Evaluation of non-invasive tests as diagnostic tools in assessment of bladder outlet obstruction severity in men with anterior urethral stricture

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Introduction The aim of this article was to evaluate non-invasive tests, which were typically used in preoperative diagnosis male patients with anterior urethral strictures in the assessing of the urethral resistance caused by urethral occlusion.

Material and methods The 63 adult male with confirmed urethral stricture and age below 55 years old were enrolled in the study. Data obtained from non-invasive tests such as uroflowmetry (UF), ultrasound examination (USG), and questionnaires such as from The International Prostatic Symptom Score (IPSS), and The Patient-Reported Outcome Measure for Urethral Stricture Surgery (USS-PROM) were analyzed.

Results Among all analyzed non-invasive tests, bladder wall thickness (BWT) showed the highest correlation with the degree of urethral occlusion described as percentage of preserved urethral lumen ($r = -0.70$; $p <0.0001$). UF variables presented medium degree of correlation, with maximum flow rate (Qmax) as the best parameter ($p = 0.45$; $p = 0.0005$). Results from both questionnaires were not shown any correlation with the severity of the urethral stricture. Multiple linear regression analysis showed that only BWT was an independent predictor in detection degree of urethral occlusion.

Conclusions UF and USG seem to be useful additional diagnostic tools in assessment severity of urethral occlusion in men suffering from anterior urethral stricture. Among them, USG had the highest correlation with degree of urethral occlusion.

Key Words: urethral stricture ‹› USG ‹› uroflowmetry ‹› non-invasive tests

INTRODUCTION

Urethral stricture is generally caused by fibrosis of the urethral epithelial tissue and corpus spongiosum leading to stenosis of the urethral lumen, which progressively narrows, varying degrees of obstruction occurs. However, the patients' symptoms are not urethral stricture-specific. Most of the cases include weak urinary stream, hesitancy, terminal dribbling, and the feeling of incomplete emptying, which can also be caused by conditions such as benign prostatic obstruction (BPO). On the other hand, most of these symptoms are directly related to decreased urethral diameter. Based on computer models, it has also been proved that a decreased functional urethral diameter, in contrast with the stricture length and location, is the most important factor linked to a decrease in urine flow and increased bladder pressure [1, 2].

Thus, one of the primary goals of a preoperative diagnosis in a patient with urethral stricture is assessing the degree of urethral occlusion to determinate the risk of urinary tract damage above the narrowing place caused by increasing intravesical pressure. Invasive imaging studies: retrograde cystourethrography (R-CUG), voiding cystourethrography (V-CUG), sonourethrography (SUG), and urethroscopy are basic tools usually used by urologists [3]. Disadvantage of these tests are often long time from order to performance. Less invasive tests, such as uroflowmetry (UF), ultrasonography (USG) or questionnaires, can give additional, indirect information about the presence and severity of urethral damage, often during first contact with urologist. But till now, the correlation between degree of urethral stricture and non-invasive tests was not analyzed.

Primary goal of our study was to assess the correlation between the non-invasive tests and urethral occlusion (described as minimal area of strictured urethra and percent of preserved urethral lumen) in group of male patients with anterior urethral stricture. Secondary goal was the comparison of ultrasonographical measurement of bladder wall between analyzed group and healthy men, and identifying predictors that may be used in determining the degree of urethral narrowing.

MATERIAL AND METHODS

The single-center prospective study was conducted from March 2018 to April 2020. The local independent Ethic Committee has approved it. Written informed consent was obtained from every patient included in the study.

Preliminary, 128 Caucasian adult male patients with the anterior urethral stricture confirmed in SUG, R-CUG and urethroscopy were qualified for the study. The study exclusion criteria were age above 55 years, complete urethral occlusion, suprapubic catheter (present or in the history), previous urethral dilatation, BPO and/or overactive bladder (OAB) diagnosis, the history of bladder cancer and/or previous bladder surgery, meatal stenosis, history of urethral stricture duration shorter than 3 months and active cystitis.

Patients who did not meet the inclusion criteria were excluded from the study (n = 65).

The same urologist performed all non-invasive tests. Every patient enrolled to the study had performed UF (analyzed data: maximal flow rate [Qmax], average flow rate [Qav] and ΔQ [Qmax-Qav]) and USG (analyzed data: bladder wall thickness [BWT], and detrusor wall thickness [DWT]). Due to previous study confirmed that SUG better estimate of stricture diameter than the R-CUG, results this examination was used as a reference [4]. Moreover, to determinate the clinical symptoms of urethral stricture, used The International Prostatic Symptom Score (IPSS), and The Patient-Reported Outcome Measure for Urethral Stricture Surgery (USS-PROM) questionnaires. The questionnaires were completed after admission to the Clinic, at the latest on day of surgery.

Sonourethrography

The sonourethrography (SUG) was performed according to the previously well-described scheme [5]. To assess the severity of the stricture, the diameter was measured in two places: the narrowest of a stenosed urethra, and the other one in the healthy area (in the penile or bulbar part of the urethra, depending on the location of the stricture) (Figure 1A). Measurements were performed on the cross-

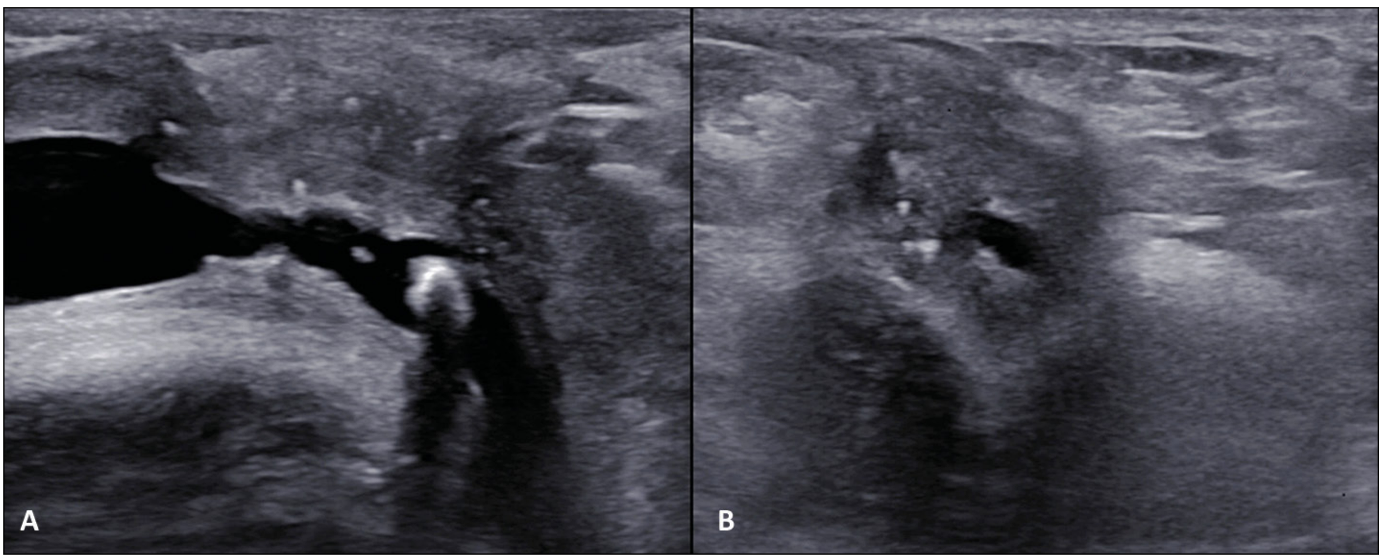

Figure 1. *Stricture in bulbar part of urethra.* **A**, *Longitudinal view. Additionally, into the urethral lumen is presented a stone.* **B**, *Transverse view (in the narrowest place of stricture).*

section of the urethra (Figure 1B). Calculations used the mathematical formula for the area of a circle ($\pi(\text{diameter}/2)^2$). The results were reported in square millimetre (mm^2) and percentages of the preserved urethral diameter and urethral area.

Ultrasonographical examination of urinary bladder

The bladder wall assessment was performed after retrograde filling the bladder with a minimum of 300 mililiter (ml). A BK Medical Flex Focus 800 equipped with a 12-18 MHz linear transducer was used. The array was positioned suprapubically in a horizontal direction. The bladder wall was observed as a three-layer linear structure, moving during breathing, just below the rectus abdominis muscle's posterior fascia. The bladder detrusor was presented as an internal, hypoechogenic structure, surrounded by two hyperechogenic layers (adventiva and mucosa, respectively) (Figure 2). The measurements were performed on the anterior wall. The results were reported as a mean of three measurements. Additionally, to correlation with analyzed group, created control group consisted of 50 men with age below 55 years old and without symptoms of bladder obstruction (inclusion criteria: Qmax >15 ml/sec and IPSS score <8 pts) and without urethral stricture confirmed in SUG.

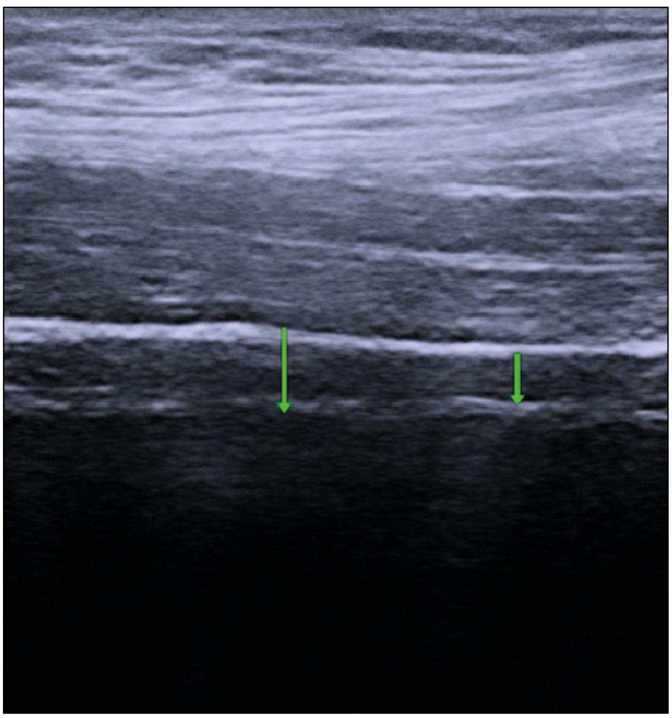

Figure 2. *Ultrasonographical assessment of bladder wall (arrow on the left – bladder wall thickness, arrow on the right – detrusor wall thickness).*

Uroflowmetry

The examination was performed just after the completion of the sonographical examination (with 300 ml as minimal bladder volume). A minimal voided volume was 150 ml. The study was performed on a Medtronic Duet Logic G2 device.

Statistical analysis

Statistical data processing was carried out using GraphPad Prism 6.05 (GraphPad Software Inc., San Diego, CA, USA) and Statistica 13 (StatSoft Inc., Tulsa, OK, USA). Descriptive variables were reported as mean and range. For evaluation of normality equality of variances, Shapiro-Wilk test was used. The Spearman's correlation analysis was used to determine the correlation between the analyzed groups. A comparison of continuous variables was carried out by an independent t-test for parametric variables, and the Mann – Whitney U-test for nonparametric variables. Forward stepwise multiple linear regression analysis was used to define independent predictors for analyzed changes. Statistical significance was considered as $p < 0.05$.

RESULTS

Finally, 63 men with an anterior urethral stricture and meeting inclusion criteria were included into the study. Demographic characteristic were recorded in the database, and shown in Table 1.

The most frequent localization of stricture was bulbar urethra (n = 33; 52%), and the most frequent etiology was iatrogenic (n = 31; 49%). Between all used procedures, urethroplasty with use buccal mucosa graft was the most frequent (n = 33; 52%).

The mean diameter and area of the urethra in the narrowest place of the stricture, measured in SUG, were 1.85 mm (0.8–4.4) and 3,1 mm^2 (0.5–15), respectively. It represented 22% (8.7–44.8%) of an intact diameter and 5.58% (0.76–20.1%) of a healthy urethral lumen. The mean bladder volume during USG was 346 (310–369) ml. The results of non-invasive tests are presented in Table 2.

The correlation coefficients for all the analyzed variables are presented in Table 3.

Among all the analyzed non-invasive tests, ultrasonographical assessment of the bladder wall showed the highest correlation with the degree of urethral damage, both when occlusion was reported as a single measurement and as a percentage of an intact lumen or area. The comparison of the two ultrasonographic variables revealed that BWT better estimated urethral occlusion than DWT. In comparison

Table 1. *Demographic data and characteristic of urethral stricture in patients included to the study*

Demographic data	Mean ±SD	Range
Age	39.96 ±10.05	20–55
Weight (kg)	85.4 ±13.4	58–124
Height (m)	1.74 ±0.07	1.6–1.95
Body mass index (kg/m^2)	28.11 ±4.45	19.37–38.97
Length of stricture (mm)	27. 5 ±12.98	6–80
	Number	%
Diabetes	7	11
Hypertension	30	48
Obesity (BMI >30 kg/m^2)	16	25
Smoking (present or past)	17	27
Location of stricture	Number	%
Penile	30	48
Bulbar	33	52
Etiology	Number	%
Trauma	5	8
Iatrogenic	31	49
Idiopatic	17	27
Lichen Sclerosus	2	3
Hypospadias	8	13
Type of surgery	Number	%
Buccal mucosa graft urethroplasty	33	52
End – to – end urethroplasty	15	24
Two – staged urethroplasty	8	13
Penile skin flap urethroplasty	3	5
Urethrotomy	4	6

BMI – body mass index; SD – standard deviation

Table 2. *Results of non-invasive tests*

Uroflowmetry	Mean ±SD	Range
Qmax (mm/sec)	7.24 ±4.34	0.5–18.6
Qav (mm/sec)	4.88 ±2.89	1–11.3
ΔQ (mm/sec)	3.34 ±1.76	0–7.6
Ultrasonographical assessment of bladder wall	Mean ±SD	Range
BWT (mm)	3.76 ±0.76	2.1–6.07
DWT (mm)	2.8 ±0.77	1.1–4.88
Questionnaires	Mean ±SD	Range
IPSS (pts.)	20.9 ±9.22	1–35
USS-PROM (pts.)	19 ±6.28	3–30

pts. – points; SD – standard deviation

two variables described urethral damage, higher correlation coefficient was presented for percentage of an intact lumen/area (BWT: -0.70 vs -0.45 and DWT: -0.54 vs -0.37).

The UF parameters (Qmax, Qav, ΔQ) presented a medium degree of correlation, and the differences between them were non-significant. For this analyzed subgroup, were no differences between a direct measurement and as a percentage of an intact lumen/area.

The disparity in the correlation between UF and ultrasonographical assessment of the bladder was most significant when a percentage of the strictured urethra to the intact diameter and area was used. For data reported in units of measure this difference decreased.

The questionnaires did not show any correlation with the severity of the urethral stricture, neither presented in units nor as percentage.

Forward stepwise multiple linear regression analysis, where the dependent variable were minimal area of strictured urethra (Table 4) and percent of preserved urethral lumen (Table 5), showed that only BWT was an independent predictor in detection of these two variables.

Table 3. *Correlation coefficients for all analyzed variables*

	Min. area of strictured urethra	% of preserved urethral lumen
BWT	-0.45 p <0.0001	-0.70 p <0.0001
DWT	-0.37 p <0.0001	-0.54 p <0.0001
Qmax	0.44 p = 0.0003	0.45 p = 0.0002
Qav	0.42 p = 0.0007	0.43 p = 0.0004
ΔQ	0.44 p = 0.0004	0.44 p = 0.0005
IPSS	-0.07 p = 0.57	-0.12 p = 0.35
PROM	-0.10 p = 0.43	-0.10 p = 0.42

ΔQ – [Qmax – Qav]; BWT – bladder wall thickness; DWT detrusor wall thickness; IPSS – International Prostatic Symptom Score; Qmax – maximal flow rate; Qav – average flow rate; SD – standard deviation; USS-PROM – Patient-Reported Outcome Measure for Urethral Stricture Surgery

Table 4. *Forward stepwise multiple linear regression analysis, where the dependent variable was minimal area of strictured urethra. Changes that had no effect on analyzed variable were omitted*

R value	R^2 value	Adjusted R^2 value	F value	p value
0.69	0.48	0.44	12.95	<0.001
	Standardized β	Standardized Error β	t value	p value
BWT	-0.56	0.10	-5.67	0.000001
Qmax	0.31	0.24	1.33	0.189606
ΔQ	0.05	0.22	0.21	0.835666
PROM	0.20	0.11	1.80	0.076671

ΔQ – [Qmax – Qav]; BWT – bladder wall thickness; DWT – detrusor wall thickness; IPSS – International Prostatic Symptom Score; Qmax – maximal flow rate; Qav – average flow rate; USS-PROM – Patient-Reported Outcome Measure for Urethral Stricture Surgery

Table 5. *Forward stepwise multiple linear regression analysis, where the dependent variable was percent of preserved urethral lumen. Changes that had no effect on analyzed variable were omitted*

R value	R^2 value	Adjusted R^2 value	F value	p value
0.64	0.41	0.37	9.68	<0.001
	Standardized β	Standardized Error β	t value	p value
BWT	-0.53	0.11	-5.04	0.00001
Qmax	0.26	0.25	1.07	0.28940
ΔQ	0.06	0.23	0.27	0.79015
IPSS	0.22	0.12	1.89	0.06438

ΔQ – [Qmax – Qav]; BWT – bladder wall thickness; IPSS – International Prostatic Symptom Score; Qmax – maximal flow rate

Comparison bladder/detrusor wall thickness between patients with urethral stricture and healthy men

Control group was created with 50 healthy men who met inclusion criteria. Mean age was 40.3 (19–55). Bladder volume was 331 (305 – 372) ml. They were not statistically significant differences between control and analyzed group.

Comparison of BWT and DWT between the analyzed and control group revealed statistically significant differences (BWT: 3.76 mm vs 1.76 mm, p <0.001, and DWT: 2.8 vs 1.14 mm, p <0.001, respectively).

DISCUSSION

Traditionally, the Qmax has usually been used as a non-invasive method to assess urethral resistance caused by urethral narrowing. However, its value and correlation to the degree of stricture has never been proved. Our study is the first one trying to determine the correlation between this and other non-invasive tests, typically used in the diagnosis and follow-up of patients with urethral damage and occlusion. Based on the results of mathematical models for urethral stricture assessment, it has been proved that the urethral occlusion, as opposed to stricture length, exerts the highest impact on the urine flow and bladder pressure [2].

Through its repeatability, UF is a widely used tool in the primary diagnosis of urethral obstruction, including by urethral stricture [6]. Because of the characteristic 'box shape' curve, in most cases this examination allows to recognize urethral occlusion. UF has high sensitivity in terms of the distinction between normal and pathological urine flow, but it is characterized by low specificity, especially when a subjective assessment of the examination curve is used [7]. A disadvantage of UF in the diagnosis of urethral stricture is a lack of a cut-off point of Qmax rate between clinically significant and non-significant occlusion. In most studies, the value of Qmax rate below 10 mL/sec or 15 mL/sec is taken as a threshold point of the urethral stricture diagnosis. With an increasing Qmax value as a cut-off point, the sensitivity of the test increases but the specificity is decreased. The difference between 10 mL/sec and 15 mL/sec is 22% and 7% for the sensitivity and specificity, respectively [8]. In order to improve the diagnostic value of UF, a mathematical, three-phasic model has been created. It increased the sensitivity and specificity of that test by 80% and 76%, respectively [9].

In this study evaluated three UF variables (Qmax, Qav and ΔQ). Generally, all three parameters revealed moderate correlation coefficients. The Qmax rate presented the highest correlation with the degree of urethral occlusion (reported as the percentage of the preserved area), but the differences between all the parameters were non-significant. With regard to assessing the role of UF in the detection of urethral resistance caused by urethral stricture, these data differ from those obtained by Tam et al., as in their study ΔQ presented the highest value, followed by Qmax [10].

The attempts to prove the usefulness of bladder USG in patients with various causes of LUTS have been well described in the literature [11, 12]. In men, the assessment of BWT or DWT was used mainly in the diagnosis of patients with benign prostatic obstruction (BPO). For this group of patients, in comparison to UF, residual urine and prostate volume, DWT proved to the best parameter to predict bladder outlet obstruction (BOO), with an area under the curve (AUC) of 0.882 [13, 14]. The disadvantage of many previous works regarding this topic is a lack of a unified method of examination. The main problem was that measurements were performed on variously filled bladder, which resulted in a problem with repeatability of measurements. The solution was provided by the study of Oelke et al., which showed that DWT decreased rapidly during the first 250 ml of bladder filling and remained almost stable until maximal bladder capacity was reached [15].

To avoid errors and to standardize the technique of examination, The International Continence Society (ICS) described a scheme of the bladder USG study. According to these data, BWT and DWT should represent an average of three anterior bladder wall measurements with the bladder filled to more than 250 ml [16]. After maintaining above mentioned guidelines, these measurements present high intra- and interobserver reproducibility [17, 18].

This study revealed that bladder ultrasonography had the highest correlation rate with urethral occlusion among all non-invasive tests. Between the two analyzed parameters, BWT was characterized by higher accuracy in estimation of urethral closure. Interestingly, higher correlation coefficient was presented for urethral occlusion described by percent of preserved lumen and diameter. It suggests that parameter better estimates the risk of bladder damage caused by obstructed urine flow. Based on this data, the authors propose using the ultrasonographical assessment of bladder wall as an additional tool in preoperative diagnosis to evaluate bladder overload.

Similarly to UF, questionnaires are the most common methods used in the evaluation of difficulty bladder emptying. The IPSS is the most popular test, typically used in patients presenting lower urinary tract symptoms (LUTS), including patients with urethral stricture. In patients with urethral damage, the highest scored questions are #2 (frequency) and #5 (weak stream) [19]. Despite a wide use of this test in patients with urethral stricture, the IPSS does not show high accuracy in the assessment of urethral damage [20]. In 2011 Jackson et al. presented the most popular questionnaire dedicated to patients after urethroplasty (The Urethral Stricture Surgery Patient Reported Outcome Measure – USS-PROM) [21]. Until now, it has been translated and validated into many languages [22, 23, 24]. However, similarly to the IPSS, also the USS-PROM score has got a low correlation with Qmax rate (0.478–0.531) [20, 23]. A correlation between the IPSS and the USS-PROM score was 0.71 to 0.9 (pre-op and post-op, respectively) [22]. Our study demonstrated a lack of correlation between the results of the questionnaires and the degree of urethral occlusion. These data confirmed low value of these tests in the assessment of the severity of urethral damage.

The study has also some limitations. The main are limited number of included patients with heterogenous etiology of urethral stricture and the inability to unequivocally exclude the coexisting obstruction due to other pathologies, especially benign prostatic hyperplasia. To reduce risk of this limitation, analyzed group was limited to men up to 55 years old. Another limitation of the above study is the assumed idealized model of urethral stricture. To ease the calculation of the area of the preserved urethral lumen, we assumed that it took the form similar to a circle in the cross-section. In fact, the occlusion has an irregular shape that could, in some cases, complicate the calculation of the area.

CONCLUSIONS

During the first visit of a patient with suspected anterior urethral stricture, an important role is to plan next steps in diagnosis and treatment for that patient. Moreover, in preoperative care in this group of patients, one of the most important things is to protect urinary tract against high pressure in bladder, caused by urethral occlusion, till the surgical treatment.

Our study confirmed a usefulness of USG and UF as valuable additional, non-invasive tests in estimation of urethral occlusion in patients with anterior urethral damage. Ultrasonography showed the greatest accuracy, where BWT showed the best correlation coefficient with degree of urethral stricture and, among all non-invasive tests, was only independent predictor in diagnosis of urethral narrowing. It proved that use of these studies, especially USG, give information about degree of resistance in urine flow below the bladder, just before performance more invasive examinations, such as R-CUG or SUG. Moreover, data obtained during these tests allow find patients with critical urethral occlusion during first contact with urologist, and offer them additionally procedures, such as cystostomy, to protect their urinary tract against irreversible changes.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

ETHICAL APPROVAL

The study was approved by the local ethics committee (Approval no: NKBBN/333/2018) and written informed consent was received from all participants. The study protocol conformed to the ethical guidelines of the 1975 Helsinki Declaration.

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