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ORIGINAL PAPER

Non-invasive diagnosis of under active bladder: A pilot study

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Summary ***Objective:** We assessed the efficacy of voiding efficiency (VE) to distinguish between underactive bladder (UB) and bladder outlet obstruction (BO) without using pressure flow studies (PFS).*
***Materials and methods:** in male patients, uroflowmetry and post-void residual (PVR) urine data and subsequent pressure flow studies (PFS) data were examined retrospectively. Bladder outlet obstruction index (BOI) and bladder contractility index (BCI) were calculated from patients' PFS values. Patients with BCI < 100 and BOI < 40 were grouped as UB group and patients with BCI > 100 and BOI > 40 were grouped as BOO group. VE was computed as a percentage of volume voided compared to the pre-void bladder volume.*
***Results:** In total we examined 93 patients, 44 in UB and 49 in BO group. There was no statistically significant difference between the two groups in relation to Q_{max} value ($p = 0.38$). However, total voiding time, time to reach the maximum urinary flow rate and voided volume showed statistically significant difference between the two groups ($p < 0.001$). Average VE was 63.6 + 2.43% and 46.2 + 2.63%) for UB and BO groups respectively and the difference was statistically significant ($p < 0.001$). UB can be diagnosed with at least 95% sensitivity and 88% specificity in men over age 80.*
***Conclusions:** Non-invasive uroflowmetry and VE measurements were able to differentiate between UB and BOO patients, presenting with identical clinic features, but different findings of PFS.*

KEY WORDS: *Underactive bladder; Bladder outlet obstruction; Voiding efficiency; Urodynamics.*

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INTRODUCTION

Reduced detrusor contraction, also named *Detrusor Underactivity* or *Underactive Bladder* (UB), means prolonged voiding at low pressure, without any obstruction from urodynamic and clinical point of view. This definition has been frequently included in the terminology. In his study published in 2015, Chapple defined UB as a symptom complex including prolonged voiding time with or without a feeling of complete bladder emptying, difficulty in initiating voiding, diminished sense of bladder filling and a slow voiding flux (1). UB may interfere with BO, which also leads to *lower urinery tract* (LUT) symptoms. This interference leads to failure of the planned surgery in these patients. Conversely, chronic retention or progression to surgery were not frequently observed during long-term conservative follow-up of these patients (2).
UB is generally seen in patients over age 80 in both genders, although identified more precisely in men, in terms of standardization. A Korean study reported higher frequencies for UB in men (40.2%) than in women (12%) over age 80 (3).
There are studies reporting symptom recovery after prostate surgery in these patients (4), although other studies claimed only slight clinical recovery (5).
Low urine flow rate is a common feature among the patients with UB and BO. Voiding pressure-flow study can be used for differentiation in indeterminate cases. (2). Because of the invasive nature of the pressure-flow study, a non-invasive method is welcomed. There may be a correlation between detrusor contraction index and the ratio of micturition volume and average physiological bladder capacity. This ratio, also known as *voiding efficiency* (VE), was addressed in the articles on pressure-flow studies and UB in the literature, although the topic is insufficiently studied.

MATERIALS AND METHODS

Clinical data of the patients and the algorithm

In the study, data of 4454 patients who underwent PFS in the period between January 2007-January 2015 was examined. Male patients having a minimum of 2 uroflowmetry and postvoid residual urine measurements were enrolled. Patients of female gender (n = 1208), patients with urological malignancies that may affect LUT symptoms (bladder cancer, prostate cancer, etc.) (n = 386), calculi in the bladder and lower end of the ureter (n = 102), active infection and asymptomatic bacteriuria (n = 406), transurethral intervention history (n = 908), previous LUT symptoms due to neurogenic causes (n = 1005), catheter before and after urodynamics or performing *clean intermittent catheterization* (CIC) (n = 155), decayed patients, bedridden patients suffering mobilization problems (n = 102), and patients with missing data (n = 89) were excluded from the study. A total of 93 patients with complete data and without exclusion criteria were included in the study.
Detailed urological history and physical examination data were evaluated in all the included patients.
Uroflowmetric measurements (*Aymed urodynamic sys-*

No conflict of interest declared.

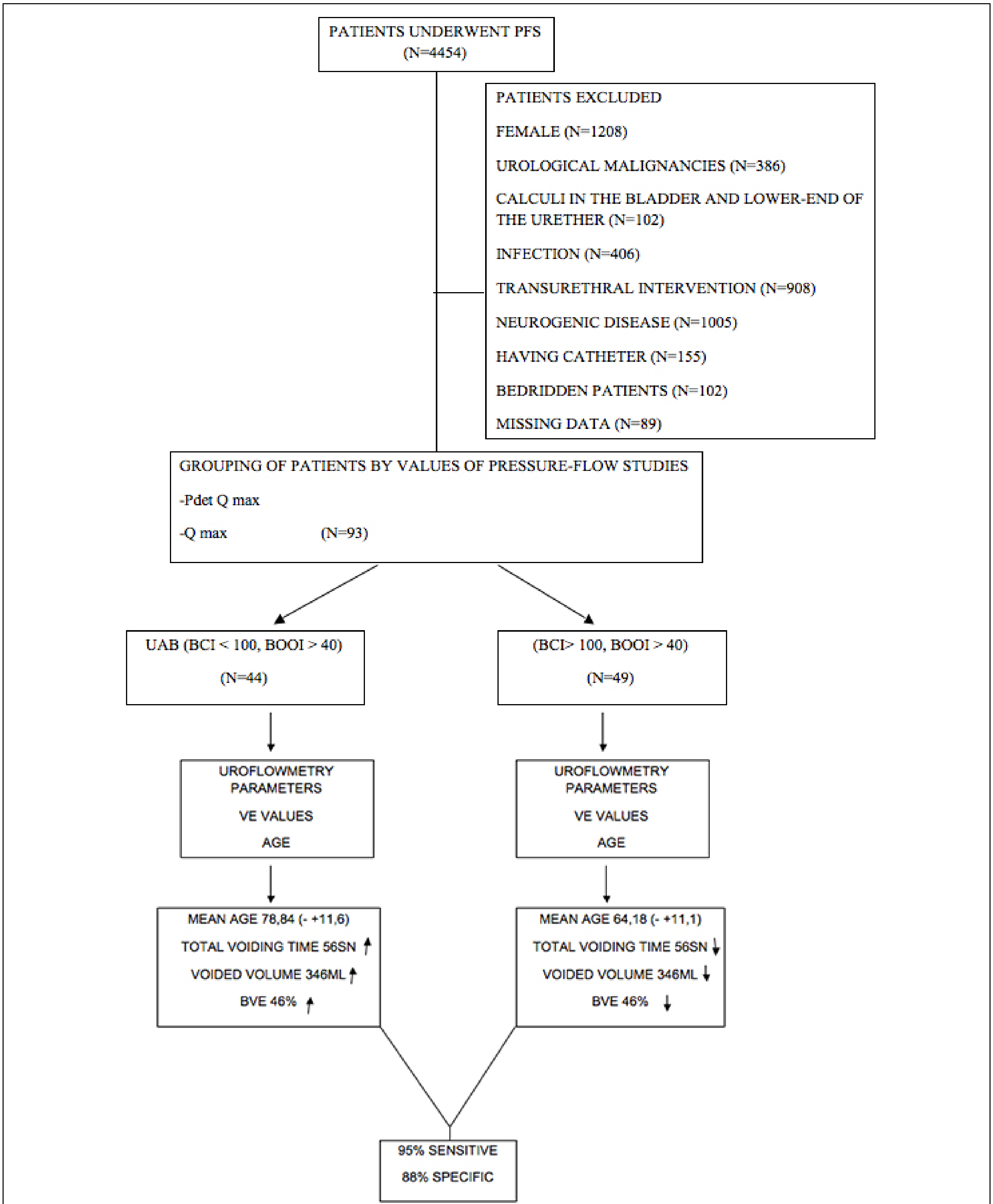
tems, Istanbul, Turkey) were performed at least two times before urodynamic testing and residual urine volume after uroflowmetry was assessed by suprapubic ultrasound measurement (*LOGIQ C2, GE medicalsystems, Jiangsu P. R. CHINA*).

Those with uroflowmetry measurement ≥ 150 ml were included in the evaluation.

Algorithm

The algorithm of the study is shown in Figure 1.

Figure 1.
Algorithm of the study.



Uroflowmetry and measurement of postvoid residual urine

All patients performed at least 2 uroflowmetric measurements prior to urodynamic evaluation and the average was calculated. They were asked to come to test with a full bladder. Uroflowmetry was performed while the patient was standing comfortably and alone.
Uroflowmetry data including maximum urinary flow rate (Q_{max}) and voided volume were noted. For each patient, postvoid residual urine volume was determined by *ultrasonography* (US) by multiplying distances at sagittal, transverse and vertical axis of the bladder by 3.14/6 and noted for all patients (6). Voiding efficacy was calculated as voided volume on uroflow/pre-void bladder capacity measured on ultrasound.

Urodynamic evaluation

Before urodynamics, patients interrupted 3 days in advance drugs that can affect LUT symptoms, in accordance with the *International Continence Society guidelines* (7). Urine culture and antibiogram were done in all cases to exclude any possible risk of infection. Patients with a negative culture were eligible for pressure flow studies with prior quinolone prophylaxis. For pressure flow studies, a two-way 6 F urodynamic catheter (*Mediana, ADS, Ankara, Turkey*) and a 12 F rectal balloon catheter (*UD-CATH, Aymed, Istanbul, Turkey*) were used. Pressure flow studies started with an empty bladder while the patient was alone in a quiet room in sitting position.
Bladder contractility index (BCI) was determined during pressure-flow studies, by adding 5 times the maximum urinary flow (Q_{max}) value following the voiding command, to the detrusor pressure at the moment of maximum flow volume following the voiding command, ($5\ Q_{max} + PdetQ_{max}$). The values ≤ 100 were defined as *Underactive bladder* (UB) (8). *Bladder outlet obstruction index* (BOI), also known as the *Abrams-Griffiths* (AG) number, was also determined during pressure-flow studies, by substracting twice the maximum flow value following the voiding command, from the value of detrusor pressure during the moment of maximum flow ($PdetQ_{max}$) - $2Q_{max}$). BOI was considered positive for the values ≥ 40 (9). BOI < 40 and BCI > 100 (healthy normal population), BOI > 40 and BCI < 100 (patients with both bladder outlet obstruction and hypoactive bladder) were excluded.

Statistical methods

SPSS 15.0 (*Statistical Package for the Social Sciences*) (*SPSS Inc, Chicago, IL, USA*) statistical package was used in the statistical analysis of the data. Kolmogorov-Smirnov goodness-of-fit test was used to assess compliance with the normal distribution of data. Descriptive statistics of the data were calculated.
Significance of differences between the groups was determined by Mann-Whitney U-test. Statistically significance was accepted as $p < 0.05$. Cut-off values of the statistically significant parameters were evaluated by the ROC curve.

Table 1.
Demographic, uroflowmetric and postvoid residual urine data of the patients.

Parameters	UB Group	BO Group	P value
Number of patients	44	49	
Mean age (year)	78.54 ± 11.6	64.18 ± 11.1	< 0.001
Uroflowmetric parameters			
Time to start voiding after the command (sec)	11.95 ± 1.82	10.89 ± 1.06	0.731
Maximum urinary flow (ml/sec)	11.36 ± 0.70	10.46 ± 0.59	0.387
Mean urinary flow (ml/sec)	7.59 ± 0.43	6.53 ± 0.40	0.061
Postvoid residual urine volume (ml)	381.4 ± 45.53	296.93 ± 25.57	0.208

Results

A total of 93 patients with eligible and complete data were assigned to group UB (BOI < 40 and BCI < 100; n = 44) and group BO (BOI > 40 and BCI > 100; n = 49). Mean age was 64.18 ± 1.66 years for group BO and 78.54 ± 1.68 years for the group UB. Mean age was higher in the UB group, with a statistically significant difference between two groups ($p < 0.001$) (Table 1).
A Korean study evaluated relationship between clinical pictures of UB and BO with age and gender, and reported higher prevalance of UB with aging when compared to BO in the male group, whereas an inverse relationship was observed for the female group that showed higher increase of BO prevalence with age compared to UB (3).
In our study which included only male patients age was higher in the UB group compared to the BO group. According to the Korean study, UB group displayed an accelerated increase with age compared to BO group.
Patients over 85 years of age constituted 40% of the UB group and 26% of the BO group. Interestingly, BO showed a decrease after the age of 75 (Figure 2).
We explain this finding as some kind of compensation caused by BO as the result of an increased effort against

Figure 2.
Patient groups by age.

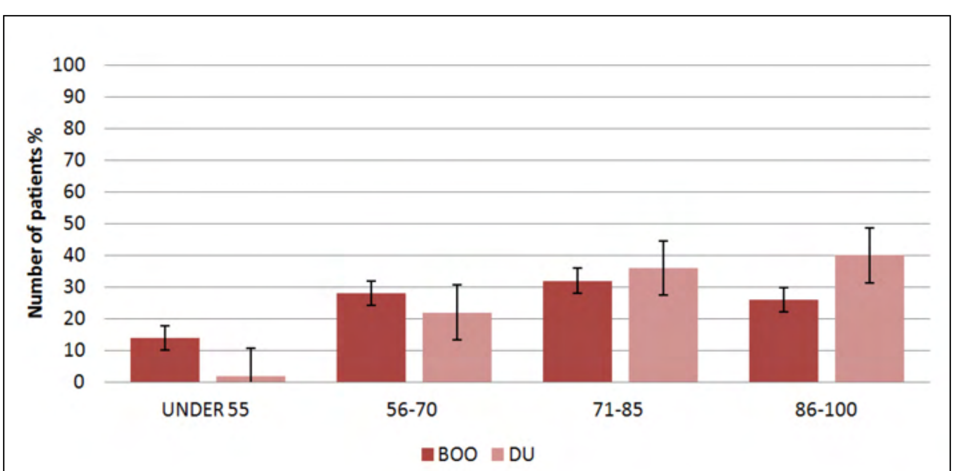
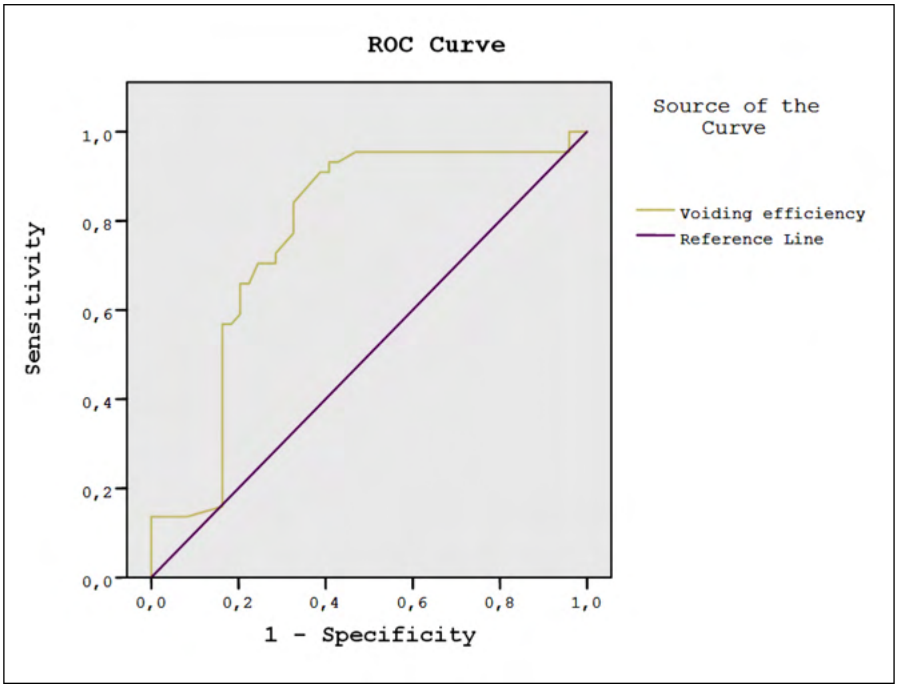


Figure 3.
ROC curves voiding efficiency.



increased resistance preventing UB development at advanced ages. In accordance with this explanation, a decreased UB incidence and an increased BO incidence was shown among female aged over 75 years in the Korean study (3). Additionally, we think UB has a closer correlation with aging but BO pathogenesis is multifactorial.
In the analysis of the two groups with regard to uroflow parameters; mean time to start voiding after the command was 11.95 ± 1.82 seconds in the UB group and 10.89 ± 1.06 seconds in the BO group and there was no statisticaly significant difference between the groups ($p = 0.731$). Mean value for maximum urinary flow was 10.46 ± 0.59 ml/sec in the UB group and 11.36 ± 0.70 ml/sec in the BO group, with a not significant difference between the groups ($p = 0.387$). Mean flow rate was 7.59 ± 0.43 and 6.53 ± 0.40 ml/sec, respectively for UB and BO, again with an insignificant difference ($p = 0.061$).
Measurement of postvoid residual urine volume showed that, mean residual volume was 381.47 ± 45.53 ml in the UB group and 296.93 ± 45.0 ml in the BO group, with an insignificant difference between the groups ($p = 0.208$). Mean voided volume was 666.90 ± 38.84 ml in the UB group and 213.46 ± 13.67 in the BO group, with a statistically significant difference between the groups ($p < 0.001$).
With regard to bladder voiding efficiency, UB group performed at 66.02 ± 2.43% and BO group at 45.53 ± 2.63% efficiency ($p < 0.001$). A statistically significant difference was detected between the two groups for VE.
In the analysis for determining the cut-off by the ROC curve, the area under the curve of maximum diagnostic value for VE was 0.771(±0.052) (Figure 3).
From this study, we can deduce that patients in the BO group were able to empty their bladders more effectively than UB group.
As the best cut-off points, separate ROC curve analysis for VE showed 93% sensitivity and 60% specificity.
In short, UB group performed voiding at high efficiency while BO at lower efficiency levels (Table 1).
In the pressure-flow study; first sensation of bladder filling (early desire to void) was detected at mean volumes of 150.8 ± 64.77 ml in UB group, although not detected in 6 patients, and 117.7 ± 64.52 ml in BO group. First desire to void occurred at average bladder filling of 243.5 ± 100.62 ml in UB group and 177.1 ± 83.86 ml in BO group. Strong desire to void (urgency) occurred at average bladder filling of 355.6 ± 130.66 ml in UB group and 294.4 ± 145.78 ml in BO group. Mean maximum bladder capacity was 544.7 ± 167.45 ml in UB group and 355.1 ± 133.48 ml in BO group. All parameters were determined to be higher, in the patients of UB group.
Mean Q_{max} valus measured during pressure-flow studies was 4.2 ± 3.96 in UB group and 6.5 ± 3.98 ml/sn in BO group. Mean vesical pressure value recorded at maximum measured flow was 34.1 ± 21.31 cm H_2O in UB group and 101.1 ± 40.02 cm H_2O in BO group. Vesical pressure values were higher in BO group, as expected.
Average bladder contractility index was 48.8 ± 27.21 in UB group and 132.5 ± 37.83 in BO group. Average A-G number was 20.0 ± 8.82 in UB group and 88.0 ± 40.69 in BO group (Table 2).

Table 2.
Urodynamic data of the patients.

Bladder sensation during filling	**UB Group**	**BO Group**
First sensation of bladder filling (early desire to void)	150.8 ± 64.77 ml absent in 6 patients	117.7 ± 64.52 ml absent in 1 patient
First desire to void	243.5 ± 100.62 ml	177.1 ± 83.86 ml
Strong desire to void (urgency)	355.6 ± 130.66 ml	294.4 ± 145.78 ml
Maximum bladder capacity	544.7 ± 167.45 ml	355.1 ± 133.48 ml
Pressure-volume studies		
Q_{max} (ml/sec.)	4.2 ± 3.96 ml/sec	6.5 ± 3.98 ml/sec
$PdetQ_{max}$ (cmH_2O)	34.1 ± 21.31 cmH_2O	101.1 ± 40.02 cmH_2O
Bladder contractility index ($PdetQ_{max} + 5Q_{max}$)	48.8 ± 27.21	132.5 ± 37.83
A-G number ($PdetQ_{max} - 2Q_{max}$)	20.0 ± 8.82	88.0 ± 40.69

Discussion

Bladder's ability to contract is well known to decrease with increasing age in both genders, causing pathologies resulting in UB and BO as well as causing LUT symptoms. Age-dependant impairment in UB is closely related with structural impairment of detrusor muscle. Structural changes are related with intense band decreases, decreased density of axonal connections, decreased colla-

gen/muscle ratio, changes in muscarinic receptors, as determined by ultrastructural studies by electron microscopy (10).
BO secondary to benign prostatic hyperplasia is well known to increase with age. Clinical features and prognosis of UB are not clearly defined and any diagnostic method has not been developed but the gold standard of urodynamics. Its prevalence in the elderly population is unclear (11). Diagnosis of BO with urodynamic testing has been shown to increase success rate of transurethral resection of the prostate.
Up to date, many studies emphasized the need for urodynamic diagnosis of BO to define three different conditions as obstructive, intermediate and non-obstructive (12). These studies are mostly based on post-operative observations of the patients who underwent an operation for BO having previously had a TUR-P. Pdet/Q_{max} values decreased postopeartively in the obstructive group, decreased insignificantly in the equivocal group and remained unchanged in the non-obstructive group (13, 14, 15).
UB and BO present with the same clinical symptoms and uroflowmetric findings although they are totally opposite clinical entities requiring completely different treatment. Surgery is usually the treatment of choice for BO, while it is rather unusual for UB, where medical treatment (cholinergic agonists, cholinesterase inhibitors, etc.), clean intermittent catheterization and conservative approach are more prominent. Urodynamic testing, which is the gold standard method, is an invasive diagnostic method used for differential diagnosis in these two clinical entities. In this context, in order to differentiate between these two types of clinical conditions, we attempted to use the non-invasive VE parameter for differential diagnosis. To the best of our knowledge, such a study has not been performed so far. VE was defined for the first time by *Abrams* in 1979 as a measure of bladder contractility against urethral resistance and presented as a percentage figure representing the degree of bladder emptying (13). Subsequent studies of *Abrams* developed a combination nomogram of 6 groups according to the BCI and the BOI. They noted that including VE to this nomogram would be more appropriate to decide both surgical and medical treatment modalities and to interpret the progression of the disease. In 1995, *Bosch* has evaluated the correlation and variation of this percentage value with aging, bladder contractility and urethral resistance (16), but voiding efficiency was calculated after urodynamic testing and was not utilized as a differential diagnostic tool.
A Korean study evaluated relationship between clinical pictures of UB and BO with age and gender, and reported higher prevalance of UB with aging when compared to BO in the male group, whereas an inverse relationship was observed for the female group that showed higher increase of BO prevalence with age compared to UB (3). In our study, which included only male patients, age was higher in the UB group compared to the BO group. According to the Korean study, UB group displayed an accelerated increase with age compared to BO group. Patients over 85 years of age constituted 40% of the UB group and 26% of the BO group. Interestingly, BO showed a decrease after the age of 75 (Figure 1). We explain this finding as some kind of compensation caused by BO as the result of an increased effort against increased resistance preventing UB development at advanced ages. In accordance with this explanation, a decreased UB incidence and an increased BO incidence was shown among female aged over 75 years in the Korean study (3). Additionally, we think UB has a closer correlation with aging bevause BO pathogenesis is multifactorial.
Our patients in the UB group displayed higher values for voided volume, total voiding time and VE percentage than those in the BO group. Average values for VE were 66.02 ± 2.43% and 45.53 ± 2.63% ($p < 0.001$) for the patients of UB and BO group, respectively.
To conclude, patients in the UB group voided larger volumes in longer time periods and more efficiently. Even if not exactly the same as in our study, in the study by *Bosch et al.*, the relationship of VE with age, urethral resistance and bladder contractility were evaluated and a closer and directly proportional relationship was determined between urethral resistance and VE (16). A nomogram with the VE values was developed in the study by *Bosch et al.* suggesting its use for analysing potential future retention risks of these patients in the future, although long-term results were not obtained in this study. Unlike our study, *Bosch et al.* measured post-voidal residual urine volume by catheterization. They checked if the bladder was completely emptied or not by instilling an opaque material obtaining much more realistic values, although the measurements were performed just after the pressure-flow studies. In our study VE was used for differential diagnosis between UB and BO achieving statistically significant difference. *Abrams et al.* developed a nomogram divided into 9 separate columns according to Q_{max} and Pdet/Q_{max} values obtained by flowmetric measurements to estimate whether medical, surgical or conservative approach is needed. It was also mentioned that addition of VE to this nomogram would provide a stronger estimation of correlations (13).
It is apparent that voiding time increases with increased voided volume for UB and BO groups, having equal average flow rates in the uroflowmetric measurements. Voided volume was found considerably higher in the UB group. We realized that our patients in the UB group had larger bladder capacity, which is the main factor affecting voided volume and voiding time. In a different way, it can be stated that patients with BO have smaller bladder capacity and thus void in lesser volumes and for shorter time.
A limitation of our study may be not having examined BOI between 20 to 40 and using a cut-off of 40 (AG-number) as in the Korean study.

Conclusions

In this retrospective study on 93 male patients, we intended to develop an alternative non-invasive diagnostic tool instead of invasive pressure-flow testing, which is recognized as the gold standard for differential diagnosis between UB and BO patients presenting with identical clinical pictures. In conclusion, UB can be diagnosed with at least 93% sensitivity and 60% specificity in men over the age of 80, with uroflowmetry measurment showing a

46% voiding efficiency. However, long-term prospective studies with larger populations are obviously needed in the follow-up of these patients to evaluate retention and upper urinary tract involvement rates.

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