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Prediction of detrusor underactivity based on non-invasive functional tests and clinical data in patients with symptoms of bladder outlet obstruction

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Abstract. – OBJECTIVE: Detrusor underactivity (DU) is a common but relatively under-researched bladder dysfunction. Recently, there has been renewed interest in this topic. The aim of the study was to develop a decision-making algorithm to predict the impaired detrusor contractility in patients with LUTS (lower urinary tract symptoms).

PATIENTS AND METHODS: A retrospective analysis covered 96 consecutive patients (aged 63 ± 8 years) treated pharmacologically for 50 ± 37 months due to LUTS (persisting for 64 ± 41 months). Functional tests included uroflowmetry and flow cystometry.

RESULTS: Weakened detrusor functioning was detected in 58 (60.4%) patients. Decision-making algorithm that included uroflowmetry, flow cystometry and clinical data, was showed to allow to diagnose impaired detrusor function with accuracy of 73% (95% CI – confidence interval: 61-83%) and specificity of 76% (95% CI: 54-90%). The positive predictive value of the classification tree graph is equal to 90% (95% CI: 78 -96%) and the negative predictive value is 50% (95% CI: 34-66%). The weakened detrusor function was more frequent in patients with: time to reach maximum flow rate higher than 13.5 s; time to reach maximum flow rate lower than 13.5 s and mean flow ratio higher than 4.5 ml/s, but time of flow longer than 44.5 s; time to reach maximum flow rate lower than 13.5 s and mean flow ratio lower than 4.5 ml/s, but time of flow longer than 52.5 s.

CONCLUSIONS: The results of the uroflowmetry can be used to predict the impaired detrusor contractility in patients with LUTS.

Key Words:
Detrusor underactivity, Uroflowmetry, Cystometry, Bladder dysfunction.

Introduction

Detrusor underactivity (DU), as defined in the recommendations of the International Continence Society (ICS) in 2002, is a contraction of reduced strength and/or duration, which results in prolonged emptying of the urinary bladder and/or a failure to achieve proper urinary bladder emptying in a time unit[1]. Clinical studies conducted in patients with non-neurogenic LUTS (lower urinary tract symptoms) showed that the DU prevalence rate is 9-28% among men under the age of 50 years, with observed growth up to 48% among men over 70 years old[2]. There are no known specific symptoms for DU diagnosis, given that signs

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like weak or intermittent urine stream, prolonged micturition time, increased post-void residual urine volume or recurring urinary tract infections can also affect patients with bladder outlet obstruction and the two pathologies cannot be distinguished based on routine laboratory tests, imaging, functional tests and International Prostate Symptom Score (IPSS)[2,3].

A significant clinical and diagnostic problem is the fact that DU is a urodynamic diagnosis and the sole test allowing for a final diagnosis of urinary tract dysfunction is the flow cystometry with a pressure flow study[2,3]. However, it is an invasive, expensive and time-consuming examination, and thus its utilization in every-day clinical practice is limited.

Therefore, the aim of this study was to evaluate a decision-making algorithm allowing to predict the occurrence of the impaired detrusor contractility in LUTS patients based on the uroflowmetry and clinical data.

Patients and Methods

The study was conducted retrospectively based on the medical records of adult patients of the Urology Ward and Specialist Outpatient Clinic of the Municipal Hospital in Sosnowiec in 2009-2015. The study group included all patients receiving pharmacological treatment for LUTS with dominant symptoms involving the voiding phase and post-micturition symptoms. These patients had undergone functional assessment with uroflowmetry and flow cystometry and were scheduled for surgical treatment of the bladder outlet obstruction.

Ninety-six patients included into the study group were adults diagnosed with benign prostatic hyperplasia (BPH) or bladder-neck dysfunction (N40 and N32 respectively, according to the ICD-10 Classification), treated pharmacologically for a minimum of 6 months and matching following functional criteria: 1) maximum urine flow rate under 15 ml/s, 2) bladder outlet obstruction with a Schafer grade of ≥1 and Bladder Outlet Obstruction Index (BOOI) ≥ 20 confirmed in cystometry.

The exclusion criteria were other than BPH and bladder-neck dysfunction (prostate cancer, urethrostenosis), prior surgical treatment for BPH or bladder-neck dysfunction, surgical treatment of colorectal cancer, radiotherapy of the lesser pelvis, chronic use of medications affecting detrusor contraction strength (antimuscarinic drugs, neuroleptics, calcium channel blockers).

The functional analysis of the patients involved the evaluation of results of the uroflowmetry test and the results of the flow cystometry. When the maximum urine flow rate (Qmax) was under 15 ml/s, the results of the flow cystometry were analyzed. Patients with maximum urine flow rate Qmax ≥ 15 ml/s in the uroflowmetry were not analyzed further, regardless of their subsequent therapy (surgical or pharmacological). Based on the results of the functional parameters 2 study subgroups were developed: I –patients with bladder outlet obstruction and impaired detrusor function (N = 58), II –patients with bladder outlet obstruction and normal detrusor function (N = 38).

Due to the technical accuracy of the device, in the uroflowmetry test, the urinary flow rate values were rounded off to the nearest whole number, while the void volume and post-void residual volume were rounded off to the nearest 10 ml.

In order to eliminate the positive and negative artifacts in the urine flow curve, the signal record was manually averaged every 2 s (1 mm on the timeline corresponds to 2 s). The examinations were carried out in intimate conditions, in a standing position, the patient was asked to urinate with a 'normal' need to pass urine. An informed consent was obtained from all of the participants. The results of patients with volume of excreted urine > 150 ml were investigated.

The flow cystometry was conducted using the Sensic Clinic G3 apparatus (Mediwatch Ltd., produced in 2008, producer's headquarters –Lumonics House, Valley Drive, Swift Valley Rugby, UK). The device was calibrated prior to every use in terms of pressure measurements, water pump functioning and the accuracy of the urinary flow rate measurements.

The intra-bladder and intra-abdominal pressures were measured using external pressure transducers connected with tubes and catheters filled with saline, zeroed at the reference value, that is the upper border of patient's pubic symphysis, and catheters: for intra - bladder pressure measurements-size 6Fr double-channel urinary catheters allowing for simultaneous pressure measurement and filling up the bladder, while for intra-abdominal pressure measurements – size 12Fr rectal catheters ended with a balloon filled with saline.

Bladder was filled with saline at room temperature at a rate of 50 ml/min. In the material presented both the recordings and values of the

Table I. Uroflowmetry in patients without and with detrusor underactivity (data shown as mean values ± standard deviation).

	DU + [N = 58]	DU – [N = 38]	*p*
Maximum flow rate [ml/s]	8.6 ± 2.2	7.9 ± 2.5	0.11
Mean flow rate [ml/s]	4.8 ± 1.2	4.8 ± 1.7	0.80
Time to reach max. flow [s]	13.2 ± 6.1	10.3 ± 4.4	**< 0.01**
Time of flow [s]	63. 4 ± 25.1	64.3 ± 25.1	0.87
Micturition volume [ml]	307.9 ± 123.3	286.3 ± 86.5	0.32
Post-void residual volume [ml]	54.1 ± 47.1	62.1 ± 53.9	0.44

EMG (electromyography) were not analyzed due to a big number of artifacts, resulting probably from the kind of surface electrodes used, and lack of EMG measurements for all analyzed patients. Tests were performed in intimate conditions, either sitting down or standing depending on patient's preferences. The research results presented in the publication were based on the evaluation of medical records and therefore did not require the approval of the Local Ethics Committee.

Statistical Analysis

Statistical analysis was performed using STATISTICA 10.0 PL (Tibco Software Inc, Palo Alto, CA, USA). Statistical significance was set at a *p*-value below 0.05. All tests were two-tailed. Nominal and ordinal data were expressed as percentages, whilst interval data were expressed as mean value ± standard deviation. Distribution of variables was evaluated by the Shapiro-Wilk test and a quantile-quantile plot and homogeneity of variances were assessed by the Fisher-Snedecor test. For comparison of data between group with and without DU, the *t*-Student test for independent data was used. The two-way ANOVA analysis with contrast analysis as post-hoc was done to compare gropups with and without DU according to surgical procedure. Categorical variables were compared using χ^2-tests. A decision-making algorithm was done with Classification and Regression Tree (CART) with the Gini index.

Results

A total of 96 men aged 63 ± 8 (range: 37-79 years) were analyzed, among whom 57 (59.4%) had an endoscopy. The duration of symptoms was equal to 64 ± 41 months (range: 10-180 months). Prostate volume in the examined group was 39.7 ± 16.1 ml (range: 15-97 ml).

Urinary hesitancy was detected in 28 (29.2%) patients, 81 (84.4%) had a prolonged micturition time, 35 (36.5%) reported a feeling of post-void urinary retention and 40 (41.7%) patients had an intermittent urine stream. The mean period of pharmacotherapy was 50 ± 37 months (range: 7-180 months). In the examined group 73 (76%) patients were treated with α-blocker (alfuzosin, doxazosin, tamsulosin) in monotherapy and 23 (24%) patients received combined treatment with α-blocker and finasteride. Impaired functioning of the detrusor was detected in case of 58 (60.4%) patients. Descriptive characteristics of the uroflowmetry and cystometry tests in the examined group are presented in the tables below (Tables I and II).

Table II. Flow cystometry in patients without and with detrusor underactivity (data shown as mean values ± standard deviation)..

	DU + [N = 58]	DU – [N = 38]	*p*
Micturition volume [ml]	330 ± 115	330 ± 107	0.98
Maximum flow rate [ml/s]	6.1 ± 2.2	8.1 ± 2.4	**< 0.001**
Time of flow [s]	91.2 ± 29.2	74.6 ± 30.2	**< 0.001**
Mean flow rate [ml/s]	3.8 ± 1.5	4.5 ± 1.2	**< 0.05**
Time to reach max. flow [s]	19.2 ± 12.8	12.6 ± 5.6	**< 0.001**
Maximum Pdet [cm H_2O]	56.7 ± 15.2	86.3 ± 21.9	**< 0.001**
Post-void residual volume [ml]	100.3 ± 95.3	60.5 ± 67.8	**< 0.05**
Pdetat the beginning of the flow [cm H_2O]	46.7 ± 16.1	68.8 ± 21.6	**< 0.001**
Pdetat the maximum flow [cm H_2O]	50.0 ± 12.0	77.1 ± 19.8	**< 0.001**
Bladder Contractility Index BCI	79.9 ± 10.3	117.2 ± 16.0	**< 0.001**
Bladder Outlet Obstruction Index BOOI	37.7 ± 15.4	61.0 ± 23.1	**< 0.001**

No significant differences were found in terms of prevalence of the urinary hesitancy in patients without and with impaired functioning of the detrusor muscle, both among operated (36.7% *vs.* 34.3%) and non-operated patients (25% *vs.* 17.4%). The frequency of prolonged micturition time was similar in patients without and with impaired functioning of the detrusor for operated (95.5% *vs.* 82.9%), as well as non-operated (81.3% *vs.* 78.3%).

There were no significant differences in the frequency of the urinary retention feeling reported by patients without and with impaired functioning of the detrusor for operated (40.9% *vs.* 28.6 %) and non-operated (31.3% *vs.* 47.8%). The incidence of intermittent urine flow was similar in men without and with impaired functioning of the detrusor, both in operated (50.0% *vs.* 40.0%) and non-operated patients (50.0% *vs.* 30.4%).

In the uroflowmetry the only significant difference was the time to reach maximum flow rate among patients without and with impaired functioning of the detrusor (10.3 *vs.* 13.2 s). In the flow cystometry significant differences between patients with and without impaired functioning of the detrusor, in the aspect of functional parameters, were found in maximum flow rate (6.1 *vs.* 8.1 ml/s), mean flow rate (3.8 *vs.* 4.5 ml/s), time of flow (91.2 *vs.* 74.6 s), time to reach maximum flow rate (19.2 *vs.* 12.6 s) and post-void residual urine volume (100 *vs.* 60 ml).

Decision-making tree graph in estimating impaired function of the detrusor: Figure 1 demonstrates a decision-making tree graph allowing to estimate patient's risk of having impaired detrusor function without performing the flow cystometry and based solely upon the results of the uroflowmetry test, age and clinical symptoms. The algorithm allows to estimate the possibility that patient's detrusor function is impaired with 73% accuracy (95% confidence interval (CI): 61-83%) and 76% specificity (95% CI: 54-90%). The positive predictive value is 90% (95% CI: 78-96%) and negative predictive value of the tree graph is equal to 50% (95% CI: 34-66%). The impaired detrusor function can be expected in patients with:

- time to reach maximum flow rate longer than 13.5 s,
- time to reach maximum flow rate lower than 13.5 s and additionally mean flow ratio higher than 4.5 ml/s, but time of flow longer than 44.5 s,
- time to reach maximum flow rate lower than 13.5 s, and additionally mean flow ratio lower than 4.5 ml/s, but time of flow longer than 52.5 s.

Comparing the parameters of the uroflowmetry test before and after the surgical procedure, both in the group without and with the weakening of the detrusor function, a statistically significant improvement was found in all measured values. Patients with weakened detrusor function had statistically significantly lower values of the change in the maximum and mean flow rate than in the group of patients with no impairment of the detrusor function (Table III).

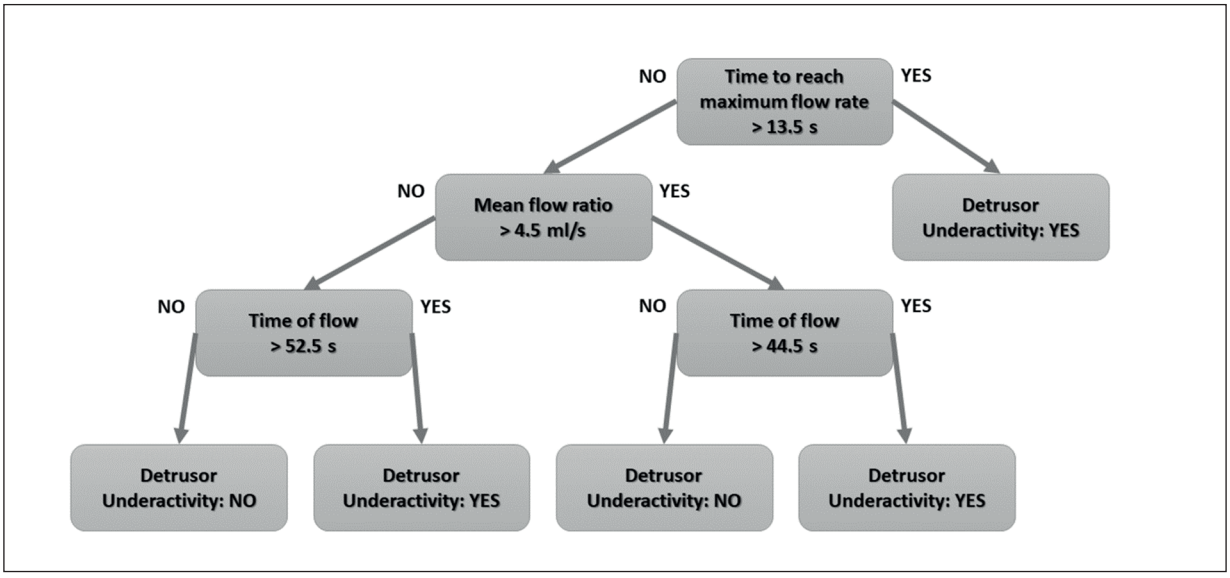

Figure 1. Decision-making tree graph allowing to estimate impaired detrusor function without performing the flow cystometry in patients with symptoms of bladder outlet obstruction.

Table III. Results of the uroflowmetry test of patients before and after surgery, both in the group without and with impaired detrusor function.

Parameter	Before Surgical procedure		After surgical procedure		*p*		
	DU +	DU -	DU+	DU -	DU	Time	Interaction
Maximum flow rate [ml/s]	8.63 ± 2.04	7.82 ± 2.46	18.94 ± 6.38	22.95 ± 6.25	0.11	**< 0.001**	**< 0.01**
Mean flow rate [ml/s]	4.91 ± 1.22	4.86 ± 1.67	12.74 ± 4.28	14.77 ± 3.54	0.12	**< 0.001**	0.054
Time to reach max. flow [s]	13.43 ± 6.27	9.68 ± 4.09	7.89 ± 4.06	6.14 ± 1.96	**< 0.05**	**< 0.001**	0.13
Time of flow [s]	62.83 ± 25.22	54.5 ± 21.46	34.49 ± 17.43	25.18 ± 9.20	0.062	**< 0.001**	0.86
Micturition volume [ml]	308 ± 123	266 ± 86	377 ± 141	293 ± 107	**< 0.05**	**< 0.05**	0.26
Post-void residual volume [ml]	58.0 ± 49.3	66.8 ± 39.7	6.3 ± 9.7	2.3 ± 4.3	0.73	**< 0.001**	0.27
	DU +		**DU -**		***p***		
Parameter	Δ ± S	± 95% CI	Δ ± S	± 95% CI			
Maximum flow rate [ml/s]	10.3 ± 5.6	8.4 ÷ 12.2	15.3 ± 6.6	12.2 ÷ 18.0	**< 0.01**		
Mean flow rate [ml/s]	7.8 ± 4.1	6.4 ÷ 9.2	9.9 ± 3.5	8.4 ÷ 11.4	**< 0.05**		
Time to reach max. flow [s]	-5.5 ± 5.3	-7.4 ÷ -3.7	-3.5 ± 3.9	-5.3 ÷ -1.8	0.13		
Time of flow [s]	-28.3 ± 19.1	-34.9 ÷ -21.8	-29.3 ± 22.7	-39.4 ÷ -19.2	0.86		
Post-void residual volume [ml]	-51.7 ± 44.2	-66.9 ÷ -36.5	-64.5 ± 39.5	-82.0 ÷ -47.0	0.27		

Δ - raw delta (after - before); S - standard deviation; CI - confidence interval.

Discussion

Urinary tract symptoms are usually related to bladder outlet obstruction in BPH in men aged over 50 years and bladder-neck dysfunction or urethrostenosis in younger men. However, LUTS that suggest these pathologies may be caused by detrusor underactivity or bladder hyperactivity, among other entities[4-6]. In our study group, detrusor underactivity was detected in 60% of patients, which represents significantly higher percentage than stated in available literature. This may arise from the selection criteria (patients with or without neurological disorders) or diagnostic criteria for DU. According to one of the proposed urodynamic definitions, detrusor underactivity can be diagnosed provided that detrusor pressure during the maximum flow rate ($P_{detQmax}$) is lower than 40 cmH_2O and the maximum flow rate (Q_{max}) lower than 15 ml/s[7]. However, when calculations (BCI – *bladder contractility index*) and Schäfer nomogram are taken into account, it can be observed that aforementioned definition used in many studies has limitations and does not consider patients with higher $P_{detQmax}$ in whom functional tests have confirmed impaired contractility of the detrusor.

Despite the limitations, the flow cystometry is still the only test that allows to define a character of the lower urinary tract functional disorders and remains a 'gold standard' in the diagnostic workup[8-11]. Therefore, from the clinical point of view there is a need for evaluation whether based on the results of non-invasive functional tests and/or patients' clinical data, it is possible to find certain qualities suggesting with high probability the occurrence of detrusor underactivity in patients with intensified LUTS and scheduled for a surgical treatment. In studies of Harding et al[11], amongst others, on the use of uroflowmetry with penile cuff test in the differentiation process of patients with and without bladder outlet obstruction and subsequent prognosis of the operative treatment effectiveness in BPH, the authors demonstrated that the unnecessary urodynamic tests could be reduced up to 50%[12-15].

The analysis of study results gives grounds to conclude that the best predictive factors of detrusor underactivity, based on uroflowmetry in correlation with cystometric analysis are: prolonged micturition time, time to reach maximum flow rate and decreased value of the mean flow rate. The use of these parameters allows for a non-invasive determination of the presence of detrusor failure, which is a new way of using uroflowmetry in the diagnosis of LUTS. This would allow to select a group of patients who should be subjects to the flow cystometry before the operative treatment, reducing the number of unnecessary tests. In the available scientific reports, the results of uroflowmetry are correlated with bladder obstruction. In studies of Harding et al[11], amongst others, on the use of uroflowmetry with penile cuff test in the differentiation process of patients with and without bladder outlet obstruction and subsequent prognosis of the operative treatment effectiveness in BPH, the authors demonstrated that the unnecessary urodynamic tests could be reduced up to 50%[11-14].

None of the remaining data, both clinical (character of the reported symptoms, duration of symptoms, treatment time, patient's age, prostate volume) and functional (maximum flow rate, micturition volume, post-void residual volume) did comply with statistical relevance criteria. Zhang et al[16] suggested based on their results that in men with a suspicion of bladder outlet obstruction, increased post-void residual urine volume is more related to impaired detrusor functioning than the obstruction due to BPH. In our study the uroflowmetric parameters mentioned above, that is micturition time, time to reach maximum flow rate and mean flow rate, gave grounds to create the decision-making tree graph allowing with 73% accuracy and 76% specificity to estimate the possibility that patient has impaired detrusor function.

Conclusions

In patients reporting intensified micturition symptoms, scheduled for operative treatment, it is possible to predict the occurrence of detrusor underactivity based on uroflowmetry with 73% accuracy and 76% specificity. Functional parameters allowing for the DU prediction are: mean flow rate, time to reach maximum flow and flow time.

Conflict of Interest

The Authors declare that they have no conflict of interests.

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