

# DOES THE COMBINATION OF INTRAVESICAL PROSTATIC PROTRUSION AND BLADDER OUTLET OBSTRUCTION NUMBER INCREASE TEST ACCURACY ACCORDING TO BENIGN PROSTATIC OBSTRUCTION AT THE INDIVIDUAL LEVEL?

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## Original paper

### ABSTRACT

**Objective:** Determine diagnostic power and intercorrelation between bladder outlet obstruction number (BOON) and intravesical prostatic protrusion (IPP) as non-invasive predictors of intravesical obstruction in patients with lower urinary tract symptoms due to benign prostatic enlargement. **Material and methods:** Prospective study during 2009-2010 analyzed data of 110 patients with proven benign prostatic enlargement. Prostate volume and IPP were determined by transabdominal ultrasound, and patients underwent complete urodynamic studies (UDS). BOON was calculated using the formula: prostate volume [cc]-3 x Qmax [ml/s]-0.2 x

mean voided volume [ml]. **Results:** There is a statistically significant correlation between the values of IPP and BOON (Spearman's rank correlation coefficient  $\rho=0.48$ ,  $p=0.0001$ ). BOON is a more sensitive (sensitivity 82.4%, specificity 66.1%), while IPP is a more specific factor (sensitivity 58.8%, specificity 81.4%) in the group-wise prediction of bladder outlet obstruction (BOO). Positive predictive value in the diagnosis of obstruction increases at the individual level combining the cut-off values for BOON > -30, with IPP > 10 mm [PPV 86.8%]. Owing to a good correlation of IPP with different definitions of urodynamic obstruction, IPP was included in the BOON formula instead of prostate volume. This number was arbitrarily called BOON2. The combination of IPP > 10 mm

and cut-off value for BOON2 > -50 showed that 88.6% of the patients were accurately classified in the zone of obstruction (mean IPP 14.9 mm), while BOON2 < -50 carried a high NPV. **Conclusion:** The combination of cut-off values for BOON and IPP increases test accuracy according to BOO at the individual level, thus facilitating clinical decision making regarding diagnostics and optimal choice of therapy in patients with BPE. Owing to its good correlation with obstruction determinants, IPP can be included in the formula for BOON instead of prostate volume.

**Key words:** Intravesical prostatic protrusion, bladder outlet obstruction number, benign prostatic enlargement, UDS

## 1. INTRODUCTION

It is well known that benign prostatic enlargement (BPE) is the most common cause of bladder outlet obstruction (BOO) in men in their 50s or older (1). Morpho-functional changes of the lower urinary tract are caused by increased prostate volume, and increased activity of alpha adrenergic receptors in the prostate stroma, prostatic capsule and bladder neck. The prostate enlargement is also manifested by the development of intravesical prostatic protrusion (IPP), as a morphological change by which the prostate protrudes into the bladder (2). It has

become known that the prostatic configuration together with the expressed IPP can influence normal urination. The IPP seems to support intravesical obstruction through the "valve ball" mechanism, in which prostatic lateral and median lobes interfere with the complete opening of the vesical neck during urination, disrupting the funnelling effect of the bladder neck and causing dyskinetic movement of the bladder during voiding (3). Further on, IPP provides information on not only the presence of urodynamic obstruction but also on its severity. Suprapubic ultrasound is a simple, non-in-

vasive and rather accurate method of assessing bladder outlet obstruction in patients with BPE, caused by prostatic protrusion. Franco et al. find good correlations between intravesical prostatic protrusion and the bladder outlet obstruction index (Spearman's  $\rho=0.49$ ,  $p=0.001$ ), and Schaefer obstruction class (Spearman's  $\rho=0.51$ ,  $p=0.001$ ) (4). Chia et al., exploring the benefit of measuring the intravesical prostatic protrusion in 200 patients, showed that the higher grade of IPP is a statistically significant predictor of bladder outlet obstruction (5).

On the other hand, the bladder

outlet obstruction number (BOON) is obtained by a simple mathematical combination of three non-invasive factors (prostate volume, uroflowmetry, and mean voided urine obtained from frequency volume chart, which is a usual part of the assessment of patients with BPE). This number is validated according to different urodynamic determinants of obstruction and it shows good group-wise sensitivity and specificity in the classification of the obstruction (6). If the number moves toward higher values, the prevalence of obstruction increases (while the number of patients decreases). According to the original study, if the chance of 80% of patients having or not having the obstruction is acceptable, then BOON should be higher than -10, or lower than -70; however, there remains a large fraction of patients (64%) that should undergo additional invasive urodynamic tests. Nevertheless, literature data on the utility of this number are very scarce; therefore, this factor needs to be further examined and compared with other reliable factors indicating the benign prostatic obstruction, in order to improve the accuracy of predicting the bladder outlet obstruction at the individual level.

Due to the above, a prospective study was conducted on the inter-correlation and utility of the combination of these non-invasive factors in patients with the lower urinary tract symptoms due to BPE, with the final aim to facilitate clinical decision making regarding the choice of additional diagnostic modalities or optimal therapy.

## 2. MATERIAL AND METHODS

During the period 2009-2010, the prospective study was carried out on 110 patients with lower urinary tract symptoms (LUTS) and confirmed benign prostatic enlargement (BPE) from Urodynamic Unit at the Urology Clinic of the Sarajevo University Hospital. The exclusive criteria were neurological abnormalities, suspicious digital rectal examination, elevated serum PSA, bladder calculosis, urethral stenosis, urinary tract infection, previous operation of the prostate, as well as the us-

Main characteristics of 110 patients	Arithmetic mean (SD); Median	Range
Age (years)	65.3 (7.4); 66.5	48-80
PSA (ng/ml)	1.8 (1.3); 0.9	0.3-4.9
PV(cc)	47.3 (19); 42	24-120
I-PSS	18.2 (5.8); 19	6-31
Q <sub>max</sub> free (ml/sec)	10.3 (3.9); 9	4-22
PVR (ml)	49.9 (52.5); 30	0-250
BOON	-17.9 (28.3); -18.5	-70.8-74.4
IPP (mm)	11.7 (6.6); 11.1	1-34
Mean Vv	167.3(42.8); 167	93-254

**Table 1.** Basic clinical and demographic characteristic of the BPE group. PSA-Prostate specific antigen, PV-prostate volume, I-PSS International prostatic symptom score, Q<sub>max</sub> free-maximum urinary flow, PVR-post void residual urine, BOON- bladder outlet obstruction number, IPP –intravesical protrusion of prostate, MeanVv-mean voided volume

age of medications which may affect voiding patterns. The transabdominal ultrasound (TAUS) determined patients prostate volume, as well as intravesical protrusion of the prostate (IPP) at the bladder volume of 150-200 ml. The IPP was defined by the distance from the tip of the prostate's protrusion into the vesical lumen to the bladder neck measured in millimetres, thus determining the three stages of IPP: <5mm grade I, 5-10 mm grade II, and >10 mm grade III. The patients completed International Prostatic Symptom Score (I-PSS) and signed the Informed Consent Form. Then, the patients underwent conventional urodynamic studies (UDS) using the Andromeda Ellipse 4 apparatus. Urodynamic studies were done according to the "good urodynamic practices" by the International Continence Society (ICS) (7). Then, the findings of pressure/flow studies (PFS) were plotted on the Schaefer obstruction class (8), ICS nomograms (9) and URA-group specific urethral resistance factor (10). Each patient had their bladder outlet obstruction index (BOOI= $P_{de-t} \cdot Q_{max} - 2Q_{max}$ ) determined (11) as well as bladder outlet obstruction number (BOON) following the formula: prostate volume (in cubic centimeters)-3 x maximal urinary free flow rate (in milliliters per second)-0.2x mean voided volume (in milliliters) (6). Mean voided urine volume was calculated for each patient as an average amount of voided urine during 24 hours, depending on the number of voidings from frequency-volume chart.

Statistical analysis was performed through rank correlation Kend-

all's tau test (relationship of IPP and prostate volume with different urodynamic nomograms), D'Agostino-Pearson test for normal distribution, calculation of area under the receiver operating characteristic (ROC) curve for predicting obstruction, while AUCs were compared via the method of DeLong (12). The best fitting associations between the clinical parameters and urodynamic obstruction were determined by step-wise logistic regression model. Statistic analysis was made using Medcalc program for Windows version 12 and Evidence based calculator (NNT calculator)-free version. The level of significance (two-tailed) was set at  $p < 0.001$ .

## 3. RESULTS

The study prospectively analyzed data on 110 patients with lower urinary tract symptoms and confirmed BPE. The average patient age was 65.3 years (49-80). The mean prostate volume was 47.3 cc (29-120), while the mean IPP value was 11.7 mm (1-34), median value of the bladder outlet obstruction number (BOON) was -17.9 (-70.8-74.4). Other clinical data are shown in Table 1.

A clinically good, statistically significant correlation was shown between the values of intravesical prostatic protrusion and bladder outlet obstruction number (Spearman's coefficient of rank correlation  $\rho = 0.481$ ,  $p < 0.0001$ ).

Kruskall-Wallis test showed a statistically significant difference between IPP grades and BOON values. Therefore, the mean value of BOON for IPP grade I (<5 mm) is -36.3, while for grade II (5-10 mm)

No pat. 110	BOON	IPP	BOON>-30 IPP>10mm
AUC	0.769*	0.708* (0.615-0.791)	0.752*
CI (95%)	(0.679 to 0.843)		(0.661-0.829)
Sensitivity (%)	82.69	59.62	61.33
CI (95%)	(69.7-91.8)	(45.1-73.0)	(49.4-72.4)
Specificity (%)	66.10	81.36 (69.1-90.3)	80.56
CI (95%)	(52.6-77.9)		(64.0-91.8)
+LR	2.38 (1.9-3.0)	3.20 (2.5-4.1)	3.15 (2.5-4.0)
-LR	0.29 (0.2-0.6)	0.50 (0.3-0.9)	0.48 (0.2-1.0)
PPV	67.7	73.8	86.8
CI (95%)	(54.7-79.1)	(57.7-86.3)	(74.5-94.6)
NPV (%)	79.6 (65.7-89.8)	69.6 (57.3-80.1)	50.0
CI (95%)			(36.6-63.4)
Number Needed to Diagnose (NND)**	2	2.4	2.4

**Table 2.** Sensitivity and specificity for different models in the prediction of obstruction. +PV-Positive Likelihood Ratio, -NPV- Negative Likelihood Ratio PPV- Positive Predictive Value, NPV-Negative Predictive Value, CI-Confidence interval, BOON- bladder outlet obstruction number, IPP -intravesical protrusion of prostate, \*p<0.001, \*\* Number Needed to Diagnose (NND) = 1 / (Sensitivity-[1-Specificity]) = 1 / (Youden's J)

and grade III (>10 mm) it is -27.7 and -6.8, respectively (p<0.001) (Figure 1). The increase of intravesical prostatic protrusion leads to the increase of BOON, i.e. increased prevalence of urodynamically confirmed obstruction.

In order to determine the discriminant value of intravesical prostatic protrusion and BOON toward obstruction, the values of receiver operating characteristic (ROC) curves were calculated, taking the value of bladder outlet obstruction index (BOOI)>40 as urodynamic obstruction, corresponding to clearly obstructed zone on the provisional ICS nomogram (9). Area under the curve (AUC) for IPP is 0.708 (95% CI 0.615 to 0.791); p<0.0001, with cut-off point of IPP> 12 mm (sensitivity 58.8%, specificity 81.4%) (Figure 2). AUC for BOON is 0.769 (95% CI 0.679 to 0.843); p<0.0001, with cut-off value with the best separation (minimal false negative and false positive results) of BOON>-27.2 (sensitivity 82.4%, specificity 66.1%) (Figure 3). Pairwise comparison of those ROC curves did not show a statistically significant difference, because the difference between the areas was 0.06 (SE 0.06, 95% CI -0.0515 to 0.169); p=0.29 (Figure 4).

After determining the cut-off value for BOON > -27.2, as the best discriminator in the classification of the obstruction, the number of patients was determined with IPP higher than 10 mm, according to

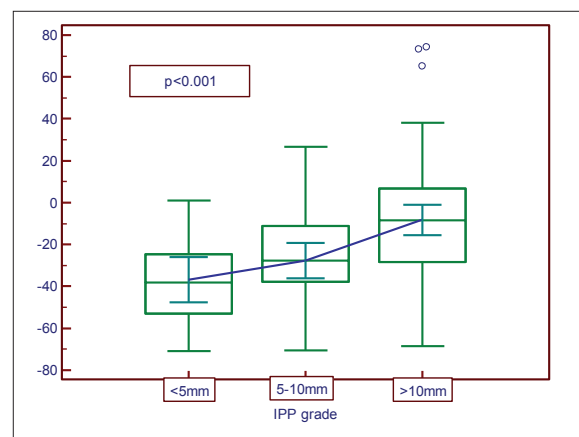
the critical point as BOON>-30. In the region of BOON <30, 29 (64.4%) patients had IPP<10 mm, while 16 (35.6%) of them had IPP higher than 10 mm. In the region of BOON>-30, 21 (32.3%) patients had IPP<10 mm, while 44 (67.7%) had IPP higher than 10 mm (Chi<sup>2</sup>=9.2, p=0.0024; Odds Ratio 3.8, and post test probability is 68%).

Table 2. shows sensitivity, specificity, positive and negative predictive values, and the number of patients needed to diagnose intravesical obstruction, depending on which model is used to predict the obstruction. It can be noticed that BOON shows higher sensitivity, while IPP shows higher specificity in the classification of the obstruction. Considering the patients with IPP higher than 10 mm, with BOON >30, the AUC of 0.752 (p=0001) is calculated, and this combination slightly increases sensitivity and significantly increases positive predictive value toward the obstruction compared with IPP alone.

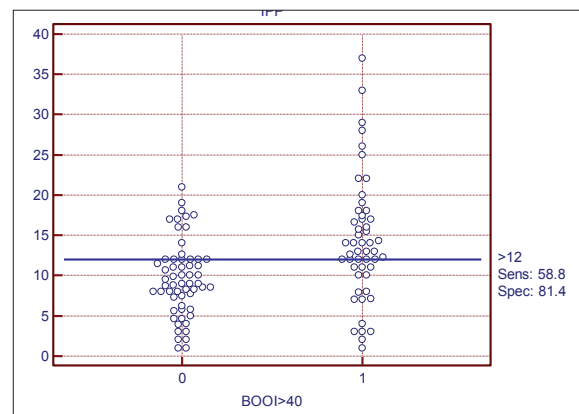
In order to deter-

mine the most independent variables indicating the obstruction (as a dependent variable), a stepwise logistic regression analysis was made. The parameters included in the mathematical formula for BOON ( $Q_{max}$ , mean voided volume, prostate volume), were taken as independent variables, as well as BOON, IPP, postvoid residual urine and age. Analysis showed that the most significant variables are the IPP (p=0.009, OR 1.12) and  $Q_{max}$  free (p<0.0001, OR -0.47) with log likelihood of 49.4, (p<0.0001). Other variables were excluded from the model. The significance level for the Hosmer & Lemeshow test is high (p=0.87; >0.1), indicating a good logistic regression model fit. The area under the ROC curve for IPP and  $Q_{max}$  was 0.862 (95% CI 0.783 to 0.920).

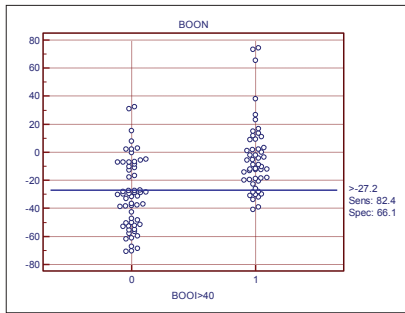
As the bladder outlet obstruction number was obtained by a mathematical combination of non-invasive clinical parameters (e.g. Prostate volume,  $Q_{max}$ , mean voided urine), the correlation between the prostate volume and IPP was deter-



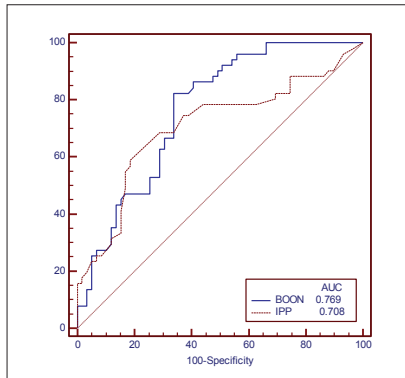
**Figure 1.** BOON value according to the IPP grades



**Figure 2.** ROC curve's dot diagram indicating the cut-off point with the best separation of IPP >12 mm in the prediction of obstruction



**Figure 3.** ROC curve's dot diagram indicating the cut-off point with the best separation of BOON >-27.2 in the prediction of obstruction

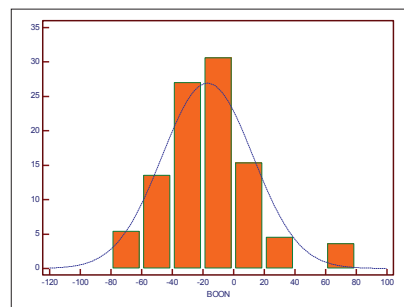


**Figure 4.** Pairwise comparison of ROC curves for the BOON and IPP

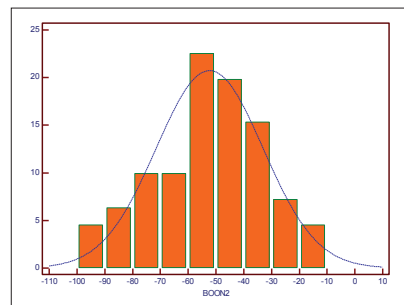
mined, and the Spearman's coefficient of rank correlation is  $\rho=0.53$  ( $p=0.0001$ ). Thus, similar correlations between the prostate volume and IPP were obtained with different obstruction determinants (Table 3). A somewhat bigger difference was observed in correlations according to Urethral resistance algorithm (URA), IPP  $\rho=0.247$  versus prostate volume  $\rho=0.289$ , but the comparison of correlation coefficients test showed that such a difference is not statistically significant ( $z$  statistics=-0.33,  $p=0.74$ ). Due to good interrelation of the prostate volume and intravesical prostatic protrusion, it was decided to replace the value of prostate volume with IPP in the formula for BOON, and arbitrarily call this number BOON2. Figure 5. shows the distribution for BOON, while Figure 6. shows the distribution for BOON2 (Arithmetic mean-52.28, SD 19.23, range -97.2 to -13.8). Two important characteristics were observed for BOON 2. First, due to a small difference in IPP values, BOON2 has distribution below zero for entire sample, while BOON widely ranges (due to considerable differences in prostate volume) from -70.8 to 74.4 (Table 1). The second

characteristic is that BOON2 shows normal distribution (D'Agostino-Pearson test  $p=0.23$ ), compared with BOON, which does not have normal distribution ( $p=0.002$ ).

ROC curve was calculated for the prediction of the obstruction for BOON2, using URA nomogram. Urodynamic obstruction is represented by the values of URA >29 cmH<sub>2</sub>O. AUC for BOON2 is 0.851 (95% CI 0.771 to 0.912; sensitivity 68.9%, specificity 89.8, +LR 6.8, -LR 0.3, PPV 87.5% and NPV 69.4%;  $p=0.001$ ) with the critical point >-47.4 (Figure 7). The number of patients needed to diagnose obstruction is 1.7. AUC



**Figure 5.** BOON distribution



**Figure 6.** BOON2 distribution

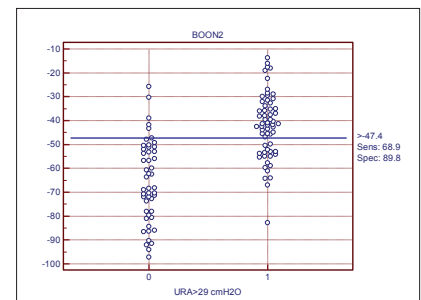
for BOON, and according to URA it is 0.816 (95% CI 0.731 to 0.884, sensitivity 78.7%, specificity 71.4%,  $p=0.001$ ). Pairwise comparison of AUCs of ROC curves for BOON and BOON2 did not show a statistically significant difference, because difference between areas was 0.0348 (SE 0.0280, 95% CI -0.0201 to 0.0897);  $p=0.21$  (Figure 8).

When the cut-off value >-50 was taken for BOON2, 71% of the patients (44/62) were accurately classified in the obstructed region, while 83.3% of the patients (40/48) were accurately classified as urodynamically unobstructed in the region BOON2 <-50. The patients with BOON2 <-50 had the mean value of IPP 9.6mm (SD 5.9), while those with BOON2

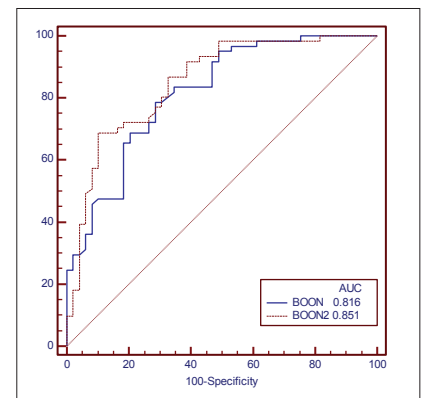
Variable	BOOI	URA	LinPURR	ICS
IPP [mm]	0.299*	0.247*	0.291*	0.258*
PV [cc]	0.311*	0.289*	0.310*	0.272*

**Table 3.** Kendall's tau correlation coefficient of prostate volume and IPP with different determinants of obstruction. PV-prostate volume, IPP- intravesical prostatic protrusion, BOOI- bladder outlet obstruction index (>40), URA- group specific urethral resistance factor (>29 cmH<sub>2</sub>O), LinPURR-Schaefer obstruction class nomogram, ICS-International Continence Society nomogram \* $p<0.001$

>50 had the mean value of IPP of 14.9 mm (SD6.6);  $T$  test=3.9,  $p=0.0002$ . In the classification of the obstruction BOON2 has the sensitivity of 84.6%, specificity 69%, +LR 2.7, -LR 0.2, and PPV of 71% and NPV of 83.3%, with NND of 1.9 and post test probability of 76%. However, of 44 obstructed patients only 5 (11.4%) patients did not have IPP higher than 10 mm, which indicates an accurate classification of obstructed patients of 88.6%. Analyzing the combination of cut-off value BOON >-30 and IPP >10 mm, it was shown that only three patients (7.1%) were not urodynamically obstructed, therefore almost 93% of the patients were accurately classified. In the zone out of obstruction, there are more significant oscillations in IPP values; therefore, the main determinant for un-



**Figure 7.** ROC curve's dot diagram indicating the cut-off point with the best separation of BOON2 >-47.4 in the prediction of obstruction



**Figure 8.** Pairwise comparison of ROC curves for the BOON and BOON2

obstructed condition is only the cut-off value  $<50$  BOON2 (83.3% of accurately classified unobstructed patients), while for BOON  $< -30$ , negative predictive value is far lower.

#### 4. DISCUSSION

The aim of this prospective study was to determine the discriminant power of non-invasive variables with regard to infravesical obstruction confirmed via pressure/flow studies, in patients with BPE, and to try to improve their sensitivity and specificity by a possible combination of the two. The IPP has recently become a very significant component in predicting the bladder outlet obstruction, as well as its progression and the need for surgical treatment (13, 14, 15). On the other hand, BOON, as a simple mathematical formula obtained by a combination of clinical, radiological and non-invasive urodynamic variables (uroflowmetry), is very seldom mentioned in the literature (16). Therefore, we consider this factor to be neglected in daily practice, though this number may fast and simply indicate to a urologist the condition of lower urinary tract (presence of infravesical obstruction) in patients with lower urinary tract symptoms, due to the presence of benign prostate enlargement. In an earlier study, covering a larger clinical sample (200 patients), we proved that the prostate volume, calculated using ellipsoid formula, may be included in the formula for BOON, using non-invasive transabdominal instead of transrectal ultrasound (17). A very good discriminant power of this number was shown, with a possibility of accurate classification of patients with regard to the obstruction in 73% of the cases, thus enabling a large fraction of patients to avoid invasive urodynamic tests. Also, we proved in the earlier study that intravesical prostatic protrusion is also a significant factor in predicting bladder outlet obstruction, and that with the increase of IPP grade, the prevalence of obstruction increases as well, and that grade III IPP shows good correlation with urodynamic factors that determine obstruction (18). At the same time, higher sensitivity and specific-

ity of this factor were proved compared with bladder wall thickness (BWT), although BWT according to other studies shows a very high accuracy in predicting infravesical obstruction (4, 19). However, accurate determination of bladder or detrusor wall thickness requires adequate maximum bladder volume, adequate place of the transducer for bladder wall measurement and optimized ultrasound transducer frequency (20).

The present study showed very good correlation between intravesical prostatic protrusion and bladder outlet obstruction number (Spearman's rank correlation coefficient  $\rho = 0.481$ ,  $p < 0.0001$ ), and that with the increase in IPP the BOON value suggestive of obstruction also increases (ANOVA test,  $p < 0.0001$ ). It was shown that BOON has higher sensitivity (82.7% vs 59.6%), but IPP has higher specificity toward the obstruction (81.4% vs 61.1%), when BOOI  $> 40$  was taken for urodynamically confirmed obstruction. When critical points were defined for each determinant, the patients were classified according to BOON  $> 30$  with IPP  $> 10$  mm (critical point  $> 12$  mm), and a slight increase of sensitivity was achieved (61.6%), but a significant increase was achieved of positive predictive value (PPV) of this combined test of 86.8% compared with PPV of 67.7% and 73.8% for BOON and IPP alone, respectively (Table 2). Why is it important to compare and combine the characteristics of these two parameters? In the editorial comment the study by Reis et al. on the utility of IPP in the prediction of bladder outlet obstruction, it was stressed that prospective and multi-centric studies are required with larger samples, as well as the comparison of IPP with other non-invasive tests in order to evaluate this recently adopted technique (3). Also, in all proposed methods involving the determination of threshold for an isolated parameter, groups of patients with high prevalence of obstruction are selected, but nevertheless, such prevalence of obstruction represents average probability to have obstruction, while the probability for an individual patient

may be higher or lower (6). It was shown that BOON is a more sensitive, while IPP is a more specific test. Tests with high sensitivity and low specificity can efficiently detect obstructed men but tend to falsely diagnose unobstructed men as obstructed (high false-positive ratio). Tests with low sensitivity and high specificity are more likely to miss obstructed men (high false-negative ratio), but can prudently exclude unobstructed men (21). By introducing a combination of BOON or BOON2 with IPP, we tried to increase the diagnostic accuracy according to obstructed/non-obstructed zone on an individual level, since observed as a group, patients with BOON  $> 30$ , and IPP higher than 10 mm, have a chance of being accurately classified in obstructed/non-obstructed zone in approximately 70% of cases, with increased accuracy if IPP increased above 12 mm.

Further on, in the present study the stepwise logistic regression analysis showed that IPP and  $Q_{\max}$  are the most independent variables in the prediction of urodynamic obstruction, and that BOON was excluded from this model (in addition to other clinical and radiological variables), probably because of pronounced fluctuation in the values of the formula's components (prostate volume, mean voided urine), and broad variation of this number within the observed group (-70.8 to 74.4).  $Q_{\max}$  in this model practically represents the most significant variable, while combining this test with IPP, very high sensitivity and specificity in the classification of the obstruction are obtained (AUC=0.862). In earlier studies we showed that  $Q_{\max}$  is a very good indicator of obstruction (as per URA nomogram), with sensitivity of 72%, specificity of 92%, and PPV of 94%, with AUC of 0.92. (22). Botker-Rasmussen *et al.* reported a 100% positive predictive value for a  $Q_{\max}$  less than 10 mL/s in a small cohort of asymptomatic men (23). However, the  $Q_{\max}$  can be influenced by a number of extraneous factors, such as learning effects, diurnal variation, fluid and medication intake, and bladder disorders (24). Further, flow rates may be particularly limit-

ed in predicting obstruction in specific situations, such as in elderly patients, individuals with low voided volumes, or men with a  $Q_{max}$  of more than 10 ml/sec, as well as in the presence of neurological disease. (25). This is why isolated observation and analysis of  $Q_{max}$  have certain justified limitations.

While analyzing the correlation of IPP with other clinical and radiological factors, a very good correlation was observed between intravesical prostatic protrusion and prostate volume (Spearman's rank correlation coefficient  $\rho=0.53$ ;  $p$  0.0001), and almost the same correlations between IPP and prostate volume were shown (Kendall's tau correlation coefficient) with different urodynamic nomograms in the definition of obstruction (e.g. ICS, URA, Shaefer nomogram and BOOI $>40$ ). This is why it was decided to insert IPP instead of prostate volume in the formula for BOON, and to arbitrarily call this new number BOON2. The calculated ROC curve for BOON2, according to URA nomogram (obstruction URA $>29$  cmH<sub>2</sub>O), showed a very good AUC of 0.851, along with increased specificity (89.8%), and positive predictive value (87.5%) toward the obstruction, while AUC for BOON2 was even higher than AUC for BOON (though not statistically significant). Again, there is a question of why include IPP into the formula (as a fraction of prostate volume) if the prostate volume is anyway determined by ultrasound. First, the prostate volume itself does not have a very pronounced predictive power towards urodynamic obstruction compared to IPP (18), secondly, due to a small range of IPP distribution values, BOON2 is in a closer range (values are negative), therefore this number has normal distribution (D'Agostino-Pearson test  $p=0.23$ ). The BOON, which has a wide range, does not have normal distribution ( $p=0.002$ ), and in statistical analysis BOON, the sample cannot accurately be described by arithmetic mean and standard deviation, and such samples should not be submitted to any parametrical statistical test or procedure. Thirdly, after including IPP in the formula for

BOON, it was shown that cut off value BOON2 $>50$ , indicating that 71% of the patients were accurately classified in the zone of obstruction, while 83.3% of the patients were accurately classified in the zone out of obstruction, implying that by using this critical value more than 76% of patients can be accurately classified in urodynamic obstruction zone. Further, by combining the values of bladder outlet obstruction number with IPP value, test accuracy would increase at the individual level since the mean value of IPP for patients with BOON2 $>50$  14.9 mm, compared to patients with BOON2 $<50$ , where the mean value of IPP is 9.6mm (significantly lower than the critical value of IPP $>12$  mm). Using BOON2  $>50$ , and BOON $>30$  in combination with IPP  $>10$  mm, accuracy is achieved according to the classification of obstruction in the range of 88-93% of patients. However, negative predictive value for isolated BOON2 $>50$  is far higher than NPV for BOON $>30$  and IPP $>10$  (non-obstructed patients). Homma states that the PPV represents the proportion of obstructed men in those testing positive, and thus it should be higher than the NPV because these tests are intended to select obstructed men (21). But, if lower values below the critical point (BOON2 $<50$ ) are observed, then non-obstructed condition is accurately indicated and patients may avoid additional invasive tests. A combination of items with distinct test characteristics might provide a more stringent exclusion of unobstructed men with less chance of missing obstructed men (21).

This method of diagnostics, i.e. a combination of two non-invasive factors, improves the diagnostics of intravesical obstruction at the individual level, thus facilitating everyday clinical decision making regarding the choice of therapy. By our best knowledge and available literature, this is the first study on intercorrelation between BOON and IPP, and including IPP in the formula for BOON. We are aware of the limitations of this study. The sample should be larger, and BOON2 should be validated by comparison

with other proposed non-invasive methods for the prediction of obstruction, e.g. clinical prostate score-CLIPS (26) or Ocrim's number (27). Nevertheless, it seems that the combination of these two non-invasive factors increases diagnostic accuracy in predicting the obstruction in individual patients with BPE (29).

## 5. CONCLUSION

A combination of non-invasive parameters as intravesical prostatic protrusion and bladder outlet obstruction number for predicting benign prostatic obstruction provides higher accuracy in diagnosing bladder outlet obstruction at the individual level, resulting in a more accurate selection of diagnostic modalities and optimization of treatment of this group of patients. IPP has shown to be a good surrogate for prostate volume in the calculation of the formula for BOON, and as such it has higher specificity compared with the original value of BOON. More research with a prospective study design and a larger sample size is needed to establish definite criteria for BOON and IPP combination.

**Conflict of interest: none declared**

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