al. In search of best pressure flow criteria to define bladder outlet obstruction in Indian females. J. Evolution Med. Dent. Sci. 2017;6(65):4686-4690, DOI: 10.14260/Jemds/2017/1014

BACKGROUND
Bladder outlet obstruction (BOO) is a bothersome problem, with significant alteration in quality of life, ranging in all ages and both sexes. In females, specific concern arises in defining the BOO accurately. Clinical symptoms alone are poor predictors of BOO, as women present with diversity of mixed symptoms.[1] Apart from routine urine testing, further evaluation is required to better characterise the nature of voiding dysfunction. These often include uroflowmetry, post-void residual (PVR), ultrasound (USG), urodynamic study and cystoscopy, depending on varying indications.[2] Overall clinical and investigational profile provides the best opportunity to assess the nature of disease. However, the difficulty arises in diagnosing the BOO confidently, due to lack of standardisation of these studies.

Urodynamic parameters in women alter significantly from men, due to different nature of voiding pattern. Women void with rather lower detrusor pressure, but higher flow rate.[3] Various nomograms based on Qmax and PdetQmax or PdetQmax have been developed in the past to quantify the BOO. However, studies differ in their pressure flow combinations to define BOO, varying from Qmax lower than 10 - 15 mL/s and PdetQmax >20 - 30 cm H_2O.[4] Similarly, no true cut-off level of PVR and maximum voided volume (MVV) has been proposed.

In the present study, we compared the different urodynamic parameters including PVR and MVV in women presenting with obstructive urinary symptoms to the patients of renal calculus disease with normal voiding, in an attempt to find a threshold pressure flow values to define BOO precisely.

MATERIALS AND METHODS
A total of 80 female patients with bothersome lower urinary tract symptoms (LUTS) presenting to the Department of

Financial or Other, Competing Interest: None.
Submission 08-07-2017, Peer Review 01-08-2017,
Acceptance 07-08-2017, Published 14-08-2017.
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DOI: 10.14260/jemds/2017/1014

Urology were included during the study period from March 2014 to December 2016. 20 patients admitted for renal calculus disease with no voiding complaints along with sterile urine were taken as control. Prospective observational study was approved by the institutional ethical committee. Patients with age <14 years, neurological disorder, UTI, malignancy and stone diseases were excluded. Study patients were divided into three groups on symptom basis. Patients with predominantly obstructive symptoms such as poor flow, intermittency, hesitancy, prolonged voiding and straining were kept in group A, while group B had the patients with predominant irritative symptoms such as frequency, urgency and nocturia. Group C acted as control.

All patients underwent clinical evaluation including history and physical examination, urine culture, non-invasive uroflowmetry and PVR measurement by Ultrasound. Last two parameters were checked twice to ensure the consistency, with a preferable interval of 2-3 hours in the same sitting. Minimum voided volume of 150 mL was considered before interpreting uroflowmetry. A written informed consent was taken prior to the evaluation. Multi-channel urodynamic study was performed using transurethral 6 F infant feeding tube and rectal balloon catheter, with a medium infusion rate of 20-30 mL/min. VCUG was not done. Urethra was assessed via 19"Fr urethroscope and findings were noted as either normal or stenosed. Stenosis was conferred as the area of narrowing visible in the urethra or gripping felt during urethroscopy. A higher value of Qmax from non-intubated uroflowmetry and lower value of PVR were taken for the analysis from 2 consecutive readings.

Descriptive analysis of Qmax, PVR, PdetQmax, MVV, DO and BOOI were obtained. ANOVA with post-hoc comparison and Chi-square test were used to check correlation of different parameters in between groups. Outcome in terms of presence or absence of obstruction was measured on the basis of combination of findings of clinical examinations, uroflowmetry, PVR and cystourethroscopy. Receiver operating characteristic (ROC) curve along with area under curve (AUC) and significance level were measured for Qmax, PVR, PdetQmax and BOOI to determine best set of values with higher sensitivity and specificity to define obstruction.

Two fixed set of pressure flow combinations were also tested to assess the obstruction accurately. Set 1 used Qmax <12 mL/s with PdetQmax >20 cm H_2O and set 2 utilised Qmax <15 mL/s and PdetQmax >30 cm H_2O. Their respective sensitivity, specificity and predictive values were calculated using crosstab chart and kappa value. Confidence interval was set at 95% and P value <0.05 was taken as significant. SPSS software version 16 was used for statistical analysis.

RESULTS

A total of 100 patients were studied, including 20 as control. Group A (obstructive LUTS) had 27 participants, while group B (irritative LUTS) and C (control) consisted of 53 and 20 participants respectively. Mean age was 43 ± 17 (years) in group A, 40 ± 14 in group B and 37 ± 12 in group C. Urodynamic parameters including PVR between groups have been presented in table 1. One way ANOVA showed significant differences among groups in Qmax [F (2, 97) = 38.58, p= 0.0005, eta squared = 0.443] and PVR [F (2, 97) = 14.8, p = 0.0005, eta squared = 0.23]. Post-hoc analysis using Dunnett T3 test further revealed lower Qmax in group A compared to group B and control both [MD_{A-B} = -5.94, p = 0.0005, 95% CI = -9.6 to -2.3 & MD_{A-C} = -15.5, p = 0.0005, 95% CI = -18.7 to -12.2] and higher PVR in group A than in other groups [MD_{A-B}= 120, p = 0.005, 95% CI = 30 to 209 & MD_{A-C} = 187, p = 0.0005, 95% CI = 105 to 268] (Figure 1a & b).

Overall difference in PdetQmax [F(2, 97) = 2.8, p = .061, eta squared = .05] and MVV [F(2, 97) = 1.3, p = .26, eta squared = 0.02] among groups was not found significant, however subgroup analysis using Dunnett T3 test showed higher PdetQmax in group A and B, compared to control [MD_{A-c} = 9.6, p = 0.001, 95% CI = 3.7 to 15.4 & MD_{B-C} = 7.5, p = 0.01, 95% CI = 1.4 to 13.5] (Figure 1c). Urethral stenosis was found in 8/27 patients in group A (29%), in 4/53 patients in group B (7.5%) and none in control group (Pearson Chi-Square value = 11.67, df = 2, p = 0.003). Uterine prolapse was noted in 4 cases of group A and 2 of group B. Cystoscopy showed obstructive changes of different grades in 17/27 of group A (63%), 14/53 cases in group B (26.3%) and none in control group [Pearson Chi-Square value= 23.52, df= 6, p= 0.001].

Based on combination of clinical, urodynamic, cystoscopic and imaging finding, bladder outlet obstruction (BOO) was found in 16/27 patients in group A (59.3%), 9/53 in group B (17%) and none in group C [Pearson Chi-Square value = 25.38, df = 2, p = 0.0005]. Urodynamic parameters in obstructed and non-obstructed group are presented in table 2. Urethral stenosis was noted in 36% (9/25) of women with BOO. ROC curve analysis for defining BOO based on BOOI, Qmax, PdetQmax, PVR and MVV revealed area under curve (AUC) of 0.956, 0.939, 0.866, 0.810 and 0.809, respectively (Figure 2). Best predictive cut-off values of different parameters were predicted while balancing for higher sensitivity and specificity in defining BOO [Table 3]. A fixed pressure flow combination of set 1 had Kappa value of 0.762, while set 2 had value of 0.690.

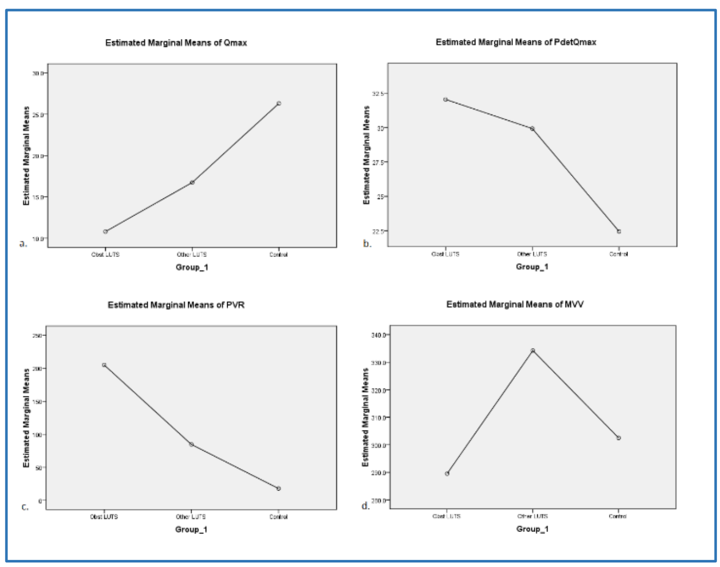

Figure 1. Graph Showing Estimated Marginal means of Qmax (a), PdetQmax (b), PVR (c) and MVV (d) In Study and Control Groups.

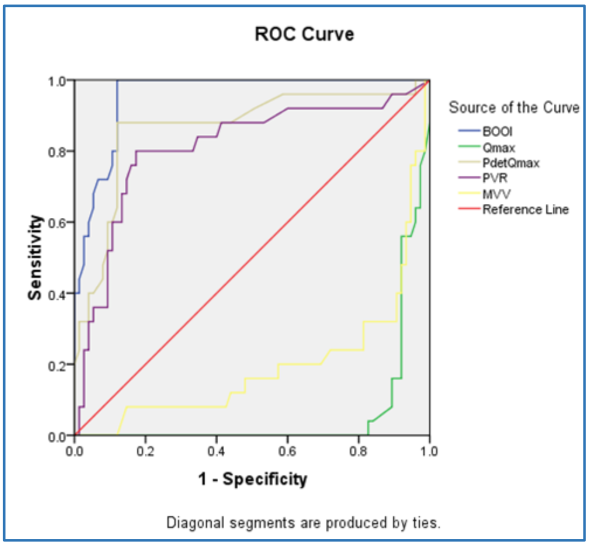

Figure 2. ROC Curve for Determining BOO based on BOOI, Qmax, PdetQmax, PVR and MVV.

Group		Qmax (mL/s)	PdetQmax (cm H_2O)	PVR (mL)	MVV (mL)
Group A (Obst LUTS) N = 27	M ± SD	10.79 ± 5.89	32.04 ± 11.67	204 ± 166	289 ± 162
Group B (Irritative LUTS) N = 53	M ± SD	16.74 ± 6.85	29.92 ± 17.43	84 ± 118	334 ± 117
Group C (Control) N = 20	M ± SD	26.31 ± 2.83	22.45 ± 2.52	17.9 ± 9.7	302 ± 45

Table 1. Baseline Urodynamic Parameters in Study and Control Groups

Group		Obstructed cases (N = 25)	Non-Obstructed cases (N = 55)	Control (N = 20)	P value	Partial Eta Squared
Qmax (mL/s)	M ± SD	8.15 ± 3.68	17.72 ± 6.19	26.31 ± 2.82	0.0005	.593
Pdet Qmax (cm H_2O)	M ± SD	43.36 ± 20.54	24.85 ± 7.94	22.45 ± 2.52	0.0005	.338
PVR (mL)	M ± SD	203 ± 160	89.8 ± 126.6	17.9 ± 9.75	0.0005	.214
MVV (mL)	M ± SD	213 ± 109	367.1 ± 117.5	302.5 ± 45.39	0.0005	.277

Table 2. Urodynamic Parameters in Obstructed, Non-obstructed and Control Groups

Test Result Variable(s)	Area	Asymptotic Sig.[b]	Asymptotic 95% Confidence Interval		Predictive cut-off value	Sensitivity	Specificity
			Lower Bound	Upper Bound			
BOOI	0.956	0.000	0.921	0.991	4.7	100%	88%
Qmax	0.939	0.000	0.894	0.984	13.15	89.3%	88.0%
PdetQmax	0.866	0.000	0.773	0.959	28.50	88.0%	86.7%
PVR	0.810	0.000	0.700	0.919	68.5	80.0%	80.0%
MVV	0.809	0.000	0.701	0.917	290.5	80.0%	76.0%

Table 3. Best Predictive values for Defining BOO, based on ROC Analysis

a- Under non parametric assumption.
b- Null hypothesis: true area = 0.5.

Authors	Cases/ Control (N)	Qmax (mL/s)	PdetQmax (cm H_2O)	PVR (mL)	Other
Farrar et al. [1976]	162	<15	>50	> = 200	
Diokno AC [1984]	3	<15	>60		Radiographic e/o BOO
Massey and Abrams [1988]	163	<12	>50	Significant	urethral resistance >0.2
Bass and Leach [1991]		<15		>100	Shape of the pressure–flow curve
Chassagne et al. [1998]	35/124	> = 15	>20	-	-
Nitti et al. [1999]	261	<15	>20		Radiographic e/o BOO
Blaivas and Groutz [2000]	600	<12	>20		Radiographic e/o BOO
Lemack GE [2000]	87/124*	=<11	>=21		
Defreitas GA, et al. [2004]	80/20	<12	>=25		
Kuo HC [2004]	70/265*/30	= <15	>=35		PdetQmax >=30 for screening
Di Grazia E, et al. [2004]	43/136	= <13	>=22	96	
Gravina GL [2007]	133/37	= <15	>=28		BOOI >= -8
Mostafa M et al. [2013]	60/27*	<15	>30	>100	MVV<170 ml
Our Series [2016]	80/20	<13.15	>=28.5	>68.5	BOOI > 4.7

Table 4. Urodynamic Criteria's to Define BOO, Suggested by Various Authors

*Patient with SUI taken as control.

DISCUSSION

Bladder outlet obstruction in females still remains a topic of curiosity, despite recent widespread research in the area. Much has been said, but general consensus on various aspects needs further discussion. Incidence has been varied, ranging from 2.7-23%, due to non-uniform definitions.[5] In our study, it measured 31.25% (25/80). Symptoms alone are insufficient in predicting BOO. Hubeaux et al found no correlation between obstructive symptoms and BOO, however, they defined BOO solely on the basis of uroflowmetry <15 mL/s and PVR >50 mL.[6] Similarly, Rivas et al showed no definite determination between SUI, UUI and BOO by AUA symptom index, but good quantification of voiding symptom.[7] However, Groutz et al reported a higher AUA symptom index score in BOO patients compared to SUI group and control (15.8 ± 8.4 versus 10.3 ± 6.4 and 2.1 ± 2.7).[8]

We found significant higher percentage of BOO in patients with predominant obstructive symptoms compared to other LUTS (59.3% v/s 17%, P = 0.0005). A significant low Qmax and high PVR were also reported in the obstructive LUTS patients, but PdetQmax and MVV didn't differ much in different symptom groups. We found good prediction capability of BOOI, Qmax and PdetQmax in defining BOO, based on AUC analysis and moderate capability of PVR and MVV [Table 3]. Though originally described for men, few authors found BOOI a useful marker in women also. Gravina et al suggested BOOI cut-off > or= -8 with sensitivity of 80.8% and specificity of 86.1% for female BOO.[9] We found a BOOI cut-off of 4.7 provided 100% sensitivity and 88% specificity. In terms of Qmax and PdetQmax, different set points have been proposed by various authors, ranging from 12 to 15 mL/s and 20 to 30 cm H_2O respectively (Table 4).[10-19] Our data showed Qmax <13.15 mL/s predicted BOO with 89.3% sensitivity and 88% specificity, while PdetQmax >= 28.5 cm H_2O had 88% sensitivity and 86.7% specificity. PVR > = 68.5 mL also showed moderate correlation with BOO.

A fixed pressure flow combination of set 1 (Qmax <12 mL/s, PdetQmax >20 cm H_2O) showed good agreement in identifying BOO accurately [Kappa value = 0.762] with sensitivity of 80% (20/25) and specificity of 94.5% (52/55). Set 2 (Qmax <15 mL/s, PdetQmax >30 cm H_2O) had moderate to good agreement [Kappa value = 0.690] with a bit higher sensitivity of 84% (21/25), but lower specificity of 87.3% (48/55). Significance of bladder trabeculations (BT) in females is not entirely clear, unlike men. Gowda et al in his study of 551 women undergoing cystoscopy found association of BT with higher degree of prolapse, increased DO and UUI.[20] We found a good correlation of increasing grade of BT with low Qmax, high PdetQmax and high PVR [p = 0.001 (Partial Eta Sq = 0.388), p = 0.001 (Partial Eta Sq = 0.29), p = 0.001 (Partial Eta Sq = 0.17) respectively].

Various aetiologies for BOO have been described, most common being anti-incontinence surgery nowadays, followed by dysfunctional voiding (DV), urethral stenosis (US), pelvic organ prolapse (POP), urethral diverticulum, cyst, carbuncle, carcinoma and pelvic tumours.[21] In our series, US (9/25) and POP (5/25) were more common than DV (4), post-surgery (3), post-RT (3) and carbuncle (1). Cystoscopy is good tool, not only for assessing site of obstruction, urethral dispensability, also the bladder wall changes.[22] We found it particularly helpful in grading of UB obstructive changes, discovered in 22 out of 25 (88%) cases of BOO (Grade 1 in 28%, grade 2 in 52% and grade 3 in 8%). So, various studies have given great insight into the female voiding patterns and a cumulative data from these might help to bring uniformity to better characterise BOO. Limitations of this study may be the non-utilisation of VUDS, which has shown promising results recently. Control population consisting more of younger cases might also bring out subtle differences in comparison. Repeat UDS have shown some benefit in unequivocal cases, not considered in our series.[23]

Limitation

Less Number of Controls Compared to Study population.

CONCLUSION

Urodynamic study considerably helps in evaluating obstructive voiding symptoms in females. Our data finds Qmax <13.1 mL/s, PdetQmax >=28.5 cm H_2O, BOOI of >=4.7 and PVR of >=68.5 mL, as a cut-off limit to define BOO. Cystoscopy adds useful information regarding bladder outlet and bladder wall changes. A fixed pressure flow combinations give variable results, with lower set of values increasing the sensitivity, but at the cost of specificity and vice versa.

ACKNOWLEDGEMENT

Dr. Aseem Kumar Dey, for assisting in conducting urodynamics.

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