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Intravesical Protrusion of the Prostate as a Predictive Method of Bladder Outlet Obstruction

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ABSTRACT

Objective: Pressure-flow study is the gold standard for diagnosis of bladder outlet obstruction (BOO). A prospective study was carried out to compare urodynamic evaluation and measurement of intravesical protrusion of the prostate for diagnosing BOO.

Materials and Methods: Patients presenting with lower urinary tract symptoms (LUTS) associated with benign prostatic hyperplasia and suspected BOO were prospectively evaluated through conventional urodynamics and classified according to the bladder outlet obstruction index (BOOI). They also underwent abdominal ultrasound measurement of the intravesical prostatic protrusion (IPP) and prostatic volume. The IPP was classified into three stages: grade I under 5 mm; grade II, between 5 and 10 mm; and grade III over 10 mm.

Results: Forty-two patients, mean age 64.8 ± 8.5 years were enrolled. Transabdominal ultrasound determined a mean prostatic volume of 45 ± 3.2 mL. Achieved IPP's values were the following: grade I - 12 (28.5%), grade II - 5 - (12%) and grade III - 25 (59.5%). The results of prostate volume differed significantly between obstructed and non-obstructed men ($p = 0.033$) and for IPP among obstructed, inconclusive and non-obstructed men ($p = 0.016$). For IPP, the area under ROC curve was 0.758 (95% confidence interval - 0.601 to 0.876), and the cutoff point to indicate BOO was 5 mm with 95 % sensitivity (75.1 - 99.2) and 50 % specificity (28.2 - 71.8).

Conclusion: IPP and prostatic volume measured through abdominal ultrasound are noninvasive and accessible methods that significantly correlate to urinary BOO, and are useful in the diagnosis of male urinary obstructive problems.

Key words: *bladder outlet obstruction; prostate; volume; flowmetry; sensitivity and specificity*
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INTRODUCTION

Bladder outlet obstruction (BOO) is characterized by increased detrusor pressure and reduced urinary flow rate. Pressure-flow studies are the gold standard for BOO determination. However, this method is an invasive and expensive procedure with limited availability.. Therefore, attempts have been made to diagnose BOO through noninvasive methods that can be divided into 2 categories: non-urodynamically based measurements and noninvasive urodynamics.

Non-urodynamically based measurements include symptoms, post-void residual urine (PVR), Prostate Specific Antigen (PSA) and ultrasound derived measurements, such as prostate volume, bladder wall thickness, bladder weight and intravesical prostatic protrusion (IPP). Noninvasive urodynamics include uroflowmetry, use of a penile cuff, the condom-method and Doppler urodynamics (1).

It is well known that the prostate's anatomic conformation together with intravesical prostatic protrusion (IPP) may affect normal voiding.

Earlier studies have previously demonstrated that the ultrasonographic measurement of IPP could identify BOO. A total of 200 patients were assessed with invasive urodynamics and transabdominal ultrasound. The relationship of IPP to BOO showed that as IPP grade increased in severity, BOO grade also increased. The sensitivity and specificity of diagnosing BOO were 76% and 92% for over 10 mm IPP, 17% and 53% for between 5 and 10 mm IPP and 7% and 56% for under 5 mm IPP, respectively. PVR more than 100 mL showed 75% sensitivity and 91% specificity for predicting BOO in the population studied (2).

The objective of this study was to define how the IPP and prostate volume, measured through abdominal ultrasound, might alter voiding and determine the accuracy of this measurement compared to conventional urodynamics in diagnosing BOO.

MATERIALS AND METHODS

A prospective study was carried out in Latin-American patients presenting with lower urinary tract symptoms (LUTS) and evaluated by urinalysis to exclude urinary tract infection.

Patients who had been previously submitted to urologic surgeries, or had urologic neoplasia, bladder calculus or presented any type of neurological abnormality or using alpha-blockers, anticholinergics, antiandrogens or another medications which may affected the voiding patterns were excluded from this study.

In the period ranging from June to August/2005, after Ethics Committee approval and written informed consent, these patients were evaluated using anamnesis, International Prostatic Symptoms Score (IPSS) and IPSS Quality of Life (IPSS-QoL) questionnaires, physical, neurological, digital rectal examination and conventional urodynamic evaluation (Dynapack, Dynamed, 2004) and classified according to BOOI.

Urodynamics were done according to the "good urodynamic practices" recommended by the International Continence Society (3). Bladder outlet obstruction index (BOOI), defined as the detrusor's pressure at the maximum urinary flow (pdet_qmax) minus two times the maximum flow (qmax): BOOI = pdet_qmax - 2 x qmax. Values below 20 were considered non-obstructed, between 20 and 40 inconclusive and higher than 40, obstructed (4). Postvoid residual urine volume was measured during urodynamic investigation, after free uroflowmetry (free flow).

After one week the patients underwent an ultrasound study performed by the same physician (J.B.) blinded to the urodynamic results performed by L.O.R. Abdominal ultrasound (Toshiba model Powervision 6000) was performed in the sagittal plane, using transductor frequencies between 3 and 6 MHz, and IPP along with the prostatic volume were measured. According to Yuen et al. (5), the bladder was filled with at least 100 mL of urine in order to consider the IPP determination; this was achieved through the ingestion of one liter of water in a two hour period after voiding. IPP was defined by the distance from the tip of the prostate's protrusion into the vesical lumen to the bladder neck measured in millimeters (Figure-1). Measurements were divided into three stages: grade I < 5 mm, grade II 5-10 mm, grade III > 10 mm (2). Prostate volumes were determined through software (Powervision 600) for automatic measurement and expressed in milliliters (mL).

The statistical analysis was performed through Kruskal-Wallis and Dunn's post test to multiple comparison, and area under ROC curve, using MedCalc version 5.00.019 and SAS System for Windows version 9.1.3.

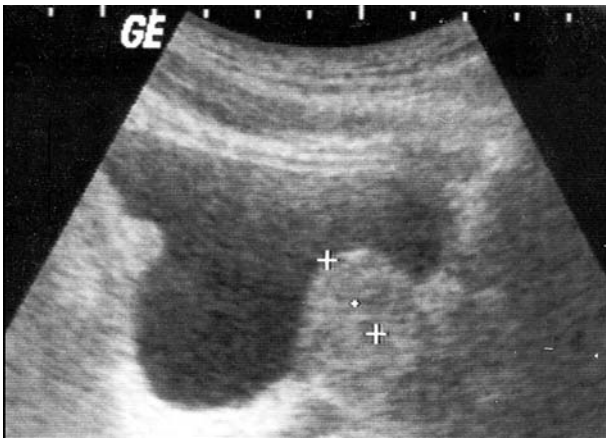

Figure 1 *– Sagittal views of bladder and prostate using transabdominal ultrasonography. Vertical distance from tip of protrusion to base of bladder is the intravesical prostatic protrusion measurement.*

Table 1 – *Clinical and demographic characteristics.*

Clinical and Demographics Characteristics	Rate
Age	64.9 (56 to 73) years
Latin-American Caucasians	100%
IPSS	13 (6 to 20)
Ultrasound transabdominal examination	45 (5.5 to 155) mL
Qmax	8.5 (5.5 to 13) mL/s
Pdet_Qmax	58.1 (35 to 126)
Post voiding residue	70 (0 to 250) mL

IPPS = International Prostate Symptom Score.

RESULTS

The clinical and demographic characteristics are shown in Table-1.

The pressure/flow study showed mean Qmax of 8.5 ± 4.3 mL/s, Pdet.qmax of 58.1 ± 26 cm H_2O, and postvoid residual urine volume after free flow of 70 ± 177 mL. Based on BOOI, 20 (47.6%) patients presented obstruction, 12 (28.5%) were inconclusive and 10 (23.9%) did not present obstruction. The mean BOOI was 28.6 (SD 13.4).

IPP's values obtained were as follows: grade I - 12 (28.5%), grade II - 5 - (12%) and grade III - 25 (59.5%).

Comparing prostatic volume and IPP with BOOI we found according to Kruskal-Wallis and Dunn's post test that the results of prostate volume differed significantly between obstructed and non-obstructed men (p = 0.033) and the results of IPP differed significantly among obstructed, inconclusive and nonobstructed men (p = 0.016), Table-2.

Table-3 demonstrates that IPP's grade III reached up to 80% sensitivity and 68 % specificity for diagnosing BOO. Positive predictive value was 70 % and the negative predictive value 79 %.

Considering the slight IPP superiority over prostate volume to detect obstruction, we calculated the IPP cutoff point to indicate obstruction as 5 mm with 95 % sensitivity (75.1 - 99.2) and 50 % specificity (28.2 - 71.8); likelihood ratio of positive test result 1.90 and likelihood ratio of negative test result 0.10.

The area under ROC curve was 0.758 (95 % confidence interval - 0.601 to 0.876) for IPP and 0.718 (95% confidence interval - 0.558 to 0.846) for prostate volume, Figure-2.

A flow diagram for IPP on diagnostic accuracy is showed in Figure-3.

Table 2 – *Prostate volume, IPP and BOOI (Kruskal–Wallis; Dunn's test).*

Prostate Volume (mL)				**IPP** (mm)			
BOOI	N	Mean	SD	BOOI	N	Mean	SD
Nonobstructed	10	29.8	19.4	Nonobstructed	10	7.6	8.5
Doubt	12	43.2	33.1	Doubt	12	8.5	7.0
Obstructed	20	53.6	32.9	Obstructed	20	15.4	6.6

p = 0.033 (prostate volume); p = 0.016 (IPP); IPP = intravesical prostatic protrusion.

Table 3 – *IPP grade III accuracy.*

Measurement	%	95% CI	N / Total
Sensitivity	80.0	55.7 ; 93.4	19/21
Specificity	68.2	45.1 ; 85.3	19/25
Positive predictive value	69.6	46.9 ; 85.9	13/19
Negative predictive value	78.9	53.9 ; 93.0	19/27
Accuracy	73.8	57.7 ; 85.6	32/46
LR +	2.51		
LR -	0.29		

CI = confidence interval; IPP = intravesical prostatic protrusion; LR = likelihood ratio; N = number of patients.

COMMENTS

LUTS are one of the most common complaints in the elderly men and benign prostate obstruction is one of the most frequent causes. Pressure flow study has been recommended before surgical treatment of prostate enlargement by many authors. Searching for new accurate methods that could substitute the gold standard pressure-flow study demonstrates the need for lowering costs, expanding accessibility and relieving patient discomfort .

Since transrectal methods can producegreat discomfort to the patient, abdominal ultrasound was demonstrated to be equivalent to rectal ultrasound for

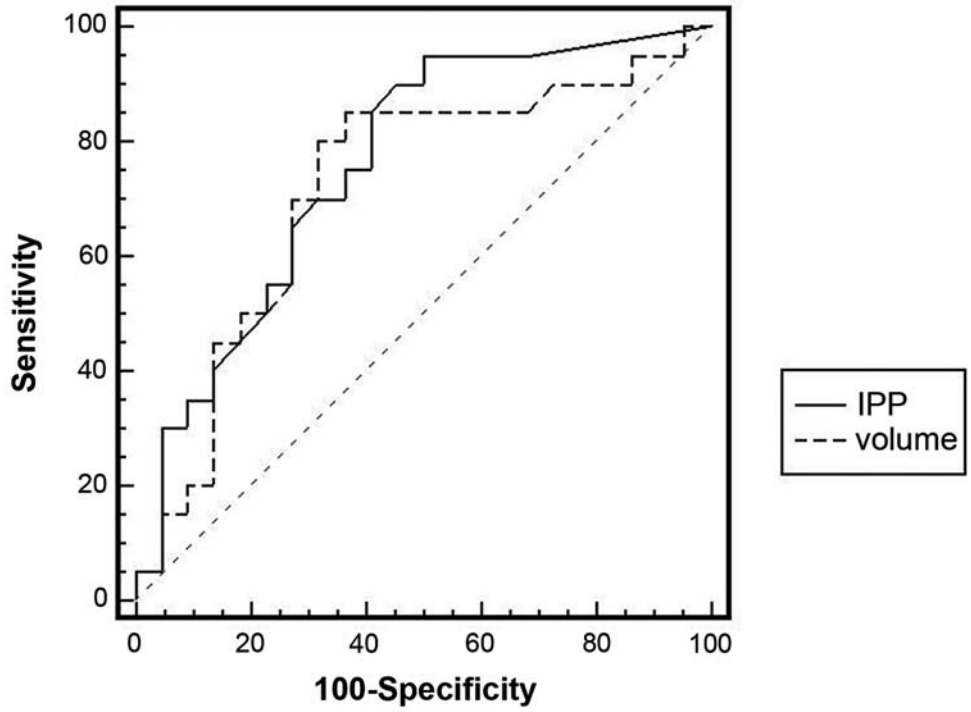

Figure 2 – *Receiver Operating Characteristic (ROC) curve for intravesical prostatic protrusion (IPP) and prostate volume.*

measuring the prostate when bladder volume is over 100 mL (5,6).

Clinical data such as IPSS, post voiding residue and flowmetry have been previously demonstrated to correlate mostly to lower urinary tract functional status rather than mechanical obstruction itself (7-9). Therefore, noninvasive measurements of the prostate intend to delineate a morpho-functional correlation in order to orient conduct towards LUTS secondary to benign prostate obstruction.

Almost all studies on IPP measurements come from Asia and it is unknown if the results in Asians are valid for Latin-Americans or Caucasians as well.

Chia et al. (2) demonstrated the possibility of using the IPP measurements for diagnosing BOO, which was also a predictor of the capacity for spontaneous voiding after acute urinary retention in Tan et al. study (10).

Other authors have suggested determining bladder weight, bladder wall width or prostate conformation through abdominal or rectal ultrasound (11-14).

Kojima et al. demonstrated, studying 104 patients, that the bladder weight more than 35 g performed thought transabdominal ultrasound is strongly associated with bladder outlet obstruction on pressure-flow studies (15).

A bladder wall thickness of 5 mm appeared to be the best cutoff point to diagnose bladder outlet obstruction, since 63.3% of patients with bladder wall thickness less than 5 mm were unobstructed while 87.5% of those with a bladder wall thickness 5 mm or greater were obstructed in a study including 174 patients of Manieri et al. at 150 mL bladder filling (16).

Hakenberg et al. (17) found that mean bladder wall thickness was 3.33 mm in healthy men and 3.67 mm in men with LUTS and BPE, measuring all patients at different bladder fillings. BOO was found in 95.5% of men with a detrusor wall thickness greater than or equal to 2 mm in Oelke et al. study, at 250 mL or more bladder filling (18).

Recently, Blatt et al. (19) who performed urodynamics evaluation and abdominal ultrasound among patients with different types bladder dysfunction, found that mean bladder wall thickness in patients with normal urodynamics, bladder outlet obstruction, detrusor overactivity and increased bladder sensation was 2.0, 2.1, 1.9 and 1.8 mm, respectively. No significant difference was found between the groups. In particular, there was no difference in bladder wall thickness between patients with normal urodynamics, and those with bladder outlet obstruction ($p = 0.31$) or detrusor overactivity ($p = 0.31$).

The inconsistency as regards the results obtained and the lack of technique standardization have limited their clinical use until now.

Intravesical protrusion seems to corroborate with urinary obstruction through a "valve ball" mechanism, in which the prostate's lateral and medium lobes interfere on the complete opening of the vesical neck while the patient urinates (10). According to this mechanism and based on the present study, it was demonstrated that the intravesical protrusion of the prostate relates not only to the urinary obstruction itself, but it also provides information concerning the severity of obstruction. It has been demonstrated that the greater the IPP, the higher BOOI (20). Still significant, but to a lesser extent, results of prostatic volume obtained through ultrasound and PSA also related to the degree of obstruction (21-24).

Utilizing receiver-operator characteristic curves, the area under the curve for IPP were 0.772, and 0.858 for Lim et al. (21) and Keqin et al. (20), respectively. The latter authors found 8.5 mm as the best cutoff value for IPP with 75.5 % of sensitivity and 82.6 of specificity.

Our findings, 0.758 for the area under the curve and 5 mm as the best cutoff value for IPP, are in agreement with these earlier investigations.

On the other hand, our study had a limited number of patients and presented great variability of results, which weakened its immediate clinical application. However, these early statistically significant results lead towards new tendencies and studies necessary to seek improved methods of diagnosing BOO as well as technique standardization.

CONCLUSION

IPP and prostatic volume measured through abdominal ultrasound are noninvasive and accessible methods that significantly correlate with urinary BOO,

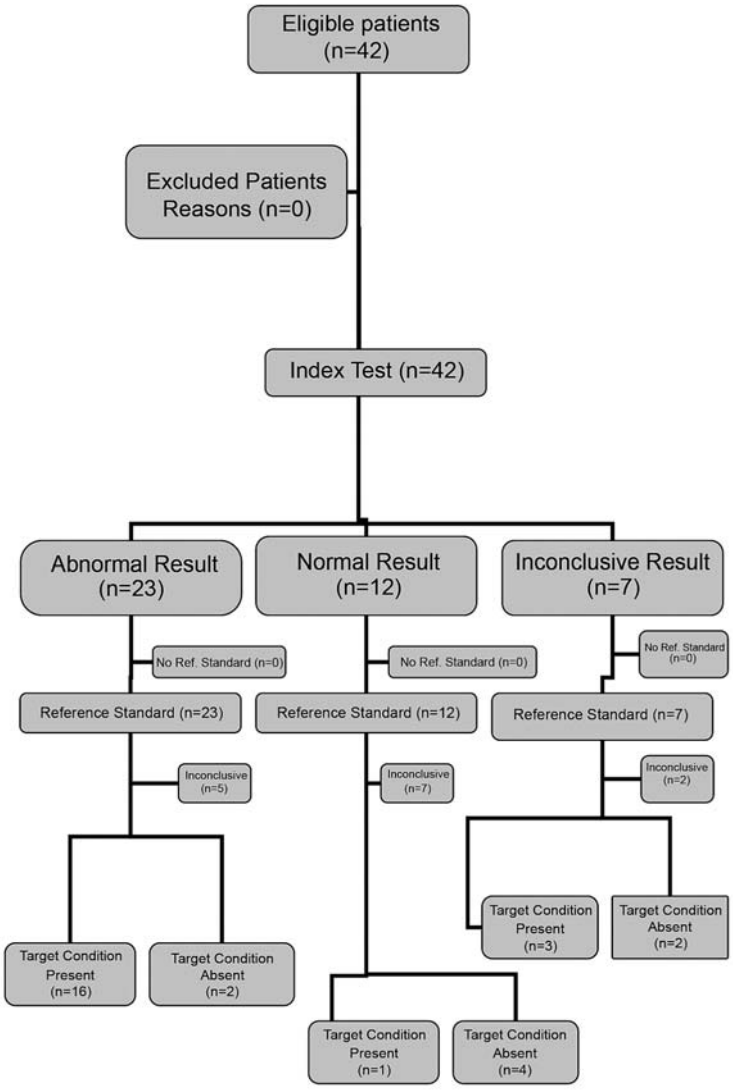

Figure 3 – *Flow diagram for intravesical prostatic protrusion on diagnostic accuracy.*

and diagnose male urinary obstructive problems. However, results are still variable and the small number of patients in this study renders further studies necessary for a final definite conclusion.

CONFLICT OF INTEREST

None declared.

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EDITORIAL COMMENT

Benign prostatic hyperplasia (BPH) belongs to the most common benign diseases in the aging men. The prevalence of histological BPH increases with age and appears in approximately 40% of men aged 51-60 years and in approximately 90% of men aged 81-90 years (1). With increasing life expectancy worldwide more men will have these histological changes in their prostate and the probability of seeking professional help will increase as well. It is doubtful if health care systems can support the financial burden associated with the assessment and treatment of BPH-related symptoms and conditions in the future. Therefore, every approach to make the assessment and treatment easier, faster, and cheaper is highly welcome. The authors of the appending article report about their attempt and introduce a new non-invasive test to a broader public (2).

The BPH disease is characterized by benign prostatic enlargement (BPE), bladder outlet obstruction (BOO), and lower urinary tract symptoms (LUTS). However, no clear correlations have been found between these three components and, therefore, each component has to be evaluated separately. Evaluation of BPE, by digito-rectal examination or transrectal ultrasound measurement, or LUTS, by history or questionnaires, is quick, cheap, easy, and without relevant morbidity. However, assessment of BOO has been more difficult until now. Only pressure-flow studies were able to detect and quantify bladder outflow resistance adequately. Urodynamic investigations are invasive, expensive, time-consuming, uncomfortable for the patients, widely unavailable, and necessitate a certain degree of education in terms of performance and interpretation of measurement results and artifacts. The morbidity of urodynamic measurements in men is in the range of 19% and includes dysuria, urinary tract infection, fever, bleeding, and acute urinary retention (3). There are even patients who died after urodynamic investigations because of urosepsis due to contaminated catheters (4). All of these factors are responsible that pressure-flow studies are only randomly performed. Therefore, there is a strong need to develop alternative techniques to measure BOO and to overcome the disadvantages of pressure-flow studies.

The article by Leonardo Reis and colleagues provides further evidence that ultrasound measurement of intravesical prostatic protrusion (IPP) is able to detect BOO in BPH patients quickly and non-invasively (2). Ultrasound machines belong to the standard armamentarium of urologists and are widely available. The IPP technique is easily applicable and the simple measurement of the distance between the bladder neck and the tip of the prostatic median lobe can qualify the patient as obstructed. IPP measurements were originally developed in Asia and results have also been limited to Asian patients (5). The authors of the current study investigated Latin-Americans with this new technique for the first time and could confirm that an IPP of 10 mm or more is a sensitive tool to detect BOO in patients from another part of the world (sensitivity 80%, positive predictive value 70%, likelihood ratio of positive test result 2.51). Therefore, no ethnical difference seems to exist and IPP measurements are of general value. The authors have to be congratulated to have presented a study, which was conducted according to all quality criteria of diagnostic accuracy tests.

Despite the achievements of the authors, the present study has to be classified as a pilot study to demonstrate the proof of principle. Only 42 patients were included in the trial which seems to be underpowered to draw general conclusions. The results are limited to BPH patients and other types of BOO cannot be studied with this technique (e.g. bladder neck stenosis, urethral strictures, or meatus stenosis). Furthermore, specificity of IPP measurements is low (68%) and, therefore, patients with an IPP distance of less than 10 mm cannot be safely classified as unobstructed. Until now, only ultrasound measurements of detrusor or bladder wall thickness have shown to have a high sensitivity (83%), specificity (95%), and likelihood ratio of a positive test result (17.6) which are superior to all other classic non-invasive tests for BOO evaluation (uroflowmetry, measurement of postvoid residual urine or prostate volume) (6). Future studies with adequate power, a multicenter and prospective evaluation approach, and the comparison of IPP with other non-invasive tests are necessary to judge the value of this emerging technique correctly.

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EDITORIAL COMMENT

The concept of measuring intra-vesical protrusion of the prostate by ultrasound as a surrogate for bladder outflow obstruction is not a new one (1). The current paper provides further confirmation of the utility of this measurement and suggests that protrusion of 10 mm or greater correlates well with urodynamic obstruction (2). Along with other ultrasound-derived measurements such as post-void residual, bladder weight, bladder wall thickness, detrusor resistive index, prostatic weight, appearance, and velocity-flow video-urodynamics, this measurement was developed to prevent the need for, and the morbidity of, multi-channel pressure-flow studies (3). The plethora of different techniques suggests that none is perfect and in fact, in individual patients, cannot yet replace 'invasive' testing. Also, the true morbidity of these studies may not be all that significant (4).

On balance, while being suggestive of bladder outflow obstruction, measuring intra-vesical protrusion of the prostate by either abdominal or trans-rectal ultrasound is likely to remain an interesting but inconclusive finding!

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EDITORIAL COMMENT

Benign prostatic hyperplasia (BPH) is one of the most common diseases in elderly men. Bladder outlet obstruction (BOO) should be well discriminated from BPH to better understand the pathology-physiology of this disease. BPH may lead to benign prostatic enlargement (BPE), BOO and lower urinary tract symptoms (LUTS). BOO might be or not be present in patients with BPH. On the other hand BOO may cause secondary bladder dysfunction and furthermore upper urinary tract damage. For these reasons, patients with BPH must be evaluated not only for LUTS but also for BOO.

Up to now, urodynamic evaluations have been accepted as the only objective method of assessing BOO. There is a lot to say about the disadvantages of pressure flow studies (PFS) which has been well described in the literature. It is invasive, uncomfortable, time-consuming and expensive. Moreover, there is a need for urethral catheterization, which causes partial obstruction during micturition and confers the undesirable consequences of possibly introducing infection and discomfort that may alter the micturition reflex. Hematuria, urinary tract infection and difficulty in urination are the side effects of this procedure (1). To avoid these disadvantages, in the last decade, the development of non-invasive evaluations for BOO has been the subject of numerous publications. Uroflowmetry, post-void residual urine, prostate volume (PV), bladder wall thickness and finally measurement of intravesical protrusion of the prostate (IPP) are used to estimate BOO in men with BPH. The rise of the idea that IPP might be a predictor of BOO can be explained by few words. IPP is caused by the enlarging lateral lobes and the median lobe, and may lead to dyskinetic movement of the bladder during voiding. This would cause more obstruction than if there were no protrusion and just bilateral lateral lobes, as the strong bladder contraction could force open a channel between the lobes.

A few investigators have considered IPP to be a useful predictor for evaluating BOO and bladder function. Chia et al. have suggested that IPP significantly correlates with BOO and is a better parameter than the other non-invasive parameters (2). Lim et al. have confirmed this study by comparing PV, prostate specific antigen (PSA) and IPP in the evaluation of BOO and IPP was the strongest predictor in this prospective study (3). In another study, it has been suggested that IPP degree is negatively correlated with Qmax and of patients with higher IPP degree, there is a higher presence of bladder overactivity and low bladder compliance.

Reis et al. provide a prospective data aiming to demonstrate whether the IPP of the prostate might replace the urodynamic evaluation, which is accepted to be an invasive and uncomfortable procedure (4). Despite the small number of patients, the results are in favor of detecting IPP might be enough to demonstrate the BOO without the need to urodynamic evaluation and comparable with the earlier investigations. These statistically significant results may lead to further investigations and force the urologists to replace measuring IPP instead of performing pressure flow studies in selected patients.

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REPLY BY THE AUTHORS

Although the current and others up-to-the-minute papers provide further confirmation of the utility of intravesical prostatic protusion (IPP) measurements and suggests that protrusion of 10 mm or greater correlates well with urodynamic obstruction, it is a limited method to accurately define obstruction (1). There are patients obstructed without IPP and unobstructed ones presenting with more than 10 mm IPP. By the other side, IPP measurements are still a science under development, and perhaps IPP measurements are more precise in determining the best patients for surgical treatment, once they were proved obstructed.

Intravesical protrusion seems to corroborate with urinary obstruction thought a "valve ball" mechanism in which the prostate's lateral and medium lobes interfere on the complete opening of the vesical neck during voiding. This way, the pharmacological response to alpha-blockers could be predicted by the IPP method (2). Men with an intravesical prostatic protrusion of 10 mm or less, compared to those with a larger intravesical prostatic protrusion, were 6 times more likely to have a successful trial without catheter after acute urinary retention (3).

Most patients in our present study presenting IPP of 10 mm or greater showed no response to alpha blockers and were submitted to surgical treatment in contrast to that presenting IPP of less than 10 mm. We are now conducting new prospective studies to prove the accuracy of this method to predict pharmacological treatment outcomes and surgical treatment suggestions.

Another minimal invasive method utilizes ultrasound measurements of detrusor or bladder wall thickness or weight. This method is inconsistent in technical standardization and there is no consensus among authors about its value (4). Bladder parameter to define obstruction is possibly not the best one, because it denotes the obstruction repercussion and imbalance in the detrusor function, which is much more than obstruction and probably occurs latter in the bladder neck obstruction process.

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