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ORIGINAL ARTICLE

A novel algorithm for the non-invasive detection of bladder outlet obstruction in men with lower urinary tract symptoms

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Urinary flowmetry

ABBREVIATIONS

AG, Abrams/Griffiths;
BWT, bladder wall thickness;
DO, detrusor overactivity;
DWT, detrusor wall thickness;

Abstract ***Objective:*** To determine the ability of bladder wall thickness (BWT) in combination with non-invasive variables to distinguish patients with bladder outlet obstruction (BOO).

Patients and methods: Patients completed the International Prostate Symptom Score (IPSS) questionnaire and prostate size was measured by transrectal ultrasonography (US). Pressure-flow studies were performed to determine the urodynamic diagnosis. BWT was measured at 250-mL bladder filling using transabdominal US. Recursive partition analysis (RPA) recursively partitions data for relating independent variable(s) to a dependent variable creating a tree of partitions. It finds a set of cuts of the dependent variable(s) that best predict the independent variable, by searching all possible cuts until the desired fit is reached. RPA was used to test the ability of the combined data of BWT, maximum urinary flow rate (Q_{max}), post-void residual urine volume (PVR), IPSS, and prostate size to predict BOO.

Results: In all, 72 patients were included in the final analysis. The median BWT, voided volumes, PVR, mean Q_{max}, and IPSS were significantly higher in patients who had an Abrams/Griffiths (A/G) number of > 40 (55 patients) compared to those

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MCC, maximum cystometric capacity;
NPV, negative predictive value;
PPV, positive predictive value;
P_{ves}, vesical pressure;
PVR, post-void residual urine volume;
Q_{max}, maximum urinary flow rate

with an A/G number of ≤40 (17 patients). RPA revealed that the combination of BWT and Q_{max} gave a correct classification in 61 of the 72 patients (85%), with 92% sensitivity and 65% specificity, 87% positive predictive value, and 76% negative predictive value (NPV) for BOO (area under the curve 0.85). The positive diagnostic likelihood ratio of this reclassification fit was 2.6.

Conclusions: It was possible to combine BWT with Q_{max} to create a new algorithm that could be used as a screening tool for BOO in men with lower urinary tract symptoms.

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Introduction

LUTS are highly prevalent in the male population and it was reported that ∼62.5% of men aged ≥40 years have at least one LUTS in a study of five European countries [1]. A pressure-flow study is the standard urodynamic test for the diagnosis of BOO. However, pressure-flow studies are invasive, expensive, and time consuming. They can also cause discomfort, UTI, and haematuria [2]. The maximum urinary flow rate (Q_{max}) measured by uroflowmetry, is a poor diagnostic method for BOO [3]. Also, although the post-void residual urine volume (PVR) is increased in patients with BOO [4], an important disadvantage of both uroflowmetry and PVR measurement is that they cannot distinguish between BOO and detrusor underactivity [5].

Ultra-structural morphological changes in the bladder wall have been studied by Elbadawi et al. [6] in a number of specimens obtained from patients with BOO. The main finding of that study was an increased smooth muscle bulk, with or without interstitial collagen deposition. Therefore, it has been assumed that the measurement of this increase in bladder wall thickness (BWT) might be an indicator for the presence of BOO. Oelke et al. [7] found that the detrusor wall thickness (DWT) decreases with increase in bladder filling until a level of 250 mL is reached, then the decrease is not statistically significant.

The aim of the present study was to investigate the diagnostic value of BWT in combination with other non-invasive variables for BOO in men with LUTS. For this purpose, recursive partition analysis (RPA), a non-parametric method [8], recursively partitions data for relating dependent variable(s) to an independent variable creating a tree of partitions. The dependent variables investigated in the present study were BWT, Q_{max}, PVR, IPSS, and prostate size. The independent variable was the urodynamics diagnosis, i.e. BOO. RPA finds a set of cuts of the dependent variable(s) that best predict the independent variable, by searching all possible cuts until the desired fit is reached. Therefore, in the present study we used RPA to test the ability of the combined data of BWT, Q_{max}, PVR, IPSS, and prostate size to predict BOO in men with LUTS.

Patients and methods

In all, 98 men with LUTS were consecutively included in the study at three centres: The Radboud University MC, Nijmegen, The Netherlands; Sohag University Hospital, Sohag, Egypt; and Minia University Hospital, Minia, Egypt. Ethical approvals were obtained from the local ethics committees at the three centres, and all patients signed a written consent and completed the IPSS questionnaire. Inclusion criteria were adult men with LUTS. Exclusion criteria were patients with neurogenic bladder, history of previous prostatic surgery, or prostatic carcinoma.

Patients were asked to stop using any medication for their urological disorders for ≥3 days before the date of investigation. TRUS was performed to measure the prostate size. Dipstick urine analysis was performed to exclude UTIs.

All patients underwent a pressure-flow study (Solar, Medical Measurement Systems, Enschede, The Netherlands, Laborie Delphis KT, Toronto, Canada). A gas- or water-filled urethral catheter (6 F) and a rectal catheter were inserted to monitor vesical pressure and abdominal pressure, respectively. Water was infused at room temperature at 50 mL/min until the maximum cystometric capacity (MCC) was reached.

The BWT was measured during filling at 250 mL of bladder volume or at the MCC for patients with small bladder capacities. The bladder wall consists of bladder adventitia, which has a bright appearance on US; the detrusor muscle layer, which has a dark appearance on US; and the innermost layer is the bladder mucosa, which has a bright appearance on US [9,10]. Therefore, the inner and outer bright lines were included in the measurement of the BWT. A curvilinear 5-MHz US transducer was positioned on the suprapubic area; the BWT measurements were made on the sharpest image obtained. Then, filling cystometry was continued until the MCC was reached. Then, the patients were asked

Table 1 Comparison of demographic and urodynamic variables between groups.

Variable	Group 1: BOO	Group 2: No BOO	P^{*}
Number of patients	55	17	
Age, years, mean (SD)	62.3 (6.6)	65.1 (12.3)	0.2
IPSS, mean (SD)	21.2 (5.1)	17.2 (5.6)	0.01
Prostate size, mL, median (range)	59 (23–130)	50 (21–296)	0.2
MCC, mL, mean (SD)	363 (94.5)	351.3 (95.7)	0.6
Voided volume, mL, median (range)	200 (100–652)	266 (129–467)	0.01
Q_{max}, mL/s, mean (SD)	6.4 (2.5)	9.7 (2.8)	< 0.001
PVR, mL, median (range)	145 (4–420)	39 (0–200)	0.001
P_{det} at Q_{max}, cmH_2O, median (range)	89 (52–165)	510 (24–66)	< 0.001
A/G number, mean (SD)	77.8 (25.3)	28.4 (7.9)	< 0.001
BWT, mm, median (range)	4 (1.9–5.8)	2.8 (1.6–5.2)	0.02

P_{det}.at Q_{max}, detrusor pressure at Q_{max}.
* Mann-Whitney *U*-test or Student's *t*-test with significance level at $P < 0.05$.

to void in the flowmeter in a sitting or standing position according to their preference.

Statistical analysis was done with JMP® 7.0.2 (SAS Institute, Cary, NC, USA). The Mann–Whitney *U*-test and Student's *t*-test were used to measure differences between groups. Spearman's rank correlation was used to test the strength of correlation between the BWT and each of the urodynamic and non-urodynamic variables of the study. For the RPA [8], BWT, Q_{max}, PVR, IPSS, and prostate size were the independent variables that were tested to best predict the dependent variable (urodynamic diagnosis), i.e. BOO.

Results

In all, 98 patients planned for urodynamic assessment were included in the study. Patients who voided < 100 mL were excluded [11], leaving 72 patients in the final analysis. Five patients had a MCC of < 250 mL, the BWT was measured at the MCC and re-calculated at 250 mL using the following equation [12]: DWT1 × R1 = DWT2 × R2. The radius (R) of the bladder was obtained from the bladder volume as 4π/3 × R3.

Patients were categorised according to the Abrams/Griffiths (AG) number into two groups: Group 1 included patients with an AG number of > 40 (i.e. BOO), while Group 2 included patients with an AG number of ≤40 (i.e. no BOO). Table 1 shows the demographic and urodynamic characteristics of the two groups.

Spearman's rank correlation revealed a statistically significant, weak-to-moderate correlation between BWT and each of the following variables: Age ($\rho = 0.44$; $P < 0.001$), IPSS ($\rho = 0.31$; $P = 0.007$), and voided volumes ($\rho = 0.45$; $P < 0.001$). Fig. 1 shows a box plot of the study variables.

In all, 23 of the 72 patients had detrusor overactivity (DO) and 18 of them had BOO. The median BWT was higher in patients without DO (49 patients) than in patients with DO (23), at 4.1 vs 3.4 mm ($P = 0.13$). In Group 1, the median BWT was higher in patients with DO (18 patients) than in patients without DO (37), at 4.5 vs 3.5 mm ($P = 0.07$). None of the above-mentioned differences were statistically significantly different.

RPA of these variables showed that the combination of BWT and Q_{max} gave a correct classification in 61 of the 72 patients (85%), with 92% sensitivity and 65% specificity, 87% positive predictive value (PPV), and 76% negative predictive value (NPV) for BOO (area under the curve 0.85). The positive diagnostic likelihood ratio (LR) of this reclassification fit was 2.6.

Fig. 2 shows the classification responses of this non-invasive combination; the computed probability of having the diagnosis 'obstructed' was 96% using a Q_{max} threshold of < 7 mL/s in 32 of 72 patients. For patients with a Q_{max} of > 7 mL/s, the BWT was checked; a threshold value of 2.7 mm had a 73% probability to be 'obstructed' in 22 of 72 patients, the program then exhaustively checked further various thresholds of Q_{max}, the computed probability of having the diagnosis 'obstructed' was 84% using the Q_{max} threshold of < 11 mL/s in 17 of 72 patients.

Discussion

In the present study, a spectrum of urodynamic, and non-urodynamic, non-invasive, variables were investigated for their ability to distinguish patients with BOO.

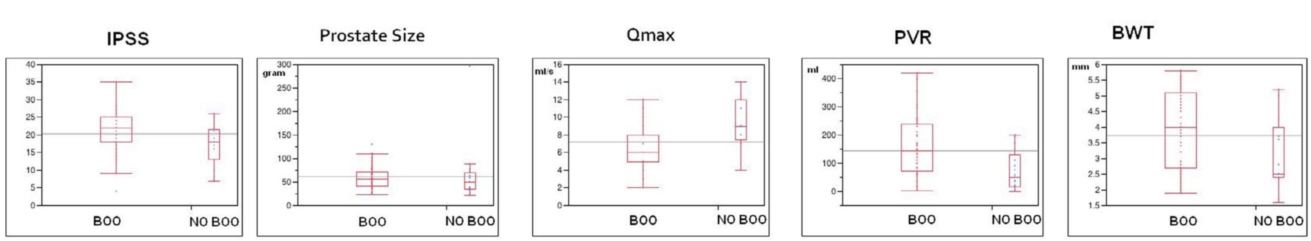

Fig. 1 Box-plots of study variables: (A) IPSS; (B) Prostate size; (C) Q_{max}; (D) PVR; (E) BWT.

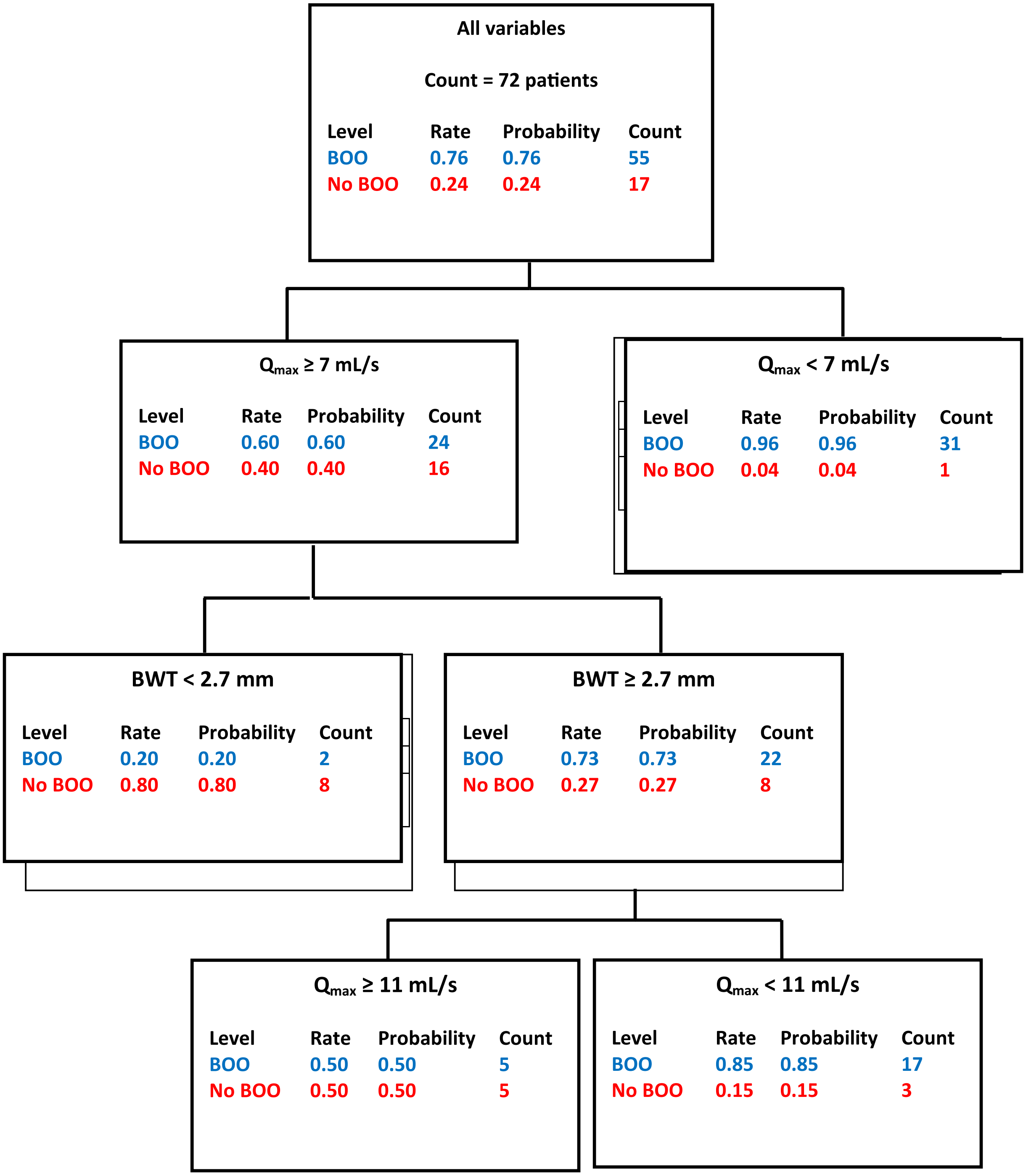

Fig. 2 Classification response of RPA. The RPA program found no suitable cuts in the PVR, prostate size, or IPSS variables that matched the desired fit and therefore, these variables were automatically excluded in this model. This model successfully classified 85% of patients with 92% sensitivity and 65% specificity, 87% PPV, and 76% NPV for BOO (area under the curve for the diagnosis of BOO 0.85). The positive diagnostic likelihood ratio (LR) of this reclassification fit was 2.6. This indicates that BWT and Q_{max} would be of value in the diagnosis of BOO independently.

BWT has been assumed to represent the hypertrophic effect of BOO on the bladder wall. Hakenberg et al. [13] reported that a mean (SD) BWT of 3.6 (0.1) mm in a group of men aged >60 years with LUTS/BPH was significantly higher than the other two healthy groups in their study, at a mean (SD) of 3.33 (0.08) mm for healthy men and 3.05 (0.06) mm for healthy women ($P < 0.002$).

Previous studies have reported that BWT independently distinguish patients with BOO [14,15]. This finding was reproducible in the present study, the median BWT was significantly higher in the group of patients with BOO (AG number >40) than in the group of patients without BOO (AG number ≤40), at 4 vs 2.8 mm, respectively.

To overcome the obstacle of the decrease in BWT with the increase in the bladder filling volume, the BWT was measured at fixed bladder filling volume of 250 mL, beyond which, the decrease in BWT is of no statistical significance. Isikay et al. [15] measured the BWT at a bladder filling of 150–200 mL and reported a mean (SD) BWT of 4.14 (1.01) mm using a 7.5-MHz linear probe. Manieri et al. [14] measured the BWT at 150-mL bladder filling in 174 patients using a 3.5-MHz curvilinear probe, which is 100 mL less than the volume at which BWT was measured in the present study. The authors reported a mean BWT (SD) of 4.5 (1.1) mm and a BWT threshold value of 5 mm was proposed to be diagnostic for BOO, i.e. above this threshold likely to have BOO. These two studies were done using US transducers of different frequencies; moreover, the measurements were done at different bladder volumes. This might explain the diversity of the outcome of the measured BWT in these studies and the present study.

An interesting finding of our present study was that the median BWT was higher in patients without DO than in those with DO. Additionally, the median BWT was higher in patients with BOO and DO than in the patients with BOO but without DO within Group 1. Although these were of no statistical significance, it may indicate that the main cause of the increase in BWT in these patients is the BOO and not DO.

Flowmetry and US assessment of PVR cannot distinguish BOO from detrusor underactivity but can still be applied for initial evaluation and follow-up of patients with LUTS. IPSS is representative of the patient perceptions but is subjective. And so, none of these abovementioned variables can yet replace conventional pressure-flow studies in clinical practice. Therefore, an exploratory analysis was further performed to explore the potential usefulness of BWT and other non-invasive variables, i.e. $Q_{\max}$, IPSS, PVR, and prostate size, in clinical practice. Results of the RPA of these variables showed the ability of the combination of BWT and $Q_{\max}$ to correctly classify 85% of patients compared to the conventional urodynamic diagnosis. The classification model was aimed to combine all the variables of BWT, $Q_{\max}$, IPSS, PVR, and prostate size, but the RPA program found no suitable cuts in the PVR, prostate size, or IPSS variables that matched the desired fit and therefore, these variables were automatically excluded. The resultant model successfully classified 85% of patients. This indicates that BWT and $Q_{\max}$ would be of value in the diagnosis of BOO independently.

Conventional pressure-flow studies are still the standard diagnostic method for BOO in men with LUTS. However, the algorithm developed in the present study could be of value as a screening tool for BOO that lessens the need for invasive pressure-flow studies in many patients with LUTS.

A limitation of the present study was that there was no control group; however, it can be ascribed to the ethical concerns about performing invasive urodynamic testing in normal subjects.

Conclusion

BWT is significantly higher in patients with BOO and significantly related to IPSS. It was possible to combine BWT with $Q_{\max}$ to produce a new algorithm for diagnosis of BOO. This new diagnostic algorithm could be used as a tool for screening of BOO in men with LUTS, which would help in reducing unnecessary invasive pressure-flow studies in these patients.

Conflict of interest

None of the contributing authors have any conflict of interest, including specific financial interests or relationships and affiliations relevant to the subject matter or materials discussed in the manuscript.

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