

A Clinical Study on Correlation of Non-Invasive Diagnostic Tests in Evaluation and Management of Patients with Symptomatic Benign Prostatic Hyperplasia

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ABSTRACT

Introduction: The gold standard for diagnosing bladder outlet obstruction is pressure flow study but it is associated with side effects of high cost, invasiveness, infection, limited availability. So non invasive diagnostic tests becomes a good option. The diagnostic accuracy of these non invasive tests, however, remains uncertain. So this study was conducted to know the role of non invasive diagnostic tests like International prostate symptom score (IPSS), Uroflowmetry (UFR), prostate volume, bladder wall thickness, post void residual urine in symptomatic patients with BPH in their evaluation and in the planning of management.

Material and methods: The present study included 108 male patients above 50 years suffering from symptomatic BPH who attended urology OPD at SVIMS, Tirupati. IPSS, Urinary flow rates, bladder wall thickness, prostate volume, post void residual urine and urodynamic study have been recorded in these patients at the time of enrollment into study.

Results: One hundred and eight men between 50 – 79 years of age with mean age of 62.4 years participated in this study. All the patients were divided into two groups as either obstructed or un obstructed based on Abraham – Griffith number calculated from the urodynamic study. Bladder wall thickness, Q max, Post void residual urine and prostate volume all had statistically significant values between obstructed and un obstructed patients. However, there was no statistical significant differences between age, IPSS in both the groups

Conclusion: This study shows that in a subset of patients with BPH with predefined inclusion and exclusion criteria, it should be possible to define obstruction with simple non invasive parameters, without using invasive pressure flow study.

Keywords: Bladder Outlet Obstruction, Benign Prostatic Hyperplasia, Urodynamic Study, Bladder Wall Thickness

The development of novel clinical measurement techniques requires progression through a number of key stages. The first requirement is that there is a clinical need for the measurement to be performed and that the results will improve patient care. Next, readings obtained by the device have to be shown to be valid – that is they measure what they are supposed to measure; they have to be demonstrated to be reliable – that is the same result is obtained on repeat testing and also it has to be established that the new test is generalizable to the range of healthcare settings in which it is likely to be used. Finally the results of the test have to be shown to make a difference to the diagnosis, management or treatment of the relevant clinical problem in a way that is an advance on existing care pathways and gold standard tests. These requirements have been recently formalized in a consensus guideline.³ Once all this has been established, purchasers of healthcare will generally require some independent assessment of the worth of the new technique in comparison to existing options prior to its introduction into routine practice.⁴

Study aimed to correlate the available non invasive diagnostic tests in patients with symptomatic BPH in their evaluation and in plan of management attending Urology OPD, SVIMS Hospital, Tirupati and objective was to study IPSS, urinary flow rates, bladder wall thickness, prostate volume, post void residual urine in patients with BPH and to compare all the parameters with urodynamic study which is the gold standard investigation for knowing the presence or absence bladder outlet obstruction.

INTRODUCTION

Pressure flow study is the gold standard investigation for detecting bladder outlet obstruction secondary to benign prostatic hyperplasia.¹ However it is associated with demerits of high cost, limited availability, restriction to specialized hospitals, risk of infection and invasive pressure flow studies are not generalizable across the range of settings where they might be needed and hence are not widely used in the assessment of men with LUTS.² In this regard a noninvasive simpler method of categorizing bladder outlet obstruction in patients with benign prostatic hyperplasia would be extremely useful for clinicians charged with assessing men with LUTS

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MATERIAL AND METHODS

This study was a Prospective observational study and it included 108 male patients above 50 years suffering from symptomatic BPH who attended urology OPD at SVIMS, Tirupati. IPSS, Urinary flow rates, bladder wall thickness, prostate volume, post void residual urine and urodynamic study have been recorded in these patients at the time of enrollment into study.

This study included 108 male patients who are above 50 years of age and suffering from symptomatic BPH and attending Urology OPD, SVIMS, Tirupati during the period between March 2016 and October 2017. The informed consent was obtained from all the patients and study has commenced after approval of Institutional ethics committee.

The exclusion criteria for this study were Carcinoma prostate, Previous pelvic surgery. Neurogenic bladder. Bladder stones, Stricture urethra. Retention on catheter. Usage of alpha blockers and 5 alpha reductase inhibitors. Chronic renal failure. And Patients who are not willing to participate in the study.

Study material

All patients included in this study underwent a comprehensive history taking and IPSS questionnaire which is used to quantify LUTS. Digital rectal examination was performed to exclude men with palpable prostate cancers and to judge the prostate size. All men with serum PSA greater than 4 ng/ml were excluded from the study. Participants who met the inclusion criteria were asked to drink water until they felt strong desire to void. When their bladders were full, a transabdominal ultrasound was done by a radiologist with the use of 7.5 M Hz linear ultrasound array and note was made of prevoid bladder volume at normal desire, post void residue, prostate volume and bladder wall thickness. Two ultrasonic measurements of the anterior bladder wall thickness in a longitudinal and transverse sections were taken and the average of the two measurements was taken as true value. Ultrasound studies were carried out independently by the radiologist, who was blinded to other reports. Bladder thickness index was obtained by dividing bladder wall thickness in millimeters by prevoid bladder volume in liters. Afterwards, all men performed a free uroflowmetry and the maximal (Q max) and average (Q avg) urinary flow rates were noted.

After one week all patients had a urodynamic investigation which was performed with LABORIE urodynamic machine which was available in Department of Urology and the recommendations of the International Continence Society were followed strictly. Bladder Outlet Obstruction was diagnosed according to Abrams – Griffith number.

AG number (BOOI) = Pdet Qmax - 2 Qmax.

If AG number was found to be greater than 40 cm H₂o it was considered as obstructed bladder and obstruction can be excluded if it is under 20 cm H₂o. Patients in equivocal group were further re-allocated to two sides based on the detrusor pressure at minimal flow. All urodynamic data used in the study were machine read, unless there was an obvious

artifact. This was done in order to avoid observer bias.

STATISTICAL ANALYSIS

The data was entered into an Excel™ (Microsoft, Redmond, WA) database and analysis performed with SPSS software. After compiling all the data, statistical analysis was performed to evaluate IPSS, UFR, prostate volume, bladder wall thickness, post void residual urine in patients with BPH who were managed medically and surgically. Chi- square test was used for comparing categorical variables. P value <0.05 was considered statistically significant.

RESULTS

- One hundred and eight men between 50 – 79 years of age with mean age of 62.4 years participated in this study
- Mean IPSS score was found to be 16.8 with a range of 2 – 30
- The mean Qmax on Uroflowmetry was found to be 10.2 ml/sec with a range of 2.5 – 38.6 ml/sec
- The mean prevoid on ultrasound scan was found to be 320 ml with a range of 92 -864 ml
- The mean post void residue urine on ultrasound was found to be 67 ml with arrange of 0- 486 ml
- The mean prostate volume on ultrasound was measured to be 42.4 ml with a range of 12 – 140 ml
- The mean bladder wall thickness on ultrasound was found to be 4.86 mm with a range from 1.2 – 9.4 mm. The baseline characteristics of patients and results after initial evaluation of patients listed in table 1.

In this study, bladder wall thickness less than 2 mm was taken normal and it was recorded in 64 patients where as bladder wall thickness equal to or greater than 2 mm was recorded in 44 patients

In this study, Q max of equal to or greater than 15 ml/sec on free uroflowmetry was taken normal and it was seen in 22 patients where as 86 patients had Q max less than 15 ml/sec For our study, post void residual urine equal to or less than 50 ml was taken normal and it was seen in 35 patients, where as 73 patients had post void residue urine greater than 50 ml For our study, Prostate volume less than 25 ml on ultrasound scan was taken normal and it was seen in 21 patients and 87 patients had prostate volume greater than 25 ml

Sl no	Parameters	Mean	Range
1	Age	62.4 years	50 -79
2	IPSS	16.8	2- 30
3	Qmax	10.2 ml/sec	2.5 – 38.6
4	Qavg	5.8 ml/sec	1.2 – 22.8
5	Pdet Qmax	76.08	22 - 178
6	Prevoid	320 ml	92 – 864
7	Post void residual urine	67 ml	0 – 486
8	Prostate Volume	42.4 ml	12 – 140
9	Bladder wall thickness	4.86 mm	1.2 – 9.4
10	Bladder thickness Index	17.3	3.82 – 91.2

Table-1: Baseline data of the patients and tests results after initial evaluation with non invasive tests.

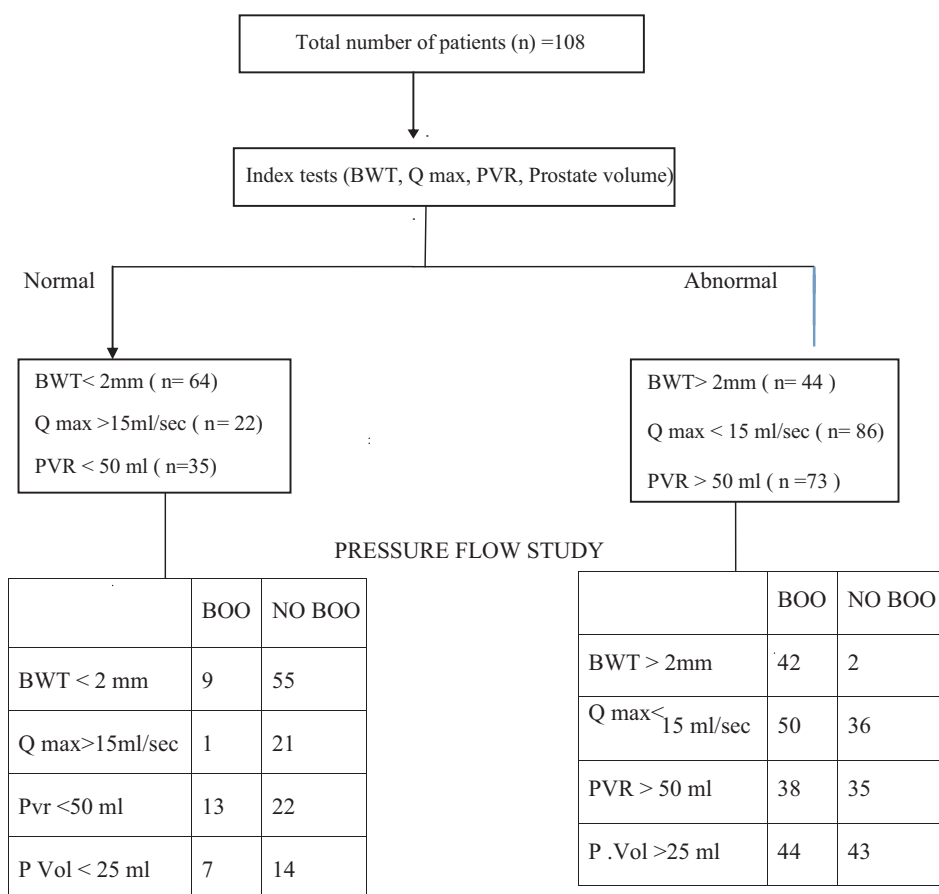


Table-2: Study design and distribution of test results

Sl no	Parameters	Obstructed mean	Unobstructed mean	P value
1	Age	63	61	0.051
2	IPSS	20.6	17.8	0.056
3	Qmax	7.3	14.8	< 0.001
4	Prostate volume	44	22	0.023
5	PVR	128	35	0.001
6	Bladder wall thickness	5.8	2.9	<0.001
7	Bladder thickness index	21.2	14.7	<0.001

Table-3: Test results of non invasive diagnostic tests compared between obstructed and non obstructed patients.

	Sensitivity	Specificity	Positive predictive value	Negative predictive value
Bladder wall thickness	82.35	96.5	95.34	85.93
Prostate volume	86.2	24.5	50.5	66.6
Q max	98.03	36.84	58.1	95.4
Post void residue	74.5	38.5	52	62.8

Table-4: Diagnostic parameters of non-invasive tests to diagnose Bladder Outlet Obstruction in patients with BPH.

On the basis of the pressure flow studies, the prevalence of bladder outlet obstruction in this study population was found to be 47.25 percentage (51 patients out of 108)

Bladder wall thickness, Q max, Post void residual urine and prostate volume all had statistically significant values between obstructed and un obstructed patients. However, there was no statistical significant differences between age, IPSS in both the groups. Patient inclusion and distribution of test results are shown in table 2. Test results of non invasive diagnostic tests compared between obstructed and non obstructed patients are shown in table 3.

Calculation of the positive predictive values demonstrated that 95.34 % of patients with bladder wall thickness greater than 2 mm had bladder outlet obstruction where as positive predictive values of other tests varied between 51 – 58 %. Calculation of the negative predictive values demonstrated that 95.4 % of patients with Q max equal to or greater than 15 ml/sec will not be having bladder outlet obstruction, where as bladder wall thickness had negative predictive value of 85.93 %, prostate volume and post void residue having negative predictive values of 66.6 % and 62.8 % respectively.

References (single parameter)	No of patients	Sensitivity %	Specificity %	Positive predictive value
de la Rosette et al symptoms ¹⁵	933			
Decreased stream		94	8	60.8
Terminal dribble		94	7	60.6
Intermittency		89	13	60.8
Hesitancy		84	19	61.1
Abrams and Griffiths (PVR > 50 ml) ¹⁶	117	87.5	35	80.3
Rosier and de la Rosette (total prostate volume > 40 ml)	571	49	32	54
Kojima et al (PCAR) ¹⁷	85	77	75	86.3
Kojima et al (RI > 0.7) ¹⁸	57	85	46	68.3
Chia et al (IPP) ¹⁹	200			
Grade 1		7	56	20.6
Grade 2		17	53	72.2
Grade 3		76	92	94.1
Manieri et al (BWT > 5 mm) ²⁰	174	54	92	89.7
Oelke et al (BWT > 2 mm)	70	64	97	95.5

Table-5: Showing single measurement methods of various studies of diagnosing bladder outlet obstruction non-invasively

Post void residual urine was found to have lowest sensitivity among all other test with 74.5% where as for other tests sensitivity varied between 82 – 98 %.

Specificity was found to be highest for bladder wall thickness which was around 96.5 % where as for all other tests it varied between 25 – 37 %. Diagnostic accuracy data are shown in table 4.

DISCUSSION

Lower urinary tract symptoms (LUTS) are among the most common cause of urological consultation, and in males are often accompanied by BPH. The role of urodynamic study in these patients has been well defined in various clinical guidelines on the management of BPH. While urodynamic study is well tolerated, it is an invasive procedure requiring bladder catheterization and it is not without morbidity in the form of hematuria, urinary tract infections, or intensification of micturition symptoms in the days following study. On the other hand Urodynamic study is more expensive than other techniques and requires considerable dedication on the part of urologist in terms of time. It is also not easily available due to high cost of the equipment. Never the less, it remains gold standard for the diagnosis of infra vesical obstruction and detrusor hyperactivity.

Numerous non- urodynamic approaches have been investigated as an alternative to pressure flow studies in men for accurately diagnosing bladder outlet obstruction. It is important that studies suggesting a new diagnostic test should follow good methodological standards to allow accurate evaluation of findings.

This study has shown that diagnostic accuracy of bladder outlet obstruction assessment is better with bladder wall thickness measurements than with measurement of Q max, post void residue, IPSS, and prostate volume. Bladder outlet obstruction can be detected with bladder wall thickness as accurately as with pressure flow studies.

The characteristics of the patients in this study were very similar to those in previous published studies. Patients of our study therefore appear to be representative of patients

who visit urologists because of benign prostatic hyperplasia. In patients with benign prostatic hyperplasia, no strict relationship exist between lower urinary tract symptoms, bladder outlet obstruction and benign prostatic enlargement. A recently published article, which reviewed the morphologic and functional changes of the bladder wall in response to bladder outlet obstruction, describes comprehensively how mechanical stretch induces gene expression and protein synthesis in epithelium and smooth muscle cells and explains how bladder outlet obstruction could cause LUTS.⁵

The ultrasound measurements of bladder wall thickness has shown high accuracy in predicting bladder outlet obstruction. The results of this study are in line with those of previous studies in which bladder wall thickness was investigated retrospectively and was not blinded to the results of pressure flow studies. A previous study in which seventy men with benign prostatic hyperplasia were evaluated with the same technique and cut off values of bladder wall thickness more than 2 mm found to have a positive predictive value of 95.5%.⁶ A recently published study including 102 men with clinical benign prostatic hyperplasia found a positive predictive value of bladder wall thickness of 89 % using a cutoff value of 2.5 mm and 100 % positive predictive value using a cut off value of bladder wall thickness more than 2.9 mm.⁷ Oelke et al which included 160 patients found 94% positive predictive value using cutoff value of 2 mm for bladder wall thickness. All the studies mentioned above demonstrated that the diagnostic accuracy of bladder outlet obstruction is higher with bladder wall thickness than with free uroflowmetry, post void residue, or prostate volume. The diagnostic accuracy of detrusor wall thickness or bladder wall thickness is remarkable in all studies. The results of our study confirms these findings.

Although the symptom of poor flow is significantly associated with a low Q max, the association is weak, as indicated by the correlation co-efficient of only -0.22 in the study by Bary et al.⁸ There was no significant association between the symptom of incomplete emptying and post void residual urine. Bary et al suggested that the poor association

between LUTS and variables such as Q max and post void residue reflected “ unreliability in the measurement of the physiologic variables ” rather than reflecting unreliability in the assessment of symptoms. Certainly test – retest validation of symptom questionnaires shows consistency in individual patients.⁹ While both Reynard et al¹⁰ and Fenely et al¹¹ have shown considerable variation in Q max measured on either the same or different days and Dunsmuir et al¹² have shown poor test – pretest reliability for the measurement of post void residue. Abnormal measurements of free uroflowmetry or post void residue can detect only voiding dysfunction, without indication bladder outlet obstruction specifically. Post void urine or reduced values of Q max can be caused by bladder outlet obstruction, detrusor under activity or in combination of both. Changing the cut off value of Q max from 15 to 10 ml/sec helps to identify more men with bladder outlet obstruction. However the detection rate of bladder outlet obstruction increased from 58% to only 69% which is clearly lower than with bladder wall thickness measurements. Thus while LUTS are important in that they are what bothers patients, their significance in terms of reflecting a demonstrable abnormality in voiding function is very limited and it is therefore important not to over interpret their significance.

Statistically significant correlation between bladder outlet obstruction and prostate volume was found in Rosier et al.¹³ Urodynamically bladder outlet obstruction was confirmed in 90 % of patients with a prostate size more than 80 cc. In 32 % of patients with a prostate smaller than 40 cc, no evidence of bladder outlet obstruction was found on pressure flow studies.

A statistically significant correlation was found between all IPSS questions (except intermittency) and objective parameters of obstruction.¹⁴ However the clinical significance of this finding is minimal because of a large overlap of symptom scores exists among patients with different grades of bladder outlet obstruction. The storage component of IPSS correlated somewhat better with obstruction than did the voiding component. Results of various studies conducted to measure diagnostic accuracy of non invasive tests in measuring bladder outlet obstruction are listed in table 5.

CONCLUSION

This study shows that in a subset of patients with BPH with predefined inclusion and exclusion criteria, it should be possible to define obstruction with simple non invasive parameters, without using invasive pressure flow study.

This study shows bladder wall thickness as a single reliable indicator for assessing bladder outlet obstruction non invasively in patients with benign prostatic hyperplasia. Although other tests like IPSS, Qmax, Uroflowmetry appears to be less reliable compared to bladder wall thickness, they remain as a useful adjunct to bladder wall thickness in assessing bladder outlet obstruction non invasively.

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