Abstract

The objective of our study was to evaluate bladder outlet obstruction number (BOON) in order to predict infravesical obstruction in patients with benign prostatic enlargement (BPE).

Two hundred patients with proven BPE from daily urological practice at the Urology Department of the Sarajevo University Clinical Centre were covered by a prospective study in period 2009-2011. All patients completed International Prostatic Symptom Score, their mean voided volume urine was determined from frequency-volume chart and their prostate volume was determined by transabdominal ultrasound. Subsequently, the patients had free uroflowmetry and they underwent complete urodynamic studies.

BOON was calculated using the formula: prostate volume (cc) - 3 x Qmax (ml/s) - 0.2 x mean voided volume (ml). A satisfactory area under the curve (AUC) was obtained for the prediction of obstruction according to bladder outlet obstruction index, Schaefer obstruction class nomogram and group specific urethral resistance factor, with AUC of 0.83 (p<0.001). Following the comparison of different cut-off values of BOON according to the obstruction, the BOON >-20 has been found to be the most accurate obstruction indicator (sensitivity 76.5% and specificity 68.2%), with posttest probability of 77%.

The BOON may be used in daily urological practice as a valid, non-invasive indicator of infravesical obstruction in patients with BPE, with a possibility of correct classification of obstruction in approximately 75% of the cases. Transabdominal ultrasound has shown to be applicable to the BOON formula in determining prostate volume. © 2012 Association of Basic Medical Sciences of FBiH. All rights reserved

Key words: benign prostatic enlargement, bladder outlet obstruction number, urodynamics

Introduction

The incidence of benign prostatic enlargement (BPE), as well as the presence of bothersome lower urinary tract symptoms (LUTS) increase with age, and these conditions are highly prevalent as early as beyond the fourth decade [1]. The evaluation of patients with LUTS requires full understanding of the physiology of voiding and of potential pathophysiologic changes [2]. Clinical and symptomatic variables are very useful for the initial evaluation of patients; however, it has been shown that they do not correlate with bladder outlet obstruction, or its degree [3]. The most accurate determination of infravesical obstruction caused by BPE is obtained by urodynamic studies; however, they are expensive, time-consuming, and often lead to patient discomfort or even to a certain degree of morbidity. The International Continence Society recommends pressure flow studies before invasive therapies, or when a precise diagnosis of bladder outlet obstruction is important [4]. This is why researchers have been seeking simple noninvasive methods or parameters that can accurately point to the bladder outlet obstruction. Recently, there has been much insistence on evaluating intravesical prostatic protrusion, measuring bladder wall thickness [5], or analyzing the accuracy of noninvasive urodynamics [6]. The bladder outlet obstruction number (BOON) is one of noninvasive modalities for the prediction of obstruction; it is obtained by using a simple mathematical formula; it is easily accessible in daily urological practice and, it has shown through its validation very good characteristics of a sensitive indicator of bladder outlet obstruction in patients with BPE [7]. However, this factor has not been analyzed enough and therefore it is not mentioned often in the literature. In addition, the BOON was originally determined according to a formula that involves transrectal ultrasound (TRUS) prostate measurement; something we regard as being impractical in daily routine. Therefore, the modality we commonly apply is transabdominal prostate mea-
Materials and Methods

Patients
In period 2009-2011, a prospective study was conducted at the Urodynamic Unit of Sarajevo University Clinical Center. Urology Department on 200 patients with the lower urinary tract symptoms suggestive of benign prostatic enlargement. Exclusion criteria were clear neurological or endocrine diseases, suspected bladder cancer or calculus, urethral stenosis, suspected prostate carcinoma, urinary infection, advanced kidney failure, previous operation of the prostate, as well as taking medication interfering with the act of voiding. Patients of an average age of 64.4 years (49-82) completed International Prostate Symptom Score (I-PSS), underwent digital rectal examination, and had their serum PSA and mean voided urine volume determined as an average amount of voided urine during 24 hours, depending on the number of voidings. Data were obtained from frequency-volume chart (voiding diary), filled out by the patients during three consecutive days.

Procedures
The patients had their prostate volume determined using transabdominal ultrasound; then free uroflowmetry was performed in a standing position (with the minimum voided volume of 150 ml), determining the maximum urinary flow rate (Qmax), and subsequently, their postvoid residual urine was determined. Having signed Informed Consent forms, the patients underwent complete urodynamic studies (UDS) using the apparatus Andromeda Ellipse 4. All patients received prophylactic Ciprofloxacin tbl. 500 mg. UDS started with cistometry. Bladder filling and measuring intravesical pressure during the filling were done by simultaneous introduction of Nelaton Ch5 catheter (Dallhausen & Co, GmbH, Köln, Germany- infusion line) and Nelaton Ch5 urethral catheter (Websinger GmbH, Wiena, Austria-transducer line) into the bladder-tandem or rail-road technique [8]. Abdominal pressure was determined by introducing standard rectal balocon catheter. Cistometry was done in a sitting position with the filling rate of 25ml/min. Prior to voiding, the patients had the Ch5 catheter removed. Then, the patients voided in a standing position, while the findings of pressure/flow studies were plotted on Schaefer obstruction class nomogram [9] and urethral resistance algorithm (URA) - group specific urethral resistance factor [10]. Each patient had their bladder outlet obstruction index (BOOI= Pdet.Qmax -2Qmax) determined [11], as well as obstruction coefficient (OCO) developed by Schaefer, which was used to quantitatively evaluate urethral resistance, following the formula: OCO = Pdet.Qmax/(40 + 2Qmax) [12]. The urodynamic studies, unless otherwise specified, were based on the International Continence Society methodology and terminology [13]. Then, for each patient the bladder outlet obstruction number (BOON) was calculated following the formula: prostate volume (in cubic centimeters) - 3 x maximal urinary free flow rate (in milliliters per second) - 0.2 x mean voided volume (in milliliters, as estimated from frequency-volume charts), or BOON=Vol prostate(cc)-3Qmax(ml/sec) - 0.2 x V void (ml) [7]. Statistical analysis was performed through rank correlation Kendall’s tau test (relationship of noninvasive parameters with urodynamic nomograms during the validation of the BOON), determination of area under the receiver operating characteristic (ROC) curve for predicting obstruction. The best fitting associations between the clinical parameters and bladder outlet obstruction were determined by stepwise logistic regression model.

Statistical analysis
Statistical analysis was made using Medcalc program for Windows version 12 and Evidence based calculator (free version). The level of significance (two-tailed) was set at p < 0.001.

Results
Due to rare reports in the literature about the utility of the BOON, and the fact that transabdominal ultrasound (rather than transrectal, as originally included in the formula) was performed, Kendall’s tau rank correlation test determined the correlation between prostate volume, Qmax and mean voided urine, as well as other clinical variables with the determinants of obstruction: URA, Schaefer nomogram and transabdominal ultrasound.

Table 1. Kendall’s tau correlation coefficient of noninvasive variables with determinants of obstruction

<table>
<thead>
<tr>
<th>Variable</th>
<th>BOOI</th>
<th>URA</th>
<th>LinPURR</th>
<th>OCO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Qmax (ml/sec)</td>
<td>-0.44*</td>
<td>-0.51*</td>
<td>-0.419</td>
<td>0.426</td>
</tr>
<tr>
<td>VP (cc)</td>
<td>0.264*</td>
<td>0.231*</td>
<td>0.294*</td>
<td>0.247*</td>
</tr>
<tr>
<td>mVV</td>
<td>-0.202*</td>
<td>-0.245*</td>
<td>-0.238</td>
<td>0.190</td>
</tr>
<tr>
<td>PVR</td>
<td>0.202*</td>
<td>0.185*</td>
<td>0.191*</td>
<td>0.194*</td>
</tr>
<tr>
<td>I-PSS</td>
<td>0.104</td>
<td>0.106</td>
<td>0.09</td>
<td>0.101</td>
</tr>
<tr>
<td>QoL</td>
<td>0.05</td>
<td>0.06</td>
<td>0.04</td>
<td>0.03</td>
</tr>
</tbody>
</table>

Qmax-maximum urinary flow, VP-prostate volume, mVV-mean voided volume, PVR-post void residual urine, I-PSS International prostate symptom score, QoL-Quality of life questionnaire, BOOI-bladder outlet obstruction index, URA-group specific urethral resistance factor, LinPURR-Schaefer obstruction class nomogram, OCO-obstruction coefficient*.p<0.001
bladder outlet obstruction index. Obstruction coefficient (OCO) was added to the analysis for the quantitative determination of urethral resistance through a continuous variable, while cut-off point for obstruction was taken at OCO≥1. Statistically significant correlations of variables included in the formula for bladder outlet obstruction number (p<0.001) were obtained. No statistically significant correlation was found between the International Prostate Symptom Score, Quality of life and the urodynamic parameters of bladder outlet obstruction (Table 1).

Having obtained significant correlations of variables and included them into the formula for the BOON (p<0.001), a BOON was calculated for each patient; Figure 1 shows the distribution of BOON values for the total of 200 patients (Arithmetic mean -113.4, SD 29.8). Subsequently, discriminant value for BOON was determined according to different definitions of obstruction, using the calculation of area under the receiver operating characteristic curve. Good values of the area under the curve were obtained, with a value above 0.80 for each obstruction determinant (p<0.001), and with high sensitivity, specificity and positive predictive value (Table 2). It has been proven that high values of BOON are very much obstruction-specific, while low values tend toward non-obstructive domain (Figure 2).

In order to prove greater benefit of BOON compared with other noninvasive parameters found in the literature, patients with a combination of International Prostate Symptom Score higher than 20 and Qmax <10ml/sec were isolated. Using this model, of the total of 200 patients, 36 (18%) of them were isolated. Of the 36 patients, 31 had the obstruction (86.6%). At the same time, using BOON>-20, 115 patients (57.5%) were found, of whom 88 had the obstruction (76.5%). Therefore, 76.5% of patients (of the total of 115 patients having the obstruction according to URA) could be correctly classified using BOON>-20, compared with 27% patients (31/115) using above applied test. A comparison of two proportions test has shown a significant difference (Chi-square =53.3, p<0.001). Further on, using the different model and taking the patients with prostate volume ≥ 40cc, Qmax ≤10 ml/sec, and International Prostate Symptom Score >20, only 22 (11%) patients of the total group were isolated. Of these 22 patients, 19 had the obstruction (86.4%), i.e. only 16.5% of the total number of obstructed patients. Thus, the difference between the BOON >-20 and this model is even more significant (Chi-square=79.5, p<0.001).

To determine the best fitting model in the relationship of variables, included in the bladder outlet obstruction number, as well as other clinical parameters used to identify infravesical obstruction, stepwise logistic regression analysis was performed. The dependent variable was the value of bladder outlet obstruction index >70 (urodynamic obstruction), while independent variables were: prostate volume, Qmax, mean voided volume, BOON, age, International Prostate Symptom Score and residual urine. It was shown that the most significant variable determining obstruction was BOON (p=0.0006, OR=1.04), followed by Qmax (p=0.009, OR=0.9), with log likelihood 73.6. (p<0.0001). Significance level for Hosmer & Lemeshow test is high (p=0.6, p<0.1), indicating a good logistic regression model fit. Area under the ROC curve for these variables is 0.824, (95% CI 0.764 to 0.874).

<table>
<thead>
<tr>
<th>Variable</th>
<th>AUC</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>+LR</th>
<th>-LR</th>
<th>PPV (%)</th>
<th>NPV (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BOOI</td>
<td>0.807*</td>
<td>71.28</td>
<td>74.53</td>
<td>2.8</td>
<td>0.39</td>
<td>71.3</td>
<td>74.5</td>
</tr>
<tr>
<td>URA</td>
<td>0.830*</td>
<td>67.83</td>
<td>81.18</td>
<td>3.6</td>
<td>0.4</td>
<td>83</td>
<td>65.1</td>
</tr>
<tr>
<td>LinPURR</td>
<td>0.807*</td>
<td>74.44</td>
<td>75.45</td>
<td>3.03</td>
<td>0.34</td>
<td>71.3</td>
<td>78.3</td>
</tr>
<tr>
<td>OCO</td>
<td>0.813*</td>
<td>73.91</td>
<td>75.93</td>
<td>3.07</td>
<td>0.34</td>
<td>72.3</td>
<td>77.4</td>
</tr>
</tbody>
</table>

BOOI-bladder outlet obstruction index, URA- group specific urethral resistance factor, LinPURR-Schafer obstruction class nomogram, OCO-obstruction coefficient, AUC- area under the curve, +PV-Positive Likelihood Ratio, -NPV-Negative Likelihood Ratio PPV- Positive Predictive Value, NPV- Negative Predictive Value *p<0.001
Finally, it was attempted to determine cut-off value for the BOON that would be the most sensitive and obstruction-specific. The values of BOON >-20; >-30; >-40, were taken as predictors of urodynamic obstruction. For the BOON >-20, 76.5% of the patients would be correctly classified; however 31.7% (27/85) would remain in a seemingly non-obstructive zone. For the BOON >-30, 71.2% (94/132) of the patients would be correctly classified, while 30.8% (21/68) of them would remain incorrectly classified; and for the BOON >-40, 67.7% (105/155) of the patients would be correctly classified, while 22.2% (10/45) of them would remain in the non-obstructive zone. Therefore, obstruction prevalence increases with higher values of the BOON, thus improving specificity and decreasing sensitivity (Table 3). With this method, the number of patients needed to diagnose (NND) the obstruction was calculated, and for the BOON >-20, it is 2.3. Area under the curve were calculated for different cut-off values for the BOON, where the area under the ROC curve for the BOON >-20 is 0.724 (95% CI 0.656 to 0.785), while for the BOON >-30 and >-40 it is 0.679 (95% CI 0.610 to 0.743) and 0.662 (95% CI 0.592 to 0.728), respectively (Figure 3). Difference between areas for BOON >-20 and >-30 were 0.0445; (p=0.04), and difference between areas for BOON >-20 and BOON >-40 were 0.0614; (p=0.037). The areas under the ROC curve for the BOON >-40 and BOON >-30 show that tests do not have sufficient accuracy (sensitivity and specificity). Only the BOON >-20 test has a moderate accuracy.

**DISCUSSION**

The aim of this study was to evaluate the bladder outlet obstruction number (BOON), as a noninvasive factor to predict infravesical obstruction in patients with lower urinary tract symptoms due to benign prostatic enlargement (BPE). Although the most accurate classification of the bladder outlet obstruction in BPE patients is based on invasive urodynamics, they are expensive, time-consuming and may cause a certain degree of morbidity. In addition, a number of urologists do not endorse the use of invasive urodynamics studies in daily clinical practice; thus, there is a need for noninvasive assessment of bladder outlet obstruction, which might assist in the optimum choice of therapy [2]. The BOON seems to be very useful in daily urological practice since it is derived from the formula obtained by a simple mathematical combination of noninvasive clinical and urodynamic variables, i.e. prostate volume, mean voided urine volume and free uroflowmetry (Qmax), as part of noninvasive urodynamics studies. Mean voided volume is easily
calculated as a mean value of voided urine volume during 24 hours. These data are obtained from frequency volume chart (simple voiding diary), which patients fill out over two or three consecutive days, and it represents a standard part of the assessment of patients with BPE. Originally, prostate volume, included in the formula, was calculated by measuring prostate transrectal ultrasound (TRUS), and according to authors, TRUS measurement is accurate, and causes patient discomfort equivalent to digital rectal examination of the prostate [7]. However, we are of the opinion that the TRUS measuring of the prostate is still an invasive component of examination (when digital rectal examination is also taken into account), the examination is prolonged, while TRUS probe is not available in every outpatients’ department. Also, it was shown that transabdominal ultrasound is equivalent to rectal ultrasound when the prostate is measured at bladder volume higher than 100 ml [15]. According to some studies, it was proven that transabdominal ultrasound is now a common clinical method, being noninvasive and easy to learn and evaluate. Using the same probe, the upper urinary tracts can be easily assessed at the same time, even the prostate fractions (such as intravesical protrusion of the prostate) can be accurately measured by this method; therefore, the diagnosis of BPE in the clinical setting can be aided by simple, noninvasive, transabdominal ultrasound [16, 17]. However, due to a different measuring technique and possible error, we had to first evaluate the correlation of transabdominal ultrasound measured prostate and other noninvasive parameters (Qmax, prostate volume, mean voided urine, International Prostate Symptom Score, residual urine) with urodynamic nomograms that characterize obstruction (Schaefer nomogram, urethral resistance algorithm and bladder outlet obstruction index). We also included in the validation the obstruction coefficient (OCO, with cut-off value ≥1), derived from pressure/flow studies, similar to Schaefer nomogram, but quantifying urethral resistance by a continuous variable (rather than by a grading system as in Shaefer nomogram). The rank correlations of observed parameters that were obtained did not differ from the correlations in the original BOON design [7]. Subsequently, the BOON for each patient was calculated, and good areas under the ROC curve were obtained (area under the curve ≥0.81), which did not significantly differ among different urodynamic determinants of obstruction. The values of the bladder outlet obstruction index corresponded to obstruction classes of the International Continence Society (ICS) nomogram, where men are obstructed when the index is higher than 40 [18]. Research done by van Venrooij et al. obtained similar values for ICS and Schaefer nomogram (area under the curve is 0.83 and 0.82, respectively), while are under the curve for urethral resistance factor is somewhat higher (0.87), but not clinically significant. Because all methods are based on the passive urethral resistance relation, all methods give the same results in classifying clearly obstructed and clearly unobstructed pressure-flow relations [7]. In the present study, it was shown that the prostate volume determined by transabdominal ultrasound did not decrease discriminant power of the BOON according to urodynamic classifications of obstruction, while good sensitivity and specificity to the bladder outlet obstruction was shown. The BOON showed to be a very applicable and simple formula able to correctly classify a large number of patients. Therefore, it is not clear enough why this predictor is not being adequately researched. By our best means of searching the literature (MedLine), we could identify only one more study that evaluated this number for the prediction of intravesical obstruction with a comparatively small number of patients, where the prostate measurement was determined by transrectal ultrasound [19]. Stepwise logistic regression analysis in the prediction of obstruction showed that the most significant independent variable is the BOON (p<0.001, OR=1.04) followed by Qmax (p=0.01, OR=0.9). This model excluded individual variables included in the formula for the BOON (prostate volume and mean voided urine), as well as other variables observed (International Prostate Symptom Score, postvoid residual and age). Qmax implies part of noninvasive urodynamic measurement, and cut-off value lower than 10 ml/sec shows a strong discriminant power to the bladder outlet obstruction diagnostics. Previous studies analyzed various combinations of noninvasive clinical and radiological parameters that would provide as accurate diagnosis of intravesical obstruction as possible, but either more parameters were used [20–22], or a complex mathematical operation was required in order to obtain the formula [23]. Also, by using the combinations of parameters with the set cut-off values, it was possible to correctly identify only a small fraction of patients. This has been proven in the present study as well, since by examining some formerly proposed models we proved that using a combination of International Prostate Symptom Score higher than 20 and Qmax <10ml/sec in the prediction of obstruction [24], only a small subset of patients (18% of patients from the entire group) could be isolated, while using the combination of prostate volume ≥ 40cc, Qmax ≤10 ml/sec, and International Prostate Symptom Score ≥20 [25], we isolated only 11% of the total of 200 patients. Unlike the BOON, which as a continuous variable is calculated for each patient and correctly classifies a greater number of patients. Van Venrooij et al. [7] were able to correctly classify as per obstruction only 10% of patients according to the cut off values proposed by Schacterle et al. [24], or only 6.3% out of the total of 160 patients with cut-off values proposed by Steele et al. [25]. Having analyzed different values of the BOON for the pre-
diction of obstruction, it has been shown that cut-off value BOON≥20 is the best discriminator, with sensitivity of 76.52%, specificity of 68.24%, positive predictive value of 76.52%, and post test probability of 77%. It is clear that moving the cutoff point to a higher BOON value will select fewer men but the prevalence of obstruction will be greater, and thus, the specificity will improve but the sensitivity will decrease. The same arguments apply to the improvement of specificity to select unobstructed men by moving the cut off point to a lower BOON value [7]. Critical point of the BOON ≥40 and BOON >30 have high specificity, on the account of lower specificity, but specificity is very important since it reduces the need for classical invasive urodynamic studies; therefore, the use of the BOON >20 could correctly classify (obstruction/non-obstruction) approximately three fourths of patients (73%). However, the calculated area under the curve for the BOON >20 has only moderate accuracy. Zhang et al. hold that the BOON >30 as critical point is the best indicator of obstruction, because the calculated sensitivity and specificity for this value were 66.1% and 82.4%, respectively [19]. The present study is first one of few studies in the literature that has evaluated a useful and simple formula (BOON) for the prediction of bladder outlet obstruction in patients with benign prostatic enlargement, using the values of prostate volume obtained by simple transabdominal ultrasound. It has shown that this method of measurement does not alter the discriminant power of the BOON according to the obstruction, as proven by urodynamic measurements.

CONCLUSION

The bladder outlet obstruction number (BOON) is calculated by using a simple formula derived from a combination of simple radiological, clinical, and noninvasive urodynamic variables. The BOON can be used in daily urological practice as a valid, noninvasive indicator of bladder outlet obstruction in patients with benign prostatic enlargement, with a possibility of detection and correct classification of obstruction in approximately 75% of cases. Transabdominal ultrasound for the determination of prostate volume has shown to be applicable for the BOON formula. However, urodynamic studies remain to be essential for a precise diagnosis of obstruction. Further research is necessary in order to examine the BOON parameters to improve its utility, probably combined with other noninvasive variables (e.g. intravesical prostatic protrusion, bladder wall thickness) that determine the obstruction.

DECLARATION OF INTEREST

The authors declare no conflict of interest.

REFERENCES


