ORIGINAL PAPER

doi: 10.5455/medarh.2019.73.81-86
MED ARCH. 2019 APR; 73(2): 81-86
RECEIVED: FEB 12, 2019 | ACCEPTED: MAR 23, 2019

Department of Urology, University Clinical Centre Sarajevo, Sarajevo, Bosnia and Herzegovina

Corresponding author: Professor Damir Aganovic, MD, PhD. Department of Urology, Clinic for Urology, University Clinical Centre Sarajevo, Sarajevo, Bosnia and Herzegovina. E- mail: dagano@lol.ba ORCID ID: https://orcid.org/0000-0002-8142-7545.

Penile Compression Release Index Revisited: Evaluation and Comparison with Other Noninvasive Tools in the Prediction of Bladder Outlet Obstruction in Men with Benign Prostatic Enlargement

Damir Aganovic, Benjamin Kulovac, Senad Bajramovic, Amel Kesmer

ABSTRACT

Aim: To determine the discriminatory power of penile urethral compression-release index (PCRI), clinical prostate score (CLIPS) and bladder outlet obstruction index 2 (BOON2) for the detection of bladder outlet obstruction (BOO), and the associated bladder abnormality in patients with benign prostatic enlargement (BPE). **Material and methods:** In study was included of 135 patients with proven BPE underwent urodynamic measurement (UDM) and PCR maneuver. PCR Index was calculated following the formula: (Qs-Qss)/Qss x 100(%). CLIPS score was calculated based on non-invasive variables (prostate volume, maximal urinary flow, residual urine and voided volume), while BOON2 was calculated using the formula intravesical prostate protrusion (IPP)-3 x Qmax-0.2 x mean voided volume. UDM results were plotted on Schaefer and URA nomograms. **Results:** A comparative analysis was made using ROC curves. The area under the curve (AUC) for PCRI is 0.85 (PTP 91.3%), while AUC for CLIPS and BOON2 is 0.8 (PTP 77.6%) and 0.82 (PTP 74.5%), respectively. PCRI with the cut-off point of 96% clearly distinguishes obstructed patients with normocontractile detrusor and the presence of detrusor overactivity (DO), versus those unobstructed. CLIPS (>10) shows good BOO prediction, but without the possibility of distinguishing between detrusor contractility grade and the occurrence of DO. BOON2 has shown that impaired contractility has influence on this number in obstructed patients. **Conclusion:** PCRI is a very good noninvasive urodynamic test for a group-wise detection of BOO in patients with BPE and associated bladder co-morbidities; it is therefore superior in comparison with to CLIPS or BOON2.

Keywords: Benign prostatic enlargement, bladder outlet obstruction, penile compression release index, clinical prostate score, bladder outlet obstruction number.

1. INTRODUCTION

Benign prostatic enlargement (BPE) is an aging disease, causing considerable deterioration in the quality of life, expressed by lower urinary tract symptoms (LUTS). There is a very good algorithm developed for the diagnosis of this disease, but from the therapy optimization perspective it is very important to prove bladder outlet obstruction (infravesical obstruction). In patients with LUTS and suspected bladder outlet obstruction, the obstruction is urodynamically proven only in 50% to 66% of cases (1).

Uroflowmetry is an additional test for diagnosing the disease, but it is not sufficiently sensitive or specific since a low flow is not necessarily caused by the obstruction; it can also be caused by detrusor underactivity (DUA) (2). For the time being, pressure-flow studies (PFS) are the only method for an accurate diagnosis of infravesical obstruction. This urodynamic test is reliable, reproducible, but also time-consuming and invasive, causing discomfort and pain to patients. This is why numerous noninvasive techniques have been developed and validated, including penile compression-release index, condom catheter method, and penile cuff technique (3), to replace invasive testing. The penile urethral compression-release (PCR) maneuver is a test which determines a possible infravesical obstruction by a simple gradual squeezing of penile urethra during urination (4). The theory is based on isobaric conduit (bladder and urethra) and the generation of isovolumetric detrusor pressure, when flow rate reduction amounts to zero, i.e. when the flow stops completely. The flow generated after the release maneuver represents surge flow (Qs), and once the flow has stabilized, quasi steady-state flow appears (Qss).

In earlier studies, we compared bladder outlet obstruction number (BOON) with modified BOON2 in the prediction of bladder outlet obstruction. BOON is calculated from 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, as estimated from frequency-volume charts) (5). Due to good interrelation of the prostate volume and intravesical prostatic protrusion (IPP), we decided to replace the value of prostate volume with IPP in the formula for BOON, and arbitrarily call this number BOON2 (6).

Rosier et al. (7) defined the Clinical Prostate Score, using the important predictors of bladder outlet obstruction (Table 1). In a study comparing the Clinical Prostate Score and I-PSS in 705 patients, it was shown that when the former was greater than 11 (48.8% of patients with symptomatic BPH evaluated), 80.7% had bladder outlet obstruction (8).

2. AIM

Due to this finding, we analyzed this score in the prediction of obstruction and in relation to PCRI, as well as its ability to make a distinction in existing bladder comorbidities.

3. MATERIAL AND METHODS

The prospective study was carried out on 140 patients with lower urinary tract symptoms (LUTS), due to BPE at the Urology Clinic of the Sarajevo University Hospital. The exclusion criteria were all conditions, illness, neurological abnormalities and medication which could interfere with the act of micturition. 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 intravesical prostatic protrusion (IPP) was measured using standard methodology described elsewhere (9, 10). The patients completed International Prostatic Symptom Score (IPSS) and signed the Informed Consent Form. After that, patients were instructed on how to perform penile compression release (PCR) manoeuvre. During the examination of flow, after the stream commenced patient should squeeze the penis gradually, to abort the flow with complete relaxation of the pelvic floor. After 2-3 seconds the patient released the compressed urethra and voiding was continued till the end. Two main points were taken; surge flow after the releasing the urethra marked as a reference point (Qs), and second point was taken, when the flow was stabilized marked as a reference point of the steady-state flow (Qss). PCR Index was calculated for each patient, following the formula: PCRI= (Qs-Qss/Qss) x 100. The index was expressed as a percentage (4). The patients with a voided volume of less than 150 ml during PCR testing were excluded because of proven poor reliability (11). The next day, 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) (12). Then, the findings of pressure/flow studies (PFS) were plotted on the Schaefer obstruction class nomogram (13) and URA-group specific urethral resistance factor (14). The Schafer nomogram was used for grading detrusor contraction strength (IV category- 0/I very weak/weak, III / IV normal/strong contractility) and for determining DAMPF (Detrusor Adjusted Mean Passive Urethral Resistance Ratio Factor), as a continuous variable, in order to determine the correlation with the observed obstruction predictors. CLIPS was calculated for each patient, depending on prostate volume, strength of Q_{max} free, volume of residual urine, and volume of voided urine (Table 1). BOON2 was calculated following the formula intravesical protrusion of prostate (IPP in centimeters)–3 x maximal urinary free flow rate (in milliliters per second)–0.2x mean voided volume (in milliliters, as estimated from frequency-volume charts).

Statistical analysis was performed through one and two-way-analysis of variance (ANOVA test), Pearson correlation coefficient, and calculation of area under the receiver operating characteristic (ROC) curve for predicting obstruction; AUCs were compared via the method of DeLong (15). Statistic analysis was made using Medcalc program for Windows version 12. The level of significance (two-tailed) was set at $p < 0.05$.

4. RESULTS

Out of the 140 patients that underwent the PCR maneuver, 135 of them were finally covered by the analysis. The drop-out 4% were the patients unable to initiate the stream (restore the flow) following the PCR maneuver, probably due to reflex inhibition of the resulting pelvic floor contraction. 70 patients (52%) had urodynamically proven obstruction, according to URA nomogram.

Prostate size (cm_3)	No. of points
< 30	0
30-60	3
>60	6
Free maximal flow (mL/s)	0
>12	0
8-12	5
4-8	10
<4	15
Post-void residual urine volume (mL)	
<30	0
30-100	2
>100	4
Voided volume (mL)	
>300	0
200-300	1
<200	2

Table 1. Clinical Prostate Score (8).

	Mean	95% CI	SD	SEM	Median	Minimum	Maximum
Age	66.1	64.906 – 67.390	7.2960	0.6279	67	51	81
IPSS	17.71	16.675 – 18.748	6.0887	0.5240	18	3	31
PV (ccm)	47.21	43.586 – 50.814	21.2286	1.8271	41	27	119
PVR (ml)	55.81	45.763 – 65.985	59.3999	5.1123	31	0	286
Q_{max} (ml/sec)	8,8	8,1365-9,3968	3,7	0,3816	8	2,9	24
IPP (mm)	10.79	10.688 – 12.868	6.4039	0.5512	11	1	31
MVvol. (ml.)	200,2	191,92-208,51	48,73	4,2	200	90	290
PCRindex(%)	100.28	90.581 – 109.996	57.0283	4.9082	80	26	266
CLIPS	11,4	10,5379-12,2473	5,02	0,4321	10	1	22
BOON2	-34,01	-37,0899 -30,9397	18,07	1,56	-31	-98,7	5,9

Table 2. Summary statistics table. IPSS International prostate symptom score, PV prostate volume, PVR post void residual urine, Qmax maximal urinary flow , IPP intravesical protrusion of prostate, MVvol. Mean voided volume, PCRindex penile urethral compression-release index, CLIPS clinical prostate score, BOON2 bladder outlet obstruction number2

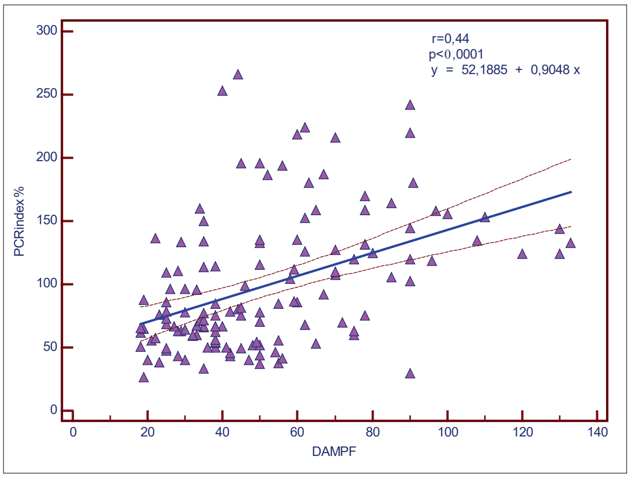

Figure 1. Linear regression for PCR Index and DAMPF

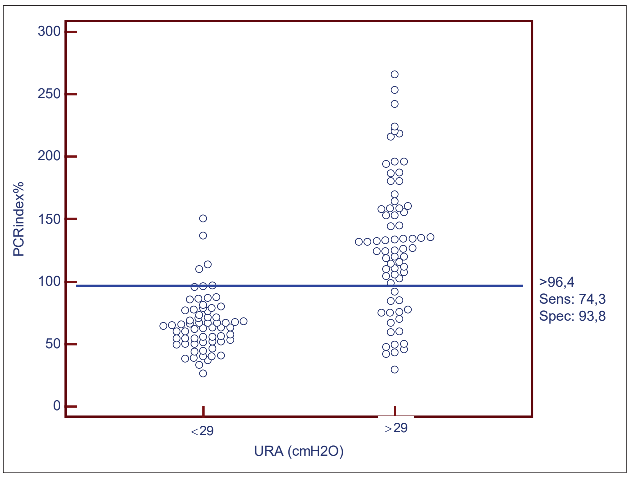

Figure 2. Interactive dot diagram for PCR Index and infravesical obstruction (URA>29CmH20)

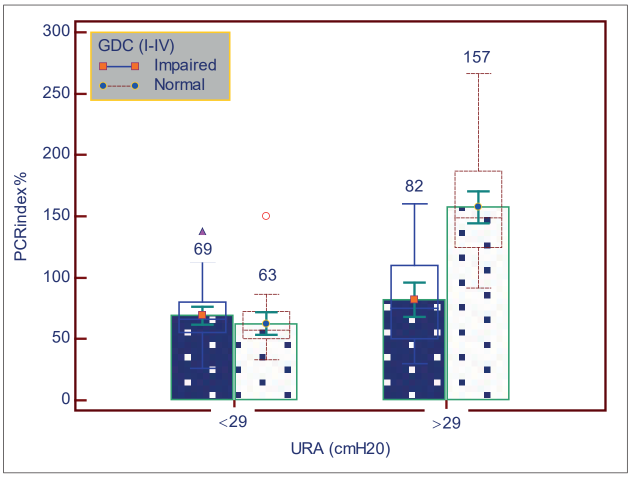

Figure 3. Mean values of PCR Index depending on detrusor contractility and obstruction

The mean age of subjects was 66 years, the average IPSS (17.7) fell within the 2nd category (moderate symptoms). The mean prostate volume amounted to 47.2 ccm, while post-void residual urine amounted to 56 ml (0-286 range), and the average PCR Index amounted to 100.3% (26-266 range). The data are shown below in Table 2.

PCRI correlates very well with the degree of urodynamic obstruction (r=0.44; p<.0001), expressed as DAMPF continuous variable (Schafer nomogram) (Figure 1).

Then, the predicted probability of this noninvasive urodynamic factor was determined according to urodynamic bladder outlet obstruction, based on URA nomogram. The cut-off point for PCRI of 96.4% gives the sensitivity and specificity of 74.3% and 93.8%, respectively, according to the obstruction, with a high positive predictive value (PPV) of 93%, and negative predictive value (NPV) of 77% , + LR 9.6 (95% CI 0.777–0.904), with NND~1.5 pat. (Figure 2).

The patients were then divided into four groups, depending on detrusor contractility and obstruction. The first group: 27 patients with normal detrusor contractility and unobstructed (20%), the second group: 38 patients with detrusor underactivity (DUA) and unobstructed (28%), 54 patients with clear obstruction and normal detrusor contractility (40%), and 16 patients with obstruction and DUA (12%) (Figure 3). A clear difference was shown between obstructed patients with preserved detrusor contractility (mean PCRI=157%) and the group of unobstructed patients with preserved detrusor contractility (mean PCRI=63%); ANOVA test (F=43, p<.00001). The patients with obstruction and DUA based on PCR Index (mean PCRI=82%) could only be statistically differentiated as a group from the group of unobstructed patients with or without DUA (PCRI 69% i 63%, respectively), via ANOVA test (F=3.8, p=0.03).

In order to analyze PCR Index only in obstructed patients, the patients from this category (No 70) were divided according to detrusor contractility and the occurrence of detrusor overactivity (DO). Out of 44 patients with preserved detrusor contractility (63%), 19 of them (43.1%) had DO. Out of 26 patients with DUA, 10 of them (38%) had the occurrence of non-inhibited detrusor contractions (Figure 4). There is a clear distinction of PCR Index in patients with the occurrence of DO and preserved detrusor contractility (mean PCRI= 187% and 141%; F=9.2, p=.005); compared with patients with DUA and the occurrence of DO, where there is no clear statistical difference (PCRI=80% and 86%, respectively); p=0.16.

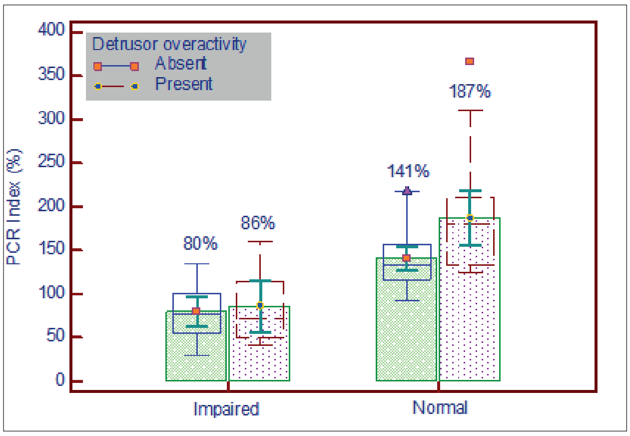

Figure 4. Detrusor contractility within the region of obstruction (URA>29CmH20), with or no detrusor overactivity

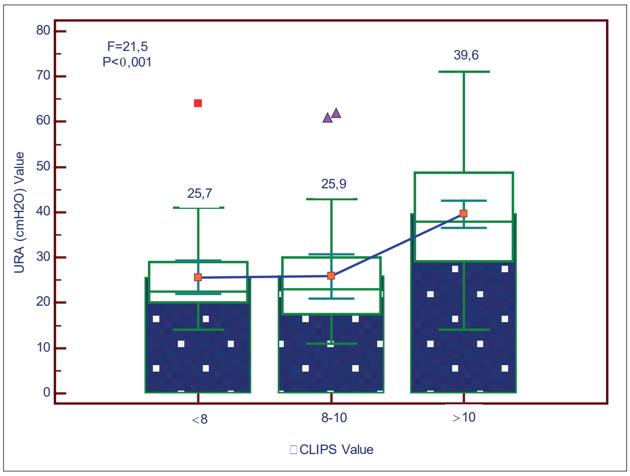

Figure 5. CLIPS values depending of obstruction

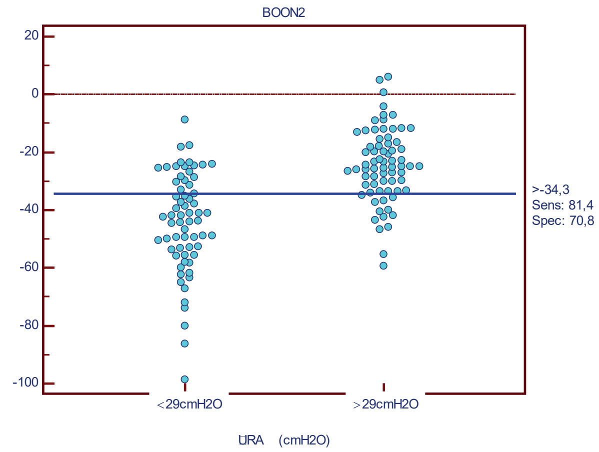

Figure 6. Interactive dot diagram for BOON2 and infravesical obstruction (URA nomogram)

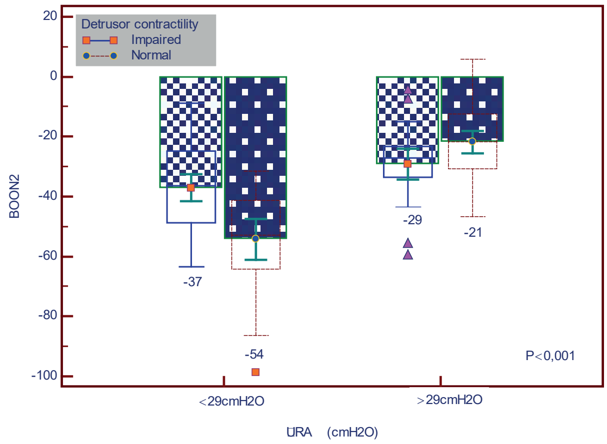

Figure 7. BOON2 mean values depending on detrusor contractility in the region in and out of the obstruction

Out of 135 patients, 70 of them (55%) had urodynamic obstruction, according to URA nomogram. Of these patients 56 had CLIPS >10 (80%). 32 patients had CLIPS <8 (23.7%), while 7 of them (21.9%) had urodynamic obstruction. The remaining 33 patients (24.4%) had CLIPS in the range of 8-10, again, of which 9 patients had UD obstruction (36.8%). Thus, sensitivity and specificity according to the obstruction of 75% and 77%, respectively, with PPV of 80%, and NPV of 70% (+LR=3.2); NND~ 1.9 pat., were shown for CLIPS (cut-off value >10). ANOVA analysis established a clear difference between the level of obstruction for CLIPS >10 (mean value of URA is 39.6 cmH2O), compared with lower categories of CLIPS, where no differences are shown (F=21.5, p<.001) (Figure 5).

The ability of CLIPS to differentiate between patients within from those out of the obstruction, depending on detrusor contractility, was tested. The mean value of CLIPS in obstructed patients with preserved detrusor contractility was 14.2 and 13.2, respectively. The mean value of CLIPS in unobstructed patients with preserved and impaired detrusor contractility was 7.2 and 9.6, respectively. ANOVA analysis showed that there was no significant difference in the values of CLIPS in the region within the obstruction, according to detrusor contractility (F=0.44, p=0.5); while in the region out of the obstruction there was slight statistical significance (F=4.1, p=0.044), with no real practical value.

Subsequently, the ability of CLIPS to differentiate between patients within from those out of the obstruction, depending on detrusor overactivity (DO), was tested. The mean values of CLIPS in obstructed patients with and without DO were 13.6 i 14; respectively. The mean values of CLIPS in unobstructed patients with and without DO were 9 i 8.7; respectively. ANOVA analysis showed that there was no significant difference in the values of CLIPS in the region within and out of the obstruction, according to the presence or absence of DO (F=0.2, p=0.65).

Interactive dot diagram of the relation of BOON2 to the obstruction showed the optimal cut-off point for the prediction of obstruction value of >-34.3. Of 135 patients, 78 of them (57%) had this value, while within this group 58 (74%) patients had UD obstruction. The remaining patients 135/57 (47%) had a lower value of the above-mentioned cut-off point. 12 patients in the latter group (22.8%) had UD obstruction, according to URA nomogram. In addition to the sensitivity and specificity of 81% and 71%, respectively, mentioned above, for the prediction of obstruction, BOON2 has PPV of 75%, and NPV of 79%, with +LR of 2.7 with NND~ 1.9 pat. (Figure 6).

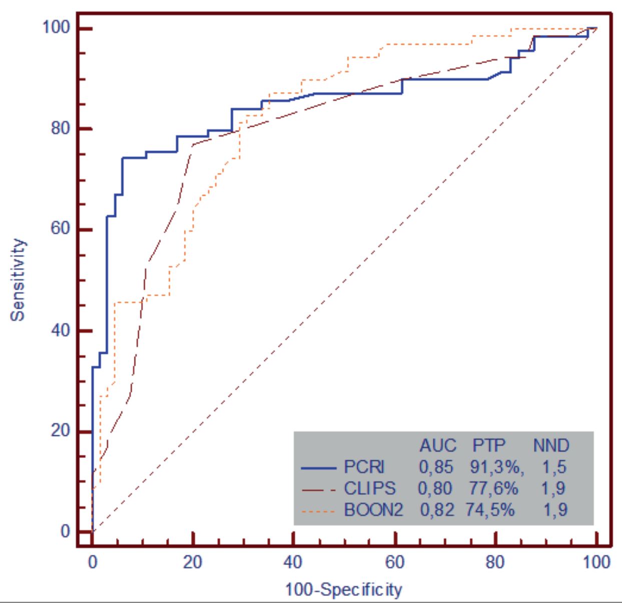

Figure 8. Comparison of the ROC curves in the prediction of obstruction according to the URA. PCRI penile compression release index, BOON2 bladder outlet obstruction number2, CLIPS clinical prostate score, AUC area under the curve, PTP post-test probability, NND number needed to diagnose

Then, the behavior of this factor was assessed in the region within and out of the obstruction, depending on detrusor contractility. In the group out of the obstruction, 38/65 (58%) patients had weak detrusor contractility with mean BOON2 -37, while the remaining patients with preserved contractility had mean BOON2 -54. In the group within the obstruction, 26/70 (37%) patients had weak detrusor contractility with mean BOON2 -29, while the remaining patients with preserved contractility had mean BOON2 -21. There is only slight statistical significance in the difference of BOON2 in patients within the obstructed group, depending on detrusor contractility (F=4; p= 0.047), while the difference in patients out of the region of the obstruction is significant (F=15, p<0.001) (Figure 7).

Then, the mean values of BOON2 were analyzed in the region within and out of the obstruction, depending on the occurrence of DO. The mean values of BOON2 in obstructed patients with and without DO were -25 and -24; respectively. The mean values of BOON2 in unobstructed patients with and without DO were -40 and -47; respectively. ANOVA analysis showed that there was no significant difference in the values of BOON2 in the region within and out of the obstruction, according to the presence or absence of DO (p>0.05).

Since the high predictive power of PCRI according to the obstruction was proven, it was compared with other observed obstruction factors, i.e. CLIPS and BOO2. A comparative analysis was made using ROC curves, and again the best discriminatory power of PCR Index according to the obstruction was shown. The area under the curve (AUC) for PCRI is 0.85 (PTP 91.3%), while AUC for CLIPS and BOON2 is 0.8 (PTP 77.6%) and 0.82 (PTP 74.5%), respectively (Figure 8). Pair-wise comparison of ROC curves using De Long method did not show a statistically significant difference between AUC for observed variables (results are not shown).

5. DISCUSSION

Sullivan and Yalla (4), using PCR index cut-off of 100%, shows the sensitivity and specificity according to the obstruction of 91% and 70%, respectively. Harding et al. while comparing standard pressure/flow studies with penile cuff test also determined PCR Index with optimal threshold for the detection of obstruction of 160%, with PPV of 69% according to bladder outlet obstruction (16). PCR Index, as confirmed by this study, provides twice as high values in obstructed patients than in those not obstructed or those obstructed, having impaired detrusor contractility. A statistically more significant increase in PCR index was shown in patients having normocontractile detrusor with DO than in those having normocontractile muscle but without DO (average value 187% vs. 141 %). There are weak statistically significant differences in patients without obstruction and those with impaired detrusor contractility. The problem of distinguishing the patients with obstruction with DUA (even those associated with DO) still remains, because these patients are not able to generate sufficient isometric pressure after voiding, to show higher values of PCR Index. Blake and Abrams found that is also very important to follow reference points during the determination of PCRI, i.e. Qs and Qss, since the patients with DO without obstruction have a high Qs, accompanied with a high Qss. Patients with detrusor underactivity neither have high Qs nor do they have high Qss (19).

CLIPS and BOON2 showed good predictive value in the detection of UD obstruction, as well as other non-invasive factors (i.e. Q_{max}, IPP, BWT) (9-11). However, CLIPS does not show significant results in the distinction of associated bladder comorbidities (i.e. DUA, DO). BOON2 is somewhat more sensitive for the distinction of detrusor contractility impairment, mainly in unobstructed patients, while the presence (or absence) of DO could not be established using this factor. BOON2 shows good sensitivity according to the obstruction, because in any model which observed contractility and DO in isolation, mean BOO2 was always higher than -30.

The value of using PCRI has been proven, as it is an easy test to perform; it is not expensive or time-consuming. While the above-mentioned indicators rely on Q_{max}, as well as other variables (symptoms, prostate volume, PVR), PCRI also shows the status of detrusor contractility (which is certainly increased by the presence of DO); therefore, the results of this and previous studies suggest that PCR index combines the measure of detrusor contractility (Qs) with the actual maximum flow rate (related to the Qss). Qs, therefore, is an important measure of detrusor contractility (isovolumetric strength) (16, 17).

6. CONCLUSION

PCR Index is shown to be a very good diagnostic instrument for the prediction of infravesical obstruction, *and to a certain extent, for proving bladder pathology.* It represents a very good introduction to other models of noninvasive urodynamic diagnostics since it shows significant specificity and PTP in the condition of infravesical obstruction caused by BPE. PCRI is useful in the study of urethra physiology, detrusor contractility and isovolumetric pressure generation in patients with BPE.

- **Declaration of patient consent:** The authors certify that they have obtained all appropriate patient consent forms.
- **Author's contribution:** D.A., B.K., S.B. gave substantial contribution to the conception or design of the work and in the acquisition, analysis and interpretation of data for the work. Each author had role in drafting the work and revising it critically for important intellectual content. Each author gave final approval of the version to be published and they agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.
- **Financial support and sponsorship:** Nil.
- **Conflicts of interest:** There are no conflicts of interest.

REFERENCES

1. Schafer W, Rubin H, Nopeney R, et al. Obstructed and non-obstructed prostatic obstruction: a plea for urodynamic objectivism of bladder outflow obstruction in benign prostatic hyperplasia. World J Urol. 1989; 6: 198-203.
2. Griffiths D. Detrusor contractility–order out of chaos. Scand J Urol Nephrol Suppl. 2004; 215: 93-100.
3. Griffiths D, Abrams P, D'Ancona CA, van Kerrebroeck P, Nishizawa O, Nitti VW. et al. Urodynamic evaluation of lower urinary tract symptoms in men. Current Bladder Dysfunction Reports. 2008; 3: 49-55.
4. Sullivan MP, Yalla SV. Penile Urethral Compression-Release Maneuver as a Non-invasive Screening Test for Diagnosing Prostatic Obstruction Neurourol. Urodynam. 2000; 19: 657-669.
5. van Venrooij GE, Eckhardt MD, Boon TA. Noninvasive assessment of prostatic obstruction in elderly men with lower urinary tract symptoms associated with benign prostatic hyperplasia. Urology. 2004; 63: 476-480.
6. Aganović D, Prcic A, Hadžiosmanović O, Hasanbegović M. Does the combination of intravesical prostatic protrusion and bladder outlet obstruction number increase test accuracy according to benign prostatic obstruction at the individual level? Acta Inform Med. 2012; 20(3): 160-166. doi: 10.5455/aim.2012.20.160-166.
7. Rosier PFWM, de Wildt MJAM, Wijkstra H, Debruyne FMJ, De la Rosette JJMCH. Clinical diagnosis of bladder outlet obstruction in patients with benign prostatic enlargement and lower urinary tract symptoms: development and urodynamic validation of a clinical prostate score for the objective diagnosis of bladder outlet obstruction. J Urol. 1996; 155: 1649-1654.
8. de la Rosette J, Perachino M, Thomas D, Madersbacher S, Desgrandchamps F, Alivizatos G,. de Wildt MJAM. Guidelines on benign prostatic hyperplasia, EAU. 2001.
9. Reis LO, Barreior GC, Baracat J, Prudente A, D'Ancona CA. Intravesical protrusion of the prostate as a predictive method of bladder outlet obstruction, Inter Braz J Urol. 2008; 34(5): 627-637.
10. Franco G, De Nunzio C, Leonardo C, Tubaro A, Ciccariello M, De Dominicis C, Miano L, Laurenti C. Ultrasound assessment of intravesical prostatic protrusion and detrusor wall thickness-new standards for noninvasive bladder outlet obstruction diagnosis?, J Urol. 2010; 183(6): 2270-2274.
11. McIntosh SL, Drinnan MJ, Griffiths CJ, Robson WA, Ramsden PD, Pickard RS. Non-invasive measurement of male bladder contractility. J Urol. 2004; 172: 1394-1398.
12. Schaefer W, Abrams P, Liao L, Mattiasson A, Pesce F, Spangberg A. et al. Good urodynamic practices: uroflowmetry, filling cystometry and pressure-flow studies. Neurourol Urodyn. 2002; 21: 261-274.
13. Schaefer W. Analysis of bladder-outlet function with the linearized passive urethral resistance relation, linPURR, and a disease-specific approach for grading obstruction: from complex to simple. World J Uro. 1995; 13: 47-58.
14. Griffiths D, van Mastrigt R, and Bosch R. Quantification of urethral resistance and bladder function during voiding, with special reference to the effects of prostate size reduction on urethral obstruction due to benign prostatic hyperplasia. Neurourol Urodyn. 1989; 8: 17-27.
15. DeLong ER, DeLong DM, Clarke-Pearson DL. Comparing the areas under two or more correlated receiver operating characteristic curves: a nonparametric approach. Biometrics. 1988; 44: 837-845.
16. Harding CK, Robson W, Drinnan WMJ, Griffiths CJ, Ramsden PD and Pickard RS: An automated penile compression release maneuver as a noninvasive test for diagnosis of bladder outlet obstruction. J Urol. 2004; 172: 2312-2315.
17. Blake C, Abrams P. Noninvasive techniques for the measurement of isovolumetric bladder pressure. J Urol. 2004; 171(1): 12-19.