

Evaluation of non-invasive diagnostic methods in male lower urinary tract symptoms using pressure-flow studies

Erkek alt üriner sistem semptomlarında non-invaziv tanı metotlarının basınç akım çalışması kullanarak değerlendirilmesi

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ABSTRACT

OBJECTIVE: This study aims to determine the importance of non-invasive diagnostic parameters such as intravesical prostatic protrusion (IPP), bladder wall thickness, prostate volume, and uroflow in the detection of bladder outlet obstruction using pressure-flow studies.

MATERIALS and METHODS: Pressure flow studies were performed on patients who presented to the outpatient clinic with lower urinary tract symptoms. Patients were divided into two groups, those with and without obstruction, according to the Bladder Outlet Obstruction Index (BOOI) parameter. Differences between the two groups were evaluated in terms of prostate volume, IPP, Bladder Wall Thickness (BWT), uroflow peak flow rate (Q_{max}), post-void residual urine volume and Bladder Outflow Obstruction Number (BOON) parameters.

RESULTS: There was a significant difference in prostate volume, IPP, BWT, uroflow peak flow rate, post-void residual urine volume and BOON parameters between the obstructed and non-obstructed groups. In the ROC analysis performed to predict the obstructed patient, the ideal cut-off value for prostate volume was determined as 71.5 ml, for IPP 10.5 mm, for BWT and 5.3 mm. Bladder outlet obstruction index parameter was positively correlated with prostate volume, IPP, BWT, residual volume and IPSS. There was a negative correlation with Q_{max}.

CONCLUSION: In the ROC curve for predicting obstructed patients, IPP showed a higher AUC (area under the curve) compared to prostate volume and BWT, indicating IPP's superior predictive value for obstruction. Uroflow parameters are also significant predictors, albeit less so than IPP. Increasing obstruction scores correlate with higher levels of prostate volume, IPP, uroflow peak flow, and IPSS, providing insights into the severity of obstruction.

Keywords: bladder outlet obstruction, benign prostate enlargement, non-invasive diagnosis

ÖZ

AMAÇ: Mesane çıkım tıkanıklığının tespiti günümüzde altın standart olarak basınç-akım çalışması ile yapılmaktadır. Fakat basınç-akım çalışmalarının invaziv bir işlem olması yaygın kullanımını sınırlamaktadır. Biz bu çalışmada İntrevezikal prostatik protrüzyonu (IPP), mesane duvar kalınlığı, prostat hacmi, üroflow gibi non-invaziv tanılabilir parametrelerin mesane çıkım tıkanıklığının tespitindeki önemini basınç-akım çalışmalarını kullanarak tespit etmeyi amaçlamaktayız.

GEREÇ ve YÖNTEMLER: Alt üriner sistem semptomları ile polikliniğe başvuran hastalara basınç akım çalışmaları yapıldı. Hastalar, Mesane Çıkış Obstrüksiyonu Endeksi (BOOI) parametresine göre obstrüksiyonu olan ve olmayanlar şeklinde iki gruba ayrıldı. İki grup arasındaki farklar prostat hacmi, IPP, Mesane Duvar Kalınlığı (BWT), üroflow zirve akış hızı (Q_{max}), işeme sonrası rezidüel idrar hacmi ve Mesane Çıkış Obstrüksiyon Numarası (BOON) parametreleri açısından değerlendirildi.

BULGULAR: Obstrüksiyonu olan ve olmayan gruplar arasında prostat hacmi, IPP, BWT, üroflow max akış hızı, işeme sonrası rezidüel idrar hacmi ve BOON parametrelerinde anlamlı fark bulundu. Obstrüksiyonu tahmin etmek için yapılan ROC analizinde, prostat hacmi için ideal kesim değeri 71,5 ml, IPP için 10,5 mm, BWT için 5,3 mm olarak belirlendi. Mesane çıkım tıkanıklık indeksi parametresi prostat hacmi, IPP, BWT, rezidüel hacim ve IPSS ile pozitif korelasyon gösterdi. Q_{max} ile negatif korelasyon bulundu.

TARTIŞMA: Obstrükte hastayı öngörmede yapılan ROC eğrisinde AUC'nin IPP'de prostat volümü ve MDK'a olan görece fazlalığı daha değerli obstrüksiyon öngörücüsü olduğunu göstermektedir. Çalışmamızda üroflow parametreleri için AUC'nin IPP kadar olmasa da kayda değer yükseklikte obstrüksiyonu öngörebilecek parametreler olduğu söylenebilir. Obstrüksiyon skoru arttıkça prostat hacmi, IPP, üroflow tepe akımı, IPSS nin korele olarak artması obstrüksiyonun şiddeti hakkında yorum yapmamızı sağlayacaktır.

Anahtar Kelimeler: mesane çıkım tıkanıklığı, benign prostat büyümesi, non-invaziv tanı

INTRODUCTION

Lower urinary tract symptoms (LUTS) are widespread among the general population, particularly in males, where age-related hormonal alterations often lead to prostatic glandular enlargement. This hypertrophy frequently precipitates bladder outlet obstruction (BOO). The incidence of Benign Prostatic Enlargement (BPE) escalates with advancing age, affecting approximately 50% of men by the age of 60 and 80% by the age of 80.^[1]

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Benign prostatic enlargement primarily manifests through voiding phase symptoms of LUTS. The severity of symptoms is quantified using the International Prostate Symptom Score (IPSS). The gold standard for BOO detection is pressure-flow studies, but their invasive nature, requirement for specialized equipment and personnel, and patient anxiety limit their widespread use. Non-invasive diagnostic options for BOO include uroflowmetry peak flow rate, prostate volume, intravesical prostatic protrusion (IPP), bladder wall thickness (BWT), detrusor wall thickness, and the penile cuff test. Research continues into refining these parameters and exploring novel diagnostic approaches.^[2]

Various nomograms have been developed so far for the diagnosis of BOO. Among these, the International Continence Society (ICS) nomogram is most used. In this nomogram, the Bladder Outlet Obstruction Index (BOOI) formula is used. In this formulation, values between 20 and 40 are considered the gray zone. Below 20 is considered non-obstructed and above 40 is considered obstructed.

This study aims to evaluate patients as obstructed or non-obstructed and determine the severity of BOO by using diagnostic methods such as IPSS, IPP, BWT, prostate volume, and uroflowmetry. In fact, although studies have been conducted on the importance of these diagnostic methods before, we aim to predict obstruction with an easier formulation by using regression analysis.

MATERIAL and METHODS

The study received ethical approval under decision number 2021-11/01 from the Ethics Committee of Cumhuriyet University. It was designed as a single-center, cross-sectional study and conducted in accordance with the criteria of the Helsinki Declaration.

Male patients who applied to the outpatient clinic with LUTS between 2021/09 and 2022/06 and volunteered to participate in the study after being informed were included in this prospectively designed study. Written consent of the patients was obtained. Patients completed the IPSS questionnaire and the results were recorded.

Prostate volume, IPP, and BWT were measured with suprapubic USG. Measurements were made on a 150–250 ml filled bladder. Intravesical prostatic protrusion was measured as the distance between the bladder neck and the prostate midline apical extension. Intravesical prostatic protrusion measurement results were grouped and recorded as <5 mm, 5–10 mm, and >10 mm according to the previously

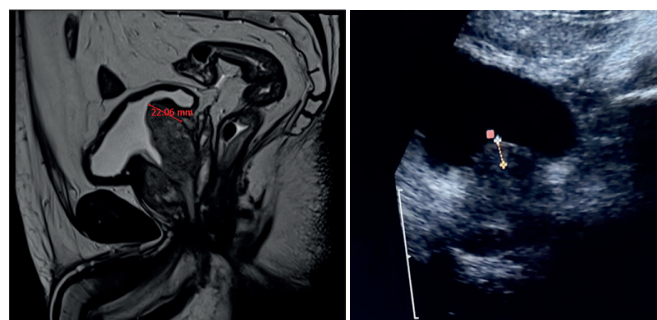


Figure 1. Magnetic resonance and ultrasonography images of intravesical prostatic protrusion.

defined grading system.^[3] For standardization, all measurements were made by a single physician (Figure 1).

Free flow uroflowmetry studies of the patients were performed under outpatient clinic conditions. Peak flow (Q_{max}) and voided volume values were recorded. Post-void residual volumes were measured by suprapubic USG.

Bladder Outlet Obstruction Number (BOON), which is a parameter to predict patients' non-invasive bladder outlet obstruction and was first developed by van Venrooij et al., was calculated. Bladder outlet obstruction number was calculated using the formula: prostate volume (cc) - 3 × Q_{max} (ml/s) - 0.2 × mean voided volume (ml). Below -20 was considered non-obstructed and above -20 was considered obstructed.^[4]

Before treatment, urodynamic studies were performed within the indications specified in the European Urology Guideline. Bladder outlet obstruction index scores of the patients were determined with the P_{det}@Q_{max} - 2 × Q_{max} (ml/s) formula. Patients with a BOOI score of 40 and above were considered obstructed, and patients with a BOOI score below 40 were considered non-obstructed (Patients suspicious of obstruction were considered non-obstructed as in previous studies).

Inclusion and Exclusion Criteria

Patients with suspicious digital rectal examination findings, high PSA levels, and malignant prostate biopsy results were not included in the study. Patients with pathological urinary USG findings (diverticula, tumor, stone, etc.), patients who have previously undergone urological surgery that may affect LUTS, and patients with findings suggestive of neurogenic bladder.

Statistical Analysis

The data were analyzed using IBM Statistical Package for Social Sciences (SPSS) program version 23.0 (IBM Inc, Chicago, IL, USA). Due to the data's non-normal distribution,

non-parametric tests were employed. Specifically, the Mann-Whitney U test compared two independent groups, while the Kruskal-Wallis test analyzed variance among more than two independent variables. A post hoc test was conducted to compare variables between groups. Receiver operating characteristic (ROC) analysis was employed with focal variables to predict obstruction. Spearman correlation analysis was utilized due to the absence of parametric variables. Given the binary nature of the categories, the binomial logistic regression method was employed to determine appropriate group allocation. G-power analysis was performed according to Cohen standards ($d=0.5$), with an error level of $\alpha: 0.05$ (95% confidence) and a power of $\beta: 0.80$. According to the analysis results, it was determined that taking 50 samples was sufficient for the study to be statistically significant. All tests were conducted at a 95% confidence level.

RESULTS

Out of the initial 79 patients recruited for the study, 9 declined participation, and 5 refused the urodynamic examination. Additionally, urodynamic artifacts were encountered in 3 patients, while catheter dislodgement prevented measurement of bladder pressure at maximum peak flow in another 3 patients. Consequently, these individuals were excluded from the study, leaving 59 patients to proceed with the research (Figure 2).

The mean age of the patients was 66.8 ± 7.3 years. The youngest individual participating in the study was 51 years old and the oldest individual was 80 years old. The average PSA value of the patients was 2.7 ± 2.1 ng/ml and the average creatinine value was 1.11 ± 0.5 mg/dl.

Bladder outlet obstruction index values of the patients showed that 14 were non-obstructed ($BOOI < 20$), 11 were suspicious for obstruction ($20 < BOOI < 40$), and 34 were obstructed ($BOOI > 40$). Patients suspicious of obstruction were considered non-obstructed as in previous studies. The BOON value of the patients measured without using a pressure-flow study demonstrated that 13 patients were non-obstructed ($BOON < -20$) and 46 patients were obstructed ($BOON > -20$).

Patients were divided into two groups, obstructed and non-obstructed, according to BOOI. There was no significant difference between the ages of the patients ($p=0.46$). A significant difference was observed between the prostate volume, IPP, BWT, Qmax, residual volume, IPSS, and BOON values of the two groups ($p=0.001, <0.001, 0.004, 0.004, 0.01, 0.003, 0.003$ respectively)(Table 1).

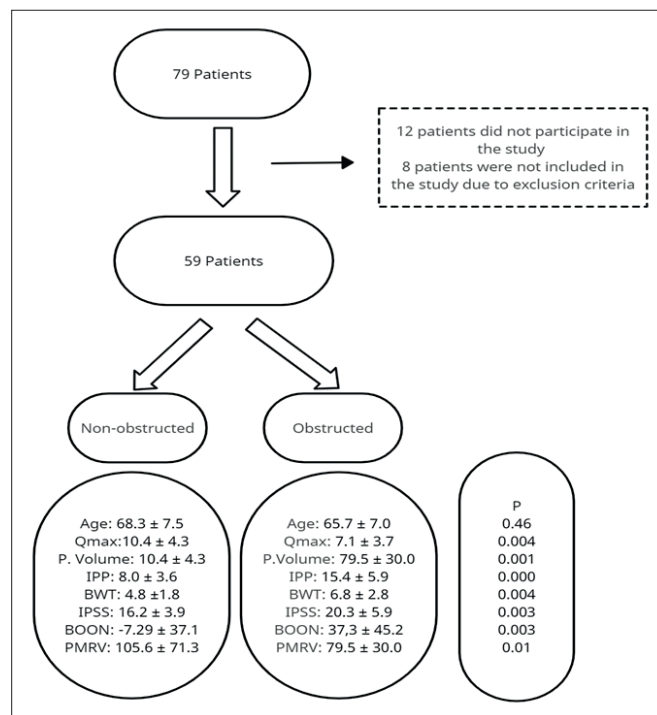


Figure 2. Distribution of patients participating in the study (P. Volume: Prostate volume).

Table 1. Comparison of mean values of obstructed and non-obstructed groups

	Non-obstructed (n=25) Mean \pm std. dev.	Obstructed (n=34) Mean \pm std. dev.	P
Age	68.3 ± 7.5	65.7 ± 7.0	0.46
Qmax (ml/sn)	10.4 ± 4.3	7.1 ± 3.7	0.004
Residual Volume (ml)	105.6 ± 71.3	181.9 ± 89.8	0.01
Prostate Volume (ml)	48.4 ± 25.6	79.5 ± 30.0	0.001
IPP (mm)	8.0 ± 3.6	15.4 ± 5.9	<0.000
BWT (mm)	4.8 ± 1.8	6.8 ± 2.8	0.004
IPSS	16.2 ± 3.9	20.3 ± 5.9	0.003
BOON	-7.29 ± 37.1	37.3 ± 45.2	0.003

In the ROC analysis used to predict obstruction according to the BOOI parameter, the best cut-off values for free uroflow peak flow and post-micturition residual volume were found to be 12.6 ml/sec and 105.2 ml, respectively, p values 0.041 and 0.031. The AUC for these values was found to be 0.761 and 0.719, respectively (Table 2). A mirror image was taken to prevent Qmax from being a negative graph in the ROC curve (Figure 3). Sensitivity, specificity, positive and negative predictive values and LHR for these cut-off values are as shown in the table (Table 2).

Table 2. Statistical data for BWT, IPP prostate volume and uroflowmetry

Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	AUC	LHR	Cutpoint	p
P. Volume (mm)							
67.6%	68.0%	74.2%	60.7%	0.754	2.8	71.5	0.022
IPP (mm)							
79.4%	68.0%	77.1%	70.8%	0.831	4.0	10.5	0.008
BWT (mm)							
61.8%	72.0%	75.0%	58.1%	0.723	3.73	5.3	0.031
Qmax							
84%	65%	46.51%	100%	0.761	3.6	12.6	0.041
Residual volume							
72%	75%	78.3%	68.2%	0.719	2.8	105.2	0.031

PPV: positive predictive value, NPV: negative predictive value, AUC: area under the curve, LHR: likelihood ratio.

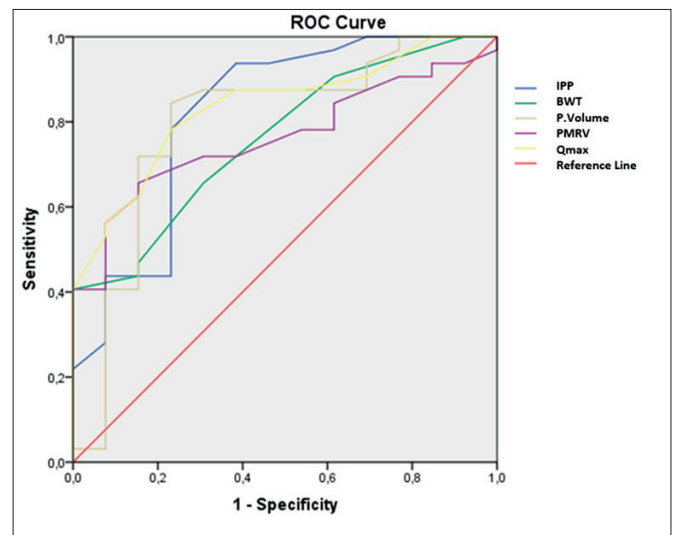
Table 3. Analysis result group assignment table

		Prediction	
		Non-obstructed	Obstructed
Actual	Non-obstructed	18	7
	Obstructed	5	29

In the ROC analysis used to predict obstruction according to the BOOI parameter, the best cut-off values for free uroflow peak flow and post-micturition residual volume were found to be 12.6 ml/sec and 105.2 ml, respectively, p values 0.041 and 0.032. The AUC for these values was found to be 0.761 and 0.719, respectively (Table 3). A mirror image was taken to prevent Qmax from being a negative graph in the ROC curve (Figure 3). Sensitivity, specificity, positive and negative predictive values and LHR for these cut-off values are as shown in the table (Table 3).

Intravesical prostatic protrusion groups were divided into groups 1, 2, and 3, respectively: <5 mm, 5–10 mm, and <10 mm. There was no notable difference observed between group 1 and group 2 (p=0.549) (Post hoc ANOVA). The difference between group 1 and group 3 reached statistical significance (p=0.006). The difference between group 2 and group 3 was also statistically significant (p=0.008).

Bladder outlet obstruction index was significantly positively correlated with prostate volume, IPP, BWT, IPSS, residual volume, and BOON. The p-values were <0.001, <0.001, <0.001, 0.029, 0.041, and 0.001, respectively. Spearman correlation coefficients were r=0.667, 0.716, 0.610, 0.484, 0.397, 0.510, respectively. There was a significant negative correlation between BOOI and Qmax (p=<0.001, r=0.554).

**Figure 3.** Receiver operating characteristic curve used for BWT, IPP, prostate volume, uroflowmetry, and residual volume.

Logistic regression analysis was used to evaluate the efficacy of non-invasive methods in detecting obstruction among patients. The model, integrating IPP, BWT, prostate volume, Qmax, residual volume, and IPSS variables, identified IPP and Qmax as key predictors of obstruction presence. To address multicollinearity and enable incorporation of multiple variables, variable selection was performed prior to regression analysis. Subsequently, the Backward method was employed to determine variable significance. Results revealed that higher Qmax values were associated with classification into the non-obstructed group, while elevated IPP values were indicative of inclusion in the obstructed group.

The mathematical model is represented as follows. A result below 1.5 indicates inclusion in the non-BOO group,

while a result exceeding 1.5 indicates inclusion in the BOO group. Proximity to the threshold value enhances decision accuracy.

$$[1,2]=0.333\cdot(\text{IPP})-0.358\cdot(\text{Qmax})$$

The numerical accuracy of the prediction values obtained as a result of logistic regression was calculated. However, positive and negative predictor values must also be calculated. Table 3 shows the accuracy of the actual values and the predicted values.

It was observed that 18 of the 25 patients included in the non-BOO group were predicted to be non-obstructed. Therefore, the specificity of correctly identifying a patient in the non-BOO group as non-obstructed was calculated as 72%. Similarly, 29 of the 34 patients in the group who actually had BOO were predicted to be obstructed. Therefore, the sensitivity of correctly identifying a patient with BOO as obstructed was calculated as 85.3%. These results show that the mathematical model obtained in detecting patients has a higher success rate than all non-invasive methods in predicting obstruction.

DISCUSSION

In urology clinical settings, pressure-flow studies offer crucial insights for diagnosing obstruction and guiding treatment decisions. However, due to their invasive nature, research persists on non-invasive diagnostic approaches, including prostate volume, IPP, BWT, free uroflowmetry parameters, and IPSS. The division of patients into obstructed and non-obstructed groups based on BOOI, along with significant parameter differences between these groups, underscores the utility of non-invasive methods in obstruction prediction. Moreover, patient stratification according to the IPP grading system revealed significant differences, particularly in the group with IPP of 10 mm and above, supporting the 10.5 mm cut-off value identified in this study.

Qmax and post-void residual urine volume were shown to be important parameters in predicting obstruction with high AUC and high LHR rates. The AUC of BWT was not found to be superior to Qmax and post-void residual urine volume and gave similar results.

BOON, designed to predict obstruction without utilizing pressure-flow studies, incorporates prostate volume, Qmax, and voided volume. It also demonstrates significant differences between groups, indicating its importance in providing relevant data. A high AUC of 0.775 was observed for predicting obstructed patients, highlighting its

significance in obstruction prediction. Typically, according to BOON, levels above -20 are considered indicative of obstruction. However, the finding of 9.6 in this study may be attributed to data collection from patients with LUTS, representing a limitation of the study.

Bladder wall thickness exhibits comparable diagnostic accuracy to free uroflowmetry parameters, boasting a high AUC in predicting obstructed patients. In Manieri et al.'s study, data were collected at a bladder volume of 150 ml, revealing a correlation between BWT and pressure flow studies, with the optimal cut-off value determined to be 5 mm. Consequently, BWT demonstrates greater diagnostic value than uroflow parameters.^[4] In our study, significant correlation was observed between BWT and BOOI scores, yet its diagnostic predictions were found to be akin to uroflow parameters.

In the study by Kessler et al., a weak to moderate correlation was identified between detrusor wall thickness (DWT) and pressure-flow parameters.^[5] The study determined a DWT cut-off value of 2.9 mm for diagnosing BOO, with a sensitivity of 43%, specificity of 100%, and a high AUC of 0.88. Our study opted for bladder wall thickness (BWT) over DWT due to several reasons. Measuring DWT is comparatively more challenging than BWT, particularly with the low to medium quality ultrasound devices typically used in outpatient clinic settings. Moreover, BWT represents a more practical examination option in daily outpatient clinic conditions.

Some articles reach negative conclusions about BWT. A hundred and eight patients were included in the study conducted by Blatt et al. There was no significant difference in BWT between the obstructed and non-obstructed groups ($p=0.309$). It was stated in the study that BWT measurement cannot be an alternative to pressure-flow studies.^[6] On the contrary, in the study conducted by Bright et al., it was stated that BWT and DWT could be non-invasive clinical parameters in the detection of BOO. However, the main problem in the studies can be stated as the methodological differences in the studies, such as the lack of standardization on which bladder capacity to measure.^[7] In our study, BWT was found to be predictive of BOO at a rate similar to uroflow parameters and a lower rate than IPP.

In the ROC curve for predicting obstructed patients, IPP showed a superior AUC compared to prostate volume and BWT, highlighting its superior predictive capability for obstruction. Despite not reaching the same level as IPP and BWT, the significantly higher AUC for uroflow parameters emphasizes their predictive capacity for obstruction. Furthermore, as the BOOI score increased, data

obtained from imaging, free uroflowmetry, and symptom scoring also increased, indicating a correlation and providing insights into the severity of obstruction.

There are various studies evaluating the correlation between IPP and BOOI. In our study, a significant correlation was found with $r=0.716$. Similarly, and Shin et al. found the correlation as 0.551, Huang et al. as 0.469, Lee et al. as 0.608, and Franco et al. as 0.491.^[8-11]

Although IPP is classified into 3 levels, the best cut-off value in predicting obstruction was found to be 10.5 mm in our study. Reis et al. found this value to be 5 mm, Franco et al. to 12 mm, Shin et al. to 5.5 mm. Sensitivity and specificity vary between studies.^[11,12] All these studies show that IPP is important in predicting obstruction. However, variable IPP cut-off, sensitivity, and specificity values indicate a lack of standardization among studies. There is a need to collect data from randomized controlled studies and collect more patient data.

In our study, all non-invasive diagnostic methods underwent regression analysis, employing a systematic approach to eliminate variables with minimal impact on BOO or lesser influence compared to others, even if they shared the same directional effect. Results showed that higher Q_{max} values correlated with increased assignment to the non-BOO group, while elevated IPP values were associated with inclusion in the BOO group. This unique formulation, specific to our study, aims to furnish clinicians with a predictive tool for BOO detection and foster further research in this area.

CONCLUSION

Pressure-flow studies are regarded as the gold standard for diagnosing bladder outlet obstruction (BOO), but their invasive nature presents challenges, requiring expertise, specialized equipment, and inducing patient apprehension. Hence, current research emphasizes non-invasive diagnostic methods. Among these, IPP provides valuable insights, while BWT shows comparable BOO detection capabilities to uroflowmetry parameters. Inconsistent data distribution across studies underscores the need for standardized data collection, prompting randomized controlled trials with larger patient cohorts. Despite non-invasive parameters not entirely predicting obstruction, their swift measurement, ease of use, and suitability for routine urology practice offer advantages. Moreover, the derived parameter from the study serves as a practical tool for obstruction prediction.

Ethics Committee Approval

The study was approved by Cumhuriyet University Faculty of Medicine Ethics Committee. (date and number of approval: 11.09.2021/2021-11/01).

Peer-review

Externally peer-reviewed.

Conflict of Interest

No conflict of interest was declared by the authors.

Financial Disclosure

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