Importance of prostate volume and urinary flow rate in prediction of bladder outlet obstruction in men with symptomatic benign prostatic hyperplasia

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KEY WORDS

prostate volume ◗ urinary flow rate ◗ bladder outlet obstruction ◗ benign prostatic hyperplasia ◗ pressure/flow study

ABSTRACT

Objectives. To predict bladder outlet obstruction with parameters of non-invasive investigations for patients with symptomatic benign prostatic hyperplasia.

Patients and methods. A sample of 122 men with moderate to severe lower urinary tract symptoms suggestive of benign prostatic hyperplasia was selected. Transrectal prostate ultrasound, free flow measurement, and transabdominal ultrasound for residual urine were carried out together with digital rectal examination for all patients. All patients underwent urodynamic pressure/flow test. Two groups of obstructed (91 patient) and equivocal/unobstructed (31 patient) were analyzed. Probabilistic model based on logistic regression was developed for prediction of obstruction.

Results. Various parameters were compared in obstructed and non-obstructed/equivocal groups, highlighting important parameters for obstruction. Correlation analysis indicates higher obstruction dependence on average and peak flow rates and lower dependence on total prostate and transition zone volumes, transition zone index. Binary logistic regression model suggests that average flow rate combined with total prostate volume is the best predictor of obstruction (83% of correct predictions; PPV = 92%; NPV = 52%) in the analyzed sample. The analyzed model suggests that peak flow rate could also be almost equally important parameter instead of average flow rate.

Conclusions. The study suggests that average/peak flow rate combined with total prostate volume can be used for prediction of obstruction. The developed probabilistic model helps to determine patients who need invasive urodynamic testing for decision on surgical treatment.

INTRODUCTION

Benign prostatic enlargement (BPE), bladder outlet obstruction (BOO) and lower urinary tract symptoms (LUTS) is the basic triad for clinical diagnosis of benign prostatic hyperplasia (BPH) [1]. BPH is rare in men younger than 40, but is present in up to 50% of men over 60 years of age and nearly 88% by 80 years of age [2, 3]. Macroscopic enlargement of the gland is found in almost half of men who have microscopic BPH.

Symptoms caused by BPH and named LUTS, can be categorized as obstructive (voiding) and irritative (storage). Obstructive symptoms are caused by enlargement of the physical mass of the gland (static component) as well as tone of smooth muscle of the prostatic stroma (dynamic component). Irritative symptoms are associated with the bladder dysfunction caused by BOO [4]. It has been estimated that 25% of men in their sixth decade of life have urinary symptoms and objective signs of BOO [2]. However, the evidence for a direct link between BPE, BOO, and LUTS is far from convincing [4, 5].

The aim of surgical treatment for BPH is to relieve or eliminate BOO. Most patients with LUTS and an enlarged prostate will benefit from prostatectomy; however, part of them still experience persistent storage symptoms [4]. Fifteen to 30% of the patients with BPH do not have a favorable outcome after transurethral resection of the prostate (TURP) if symptoms are considered [6]. One of the main causes of unfavorable results is absence of obstruction before surgery.

Pressure-flow urodynamic studies remain the most definitive method of objective documenting BOO. It serves as the best instrument to find out if the symptoms are caused by prostatic obstruction or bladder dysfunction [7]. Preoperative investigations with pressure-flow study has been demonstrated that 20-50% of patients with LUTS had no urodynamic evidence of obstruction [7-9]. However suitability of urodynamics in assessing BPH is controversial in terms of invasiveness, cost, time consumption, and, both, reproducibility and variability of results [7]. Therefore these studies still are not routinely recommended in BPH.

It has been proven that the diagnosis of BOO cannot be made by symptomatic assessment alone [8]. Size of prostate and post-void residual (PVR) of urine are important in evaluation of BPH, but not critical for diagnosis of obstruction. It has been confirmed by studies that the best single predictor of BOO is urinary flow rate. Approximately 70% of men with peak flow rate (Qmax) less than 15 ml/s are obstructed [10]. Value of other parameters of free flow is more controversial. Recent studies show that ultrasound estimated prostate weight or prostate transition zone volume can also predict obstruction [11, 12].

Better prediction of obstruction using parameters of non-invasive investigations aimed to improve results of BPH surgery is an important topic for more than two decades, but there is no worldwide-accepted model. Some studies show that predictability of conventional tests alone or in combination for BOO is only 60-70% [13]. The aim of our study was to look for possibly better simple predictors.

MATERIAL AND METHODS

There were 122 men aged 45-85 years with moderate to severe LUTS suggestive for BPH involved in this prospective study during the period from March 2003 to December 2004. Permission for the study was obtained from the Regional Ethics Committee. Informed consent was received from all patients. Only subjects with International Prostate Symptom Score (IPSS) ≥7 and Qmax in range 3-20 ml/s in total voided volume of 120 ml or greater were included. Symptoms were measured according IPSS together with quality of life (QoL) question. All uroflow traces were reviewed by a single investigator for correction of artifacts.

Individuals who had undergone previous prostate or lower urinary tract surgery or who had prostate cancer or PSA level exceeding 10 ng/ml were excluded. Carcinoma of the prostate in case of PSA range 4 to 10 ng/ml had to be excluded by prostate biopsy. Patients with bladder stones, urinary tract infection, and suprapubic drainage as well as evidence of neurogenic bladder were excluded from the study.

Uroflowmetric free urinary flow measurement (Urodyn 1000, Medtronic) was performed for flow parameters. Prostate size was measured by transrectal ultrasound (Siemens Sonoline SI-250 with probe of 5-7.5 MHz) evaluating total prostate volume (TPV) as well as transition zone volume (TZV). For calculation of prostate volume, the ellipsoid formula (0.52 x width x height x length) was used [14]. Transition zone index (TZI) was calculated by dividing TZV/TPV. Post void residual (PVR) was measured by transabdominal ultrasound using bladder measurements in transverse and sagittal plains immediately after free flow measurement. Eventually all patients underwent urodynamic pressure-flow study (Duet® Logic, Medtronic, software Duet 8.37, 1995-2001 Medtronic Functional Diagnostics A/S). Bladder filling with subsequent pressure-flow study was performed in rate of 30 ml/min with 37°C saline via transurethral two-channel 7 F urodynamic catheter. The test was repeated two times and lower degree of obstruction showing data was taken to account. The International Continence Society (ICS) nomogram was used for obstruction evaluation. According to this nomogram the patients were classified into two groups: obstructed (Abrams-Griffiths number – AG >40) and unobstructed/equivocal (AG ≤40). Comparing to Schafer nomogram these groups were separated by line between categories two and three.

Urodynamic studies were performed and evaluated according ICS recommendations by one investigator (DT).

Statistical analysis was performed using SPSS software. Mean, standard deviation (SD), 10-90 percentiles, median, and correlation coefficients (r) were calculated. Significant differences in groups were analyzed by t-test for independent normally distributed samples and by Mann-Whitney U test for non-normally distributed samples. The binary logistic regression model was developed for obstruction probability estimation and identification of the most important predictors. A level of statistical significance was chosen to be 95%.

RESULTS

There were 91 obstructed and 31 unobstructed/equivocal out of 122 tested patients. Age of patients was not statistically different between the groups (p = 0.088). Qmax in range of 4-15 ml/s was determined in 85.3% of patients. The characteristics of parameters for both groups are summarized in Table 1. A statistically significant difference between the groups was reached for total IPSS score, score of obstructive symptoms evaluated by ques-

Table 1. Characteristics of obstructed and unobstructed/equivocal patients

	All patients, n = 122				Obstructed, n = 91				Unobstructed/equivocal, n = 31				p-values
	Mean	SD	10-90 percentiles	Median	Mean	SD	10-90 percentiles	Median	Mean	SD	10-90 percentiles	median	
Age (years)	67.6	8.5	58.0-77.7	68.5	68.4	8.1	59.0-79.0	69	65.4	9.3	51.5-76.8	66	0.09
Duration of symptoms (years)	5.1	3.8	1.0-10.0	4.0	5.0	3.5	1.0-10.0	4.0	5.5	4.8	1.1-12.4	4.0	0.99
Irritative symptoms (2,4,7 of IPSS)	7.6	3.3	4.0-12.0	7.0	7.7	3.2	4-12	7.0	7.2	3.5	3-13	7.0	0.34
Obstructive symptoms (1,3,5,6 of IPSS)	10.5	5.0	4.3-18.7	10.0	11.2	4.7	5-19	11.0	8.3	5.1	2-16	7.0	0.002
IPSS	18.0	6.8	10.0-27.0	17.0	18.9	6.6	10-29	19.0	15.4	6.5	8-26	14.0	0.01
QoL	3.9	1.3	2-6	4.0	4.0	1.3	2-6	4.0	3.5	1.1	2-5	4	0.04
PSA (ng/ml)	3.6	3.1	0.9-7.6	2.6	3.9	3.2	0.9-7.9	2.9	2.8	2.5	0.8-6.9	1.9	0.05
Post void residual (ml)	76.5	88.0	2-213	45.0	87.1	93.0	6-234	50.0	45.6	63.2	0-122	30.0	0.002
Total prostate volume (ml)	53.8	32.1	24.9-84.9	45.5	58.8	34.2	28.0-89.8	50.0	39.2	18.3	17.2-70.0	33.0	0.001
Transition zone volume (ml)	28.6	24.8	6.5-50.7	23.6	32.6	26.5	9.4-56.3	26.8	16.8	13.4	3.5-36.8	12.0	0.0001
TZI	0.48	0.15	0.28-0.66	0.49	0.51	0.13	0.33-0.68	0.51	0.38	0.14	0.16-0.60	0.40	0.0001
Qmax free (ml/s)	10.1	4.5	5.2-16.8	9.2	8.8	3.7	5.0-13.3	8.2	13.6	5.0	7.5-19.4	13.4	0.0001
Qave free (ml/s)	5.2	2.5	2.7-8.8	4.5	4.4	1.9	2.3-6.3	4.0	7.3	2.9	3.8-11.3	7.6	0.0001
AG number	67.7	37.1	25.0-120.3	65.6	82.5	31.0	47.3-127.7	77.8	24.9	10.4	11.7-36.1	28.0	0.0001
pdetQmax (cm/H_2O)	85.5	33.3	47.3-135.2	80.0	97.8	29.4	61.2-142.8	94.0	49.4	9.8	34.2-62.6	51.0	0.0001

IPSS – International Prostate Symptom Score, QoL – Quality of Life score, TZI – transition zone index (transition zone volume/total prostate volume), Qmax free – free peak flow rate, Qave free – free average flow rate, AG number – obstruction number, if over 40 – obstruction (AG number = pdetQmax – 2 Qmax), pdetQmax – detrusor pressure at peak flow).
p - values were calculated to test significant differences between the groups (difference considered statistically significant if p <0.05), SD – standard deviation.

tions 1, 3, 5, and 7 of IPSS, TPV, TZV, TZI, peak (Qmax) and average (Qave) flow rates, as well as PVR. These variables correlated with the degree of obstruction evaluated by the AG number, but high correlation was observed only with Qave and Qmax (r respectively -0.501 and -0.496, p = 0.0001). AG number correlated with TZI (r = 0.29, p = 0.001), total prostate and transition zone volumes (r = 0.27 for both, p = 0.003) as well. Correlation with residual urine was considerably lower (r = 0.198, p = 0.03). No statistically significant correlation between age of patients and obstruction was observed.

Logistic regression model suggests that obstruction is best predicted when combination of Qave and TPV are used. Overall prognostic power of this combination for detecting correct results was 83% (with probability cut value of 0.6). PPV (positive predictive value) = 92%; NPV (negative predictive value) = 52%. Prognostic power for prediction of obstruction in the first group reached 91%. Unobstructed/equivocal subjects were predicted correctly in 61% of cases in the second group. Analysis of odds ratio (OR) for each variable shows that in case of Qave and TPV it was respectively 0.61 (95% CI 0.49-0.76) and 1.04 (95% CI 1.01-1.07). It means that increase of Qave by 1 ml/s decreases obstruction probability by 1.6 times and increase of total prostate volume by 1 ml increases it by 1.04.

The developed binary logistic model for prediction of obstruction is the following:

$$P = \frac{e^z}{1+e^z},$$

where

P – probability of obstruction;

z = 2.149 + 0.037 TPV – 0.501 Qave

It can be calculated that in case of total prostate volume 40 ml and Qave 5 ml/s probability of obstruction equals to 0.75 (75%).

Predictive power of Qmax in combination with TPV was slightly lower – small difference is seen only in the group of unobstructed/equivocal subjects (58% of correct predictions) with the almost same rate of correct results in total and in the group with obstruction. Compatibility of model with the data (Cox Snell and Nagelkerke coefficients of determination) was slightly lower in case of Qmax and TPV. Equation for prediction of obstruction with Qmax in combination with TPV is the following:

$$P = \frac{e^z}{1+e^z},$$

where

z = 1.952 + 0.039 TPV – 0.249 Qmax

Combinations of TZV or TZI with Qmax or Qave were not superior in prediction of obstruction compared to TPV.

The free flow pattern of a patient with TPV of 51 ml (Fig. 1) and computer based calculation of obstruction probabilities (Fig. 2) are presented. Changes in obstruction probability due to value of parameters are shown in Figs. 3 and 4. Fig. 3 visualizes obstruction probability as function of average flow rate and TPV. Figure 4 presents isolines of selected obstruction probability. Figure 4 also visualizes the area of obstruction probability being more than 0.9 isoline (upper left corner of the plot).

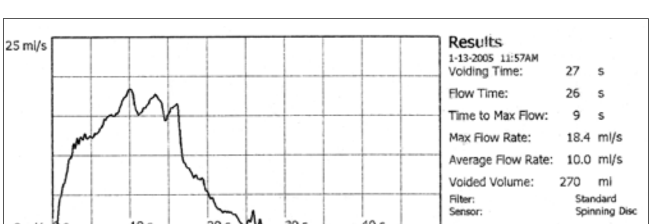

Fig. 1. Uroflowmetric trace of a 59-year-old patient with total prostate volume of 51 ml: peak flow rate 18.4 ml/s, average flow rate 10 ml/s.

Variables		
TPV (cc)	**51**	
Qave (ml/s)	**10**	
Qmax (ml/s)	**18.4**	
Intermediate calculations		
-0.97	**-0.64**	
Probability of obstruction according Qave		**0.27**
Probability of obstruction according Qmax		**0.35**

Fig. 2. Obstruction predicted for the same 59-year-old patient. Total prostate volume 51 ml, peak flow rate 18.4 ml/s, average flow rate 10 ml/s. Probability of obstruction 27-35%.

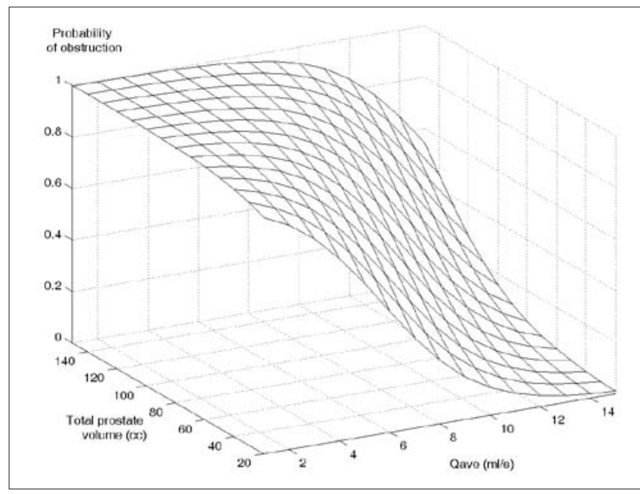

Fig. 3. Bladder outlet obstruction probability dependence on total prostate volume (TPV) and average flow rate (Qave).

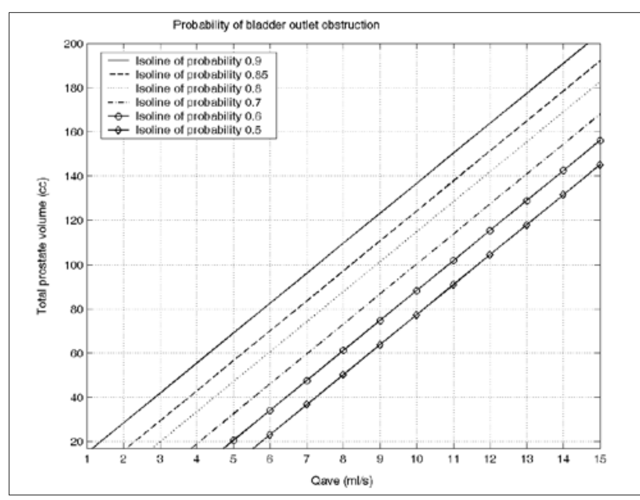

Fig. 4. Bladder outlet obstruction probability isolines due to total prostate volume (TPV) and average flow rate (Qave).

DISCUSSION

In face of numerous micro-invasive techniques for BPH treatment, transurethral resection is still the main and the best option. TURP is performed in approximately 95% of surgical procedures and open procedures are reserved only for very large prostates [15].

Table 2. Approximate probabilities of bladder outlet obstruction

Qave (ml/s)	Total prostate volume (ml)								
	20	30	40	50	60	70	80	90	100
2	0.87	0.91	0.93	0.95	0.97	0.98	0.98	0.99	0.99
3	0.8*	0.85	0.89	0.92	0.95	0.96	0.97	0.98	0.99
4	0.71*	0.78*	0.84	0.88	0.91	0.94	0.96	0.97	0.98
5	0.59*	0.68*	0.75*	0.82	0.87	0.9	0.93	0.95	0.97
6	0.47*	0.56*	0.65*	0.73*	0.8*	0.85	0.89	0.92	0.94
7	0.35	0.44*	0.53*	0.62*	0.7*	0.77*	0.83	0.88	0.91
8	0.25	0.32	0.41*	0.5*	0.59*	0.68*	0.75*	0.81	0.86
9	0.17	0.22	0.29	0.38	0.47*	0.56*	0.65*	0.73*	0.79*
10	0.11	0.15	0.2	0.27	0.35	0.43*	0.52*	0.62*	0.7*

*suggested indication for pressure/flow study; Qave – average flow rate

In the Department of Urology at Kaunas Medical University Hospital, 150-160 prostatectomies due to BPH are performed annually, TURP comprise 60-70%. Though TURP is an effective procedure with good or excellent results in 80-85% of cases [6, 16, 17], the possibility of an unfavorable outcome is still high. One of reasons for unfavorable results is unsatisfactory preoperative selection of patients. Prediction of obstruction in terms of postoperative effect would be of most important value.

According to literature, the most valuable parameter for prediction of obstruction is peak flow rate (Qmax). In case of Qmax <10 ml/s, likelihood of obstruction is 90%, in range of Qmax 10-14 ml/s – 67% and in Qmax >15 ml/s – only 30% [15]. Approximately 1/3 of patients with Qmax over 10 ml/s are unobstructed. Probability of obstruction in case of Qmax >10 ml/s for elderly man (>80 years) falls to 40% [15]. In some studies, on the basis of uroflow alone, 21% of the patients were misclassified [6]. Single or combined conventional tests can predict correctly just in 60-70% of cases [13]. According to our study, misclassifications in 21-25% is possible if only a single free flow parameter, Qmax or Qave, is used.

Traces of uroflow often have peaks and registered Qmax is not reliable. Such artifacts need to be corrected. Average flow rate is a quite steady parameter and should be important in case of continuous flow without terminal dribbling [3]. Our study shows, that Qave predicted obstruction even better than Qmax, but the difference compare to Qmax was not pronounced.

Combination of Qave and TPV had the best predictive power in our sample. Combinations of Qmax – TPV or Qmax – TZV were not superior.

As has been shown in many of studies PVR is not important predictor of obstruction. Our data also confirm that post-void residual volume is not of paramount importance in terms of obstruction. Though we found statistically significant difference for PVR between the groups, correlation of PVR with obstruction was weak. Predictive models usually use PVR as one of important parameters (Clinical Prostate score model developed by Rosier et al. as well as models developed by Van Venrooij et al. and Madersbacher S. et al.), but we did not find its importance for prediction [8]. A big volume of residual urine indicates bad detrusor contractility rather than obstruction [10]. From the other hand, bad contractility shows terminal phase of obstructive process.

Transition zone volume more than total prostate volume represents processes of benign hyperplasia. Therefore, measurement of transition zone volume is essential, especially in terms of treatment options [12]. Transition zone volume correlates well with resected volume of the prostate [12]. It was shown by studies of Kaplan that transition zone volume is directly associated with urodynamic obstruction of the bladder and this correlation is mostly reliable when transition zone index is over 0.5 [11]. Though it was shown that transition zone index is important on prediction of outcome after TURP [17], recent study did not confirm superiority of TZV or TZI for prediction of urodynamic obstruction compare to TPV.

There are less correct predictors in the group of unobstructed/equivocal subjects, which directly worsens total rate of correct predictions. Better prediction in this group would be very important because it would let us improve surgical results. Unfortunately there are no clear parameters for prediction of bad contractility/unobstructed. We guess that in case of calculated probability of obstruction 0.4-0.8, an invasive urodynamic pressure/flow study would be beneficial, especially if surgical treatment is considered (Table 2).

Though combination of Qmax and TPV was not superior, the predictive power of it was almost the same as Qave combined with TPV. Considering flow pattern either Qave or Qmax should be used. Probabilities should be calculated using both models and results compared. We suppose that similar results show reliable prognosis. In case of difference, uroflowmetry should be repeated and probabilities re-evaluated. Pronounced difference and/or probability around 0.5 would be indicative for invasive pressure flow study. In case of high probability of obstruction, urodynamic pressure flow study could be spared. Our study shows that Qave is as good as Qmax and can be used more often.

CONCLUSIONS

A binary logistic regression model was developed, which suggests that average flow rate and total prostate volume are the best predictors of obstruction (83% of correct predictions; PPV = 92%; NPV = 52%) in the analyzed sample. The analyzed model suggests that peak flow rate could also be an almost equally important parameter instead of average flow rate. The above parameters could be obtained from simple ultrasound and free flow measurements. The developed probabilistic model also provides information that is useful to select patients who need invasive urodynamic testing for decision on surgical treatment. It is suggested to perform invasive urodynamic testing in case obstruction probability is in the range of 0.4-0.8.

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