

DOI: 10.5455/medarh.2012.66.324-328

Med Arh. 2012 Oct; 66(5): 324-328

Received: June 18th 2012

Accepted: August 29th 2012

CONFLICT OF INTEREST: NONE DECLARED

ORIGINAL PAPER

Which Is a Better Indicator of Bladder Outlet Obstruction in Patients with Benign Prostatic Enlargement – Intravesical Protrusion of Prostate or Bladder Wall Thickness?

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Objective: to determine the correlation of intravesical prostatic protrusion (IPP) and bladder wall thickness (BWT) with clinical and urodynamic parameters, as well as their sensitivity and specificity with regard to bladder outlet obstruction in patients with a benign prostatic enlargement (BPE). **Materials and methods:** 111 patients with lower urinary tract symptoms and confirmed BPE completed the International Prostatic Symptom Score (I-PSS), as well as a transabdominal ultrasound to determine their prostate volume, a grade of IPP and BWT. All the patients were then subjected to the complete urodynamic studies (UDS). **Results:** the IPP showed a good correlation with the prostate volume ($r=0.61$) and serum PSA ($r=0.48$); $p=0.0000$, free uroflowmetry ($r=-0.27$; $p=0.004$), as well as the determinants of urodynamic obstruction: bladder outlet obstruction index–BOOI ($r=0.36$; $p<0.0001$), and ICS and Schaefer obstruction class nomograms ($\rho=0.33$ and $\rho=0.39$, respectively; $p<0.001$), while the BWT showed only a statistical correlation with age ($r=0.23$; $p=0.02$) and serum PSA ($r=0.4$; $p=0.0000$), regardless of an significant correlation with the IPP ($r=0.45$; $p=0.0000$). The ANOVA test showed a significant difference between the IPP grades for the observed clinical and urodynamic variables with an increase in significance for IPP>10 mm. The area under the ROC curve in the prediction of obstruction for the IPP is 0.71 (sensitivity 59.6, specificity 81.4), while the AUC for the BWT is 0.61 (sensitivity 64.5, specificity 59.2). The stepwise logistic regression model shows that most significant independent variables for the obstruction are the IPP, Q_{max} free and age, with the area under the ROC curve of 0.78 (95% CI 0.695 to 0.856). **Conclusion:** The IPP higher than 10 mm as a non-invasive predictor of infravesical obstruction shows good correlations with clinical and urodynamic parameters, while the specificity and PPV against obstruction are significant. Despite a good correlation with IPP, the BWT is only a modest indicator of obstruction. **Key words:** benign prostatic enlargement, intravesical prostatic protrusion, bladder wall thickness, UDS.

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1. INTRODUCTION

A benign prostatic enlargement shows an increase in incidence with age, causing lower urinary tract symptoms (LUTS) and infravesical obstruction (1). The most precise tool of diagnosing a bladder outlet obstruction are urodynamic studies (UDS), which are, however, invasive, costly, time consuming, and can also lead to a certain degree of morbidity (2). Furthermore, the relationships among urodynamic parameters, treatment outcome and symptom relief are still a subject of controversy. The ISC recommends pressure flow studies before invasive therapies or when a precise diagnosis of bladder outlet obstruction is important (3). Considering the above, it has recently been insisted on searching for non-invasive modalities in bladder outlet obstruction prediction. They rely on a combination of radiological and clinical indicators or on non-invasive urodynamics (4). One of such non-invasive indicators is the ultrasound-confirmed intravesical prostatic protrusion (IPP) and bladder wall thickness (BWT), which according to some studies show a good prediction

towards obstruction (5, 6), compared to urodynamic studies.

Owing to the above, a prospective study was conducted in order to determine the correlation between these determinants with clinical and urodynamic variables and to assess the sensitivity and specificity of IPP and BWT in relation to intravesical obstruction due to BPE.

2. MATERIALS AND METHODS

During the period 2009-2010, the total of 111 patients from daily urological practice were selected at the Urology Clinic of the Sarajevo University Hospital. The patients' mean age was 65.4 years (48-82), and they had lower urinary tract symptoms (LUTS) and confirmed benign prostatic enlargement (BPE). The exclusive criteria were clear neurological or endocrine diseases, suspect bladder cancer or calculosis, urethral stenosis, suspect prostate carcinoma, urinary infection, advanced kidney failure, previous operation of the prostate, as well as taking medications interfering with urination. The transabdominal ultrasound (TAUS) determined their prostate volume, as well as intravesical protrusion of the prostate (IPP). The IPP was determined at the bladder volume of 150-200 ml, moving the sagittal scan of the ultrasound probe horizontally and longitudinally, examining the vesical neck in terms of prostate protrusion into the bladder. The IPP was defined by the distance from the tip of the prostate's protrusion into the vesical lumen to the bladder neck measured in millimetres, determining the following three stages of IPP: <5mm grade I, 5-10 mm grade II, and >10 mm grade III. Bladder wall thickness (BWT) was determined at the full bladder capacity. Prior to the urodynamic studies (UDS), the patients signed the Informed Consent and completed International Prostatic Symptom Score (I-PSS). All the patients were prophylactically given Ciprofloxacin tbl a 500 mg. This was followed by free uroflowmetry (with the minimum of 150 ml of urine voided) and determination of the postvoid residual urine (PVR). The examination continued with cystometry (CMG). The bladder filling

and measuring of the intravesical pressure during filling and urination were performed by introducing the Nelaton Ch8 catheter (Dalhausen & Co, GmbH, Koln, Germany- infusion line) and Nelaton Ch5 urethral catheter (Web-singer GmbH, Wiena, Austria-transducer line) into the bladder – tandem or rail-road technique (7). The abdominal pressure was determined by introducing the standard rectal balloon catheter. The CMG was performed in sitting position with the filling rate of 25ml/min. Before urination, the patients' Ch8 catheters were removed. Then the findings of pressure/flow studies (PFS) were plotted on the Schaefer obstruction class and ICS nomograms, followed by the determination of the bladder contractility index ($BCI = P_{det} Q_{max} + 5Q_{max}$), bladder voiding efficiency ($BVE = \text{voided volume} / \text{total bladder capacity} \times 100$), and the bladder outlet obstruction index ($BOOI = P_{det} Q_{max} - 2Q_{max}$) (8). The UDS, unless otherwise specified, were based on the International Continence Society methodology and terminology (9). Statistical analysis was performed through correlation tests, ANOVA test, area under ROC curve, stepwise logistic regression model using Medcalc program for Windows version 12. The level of significance (two-tailed) was set at $p < 0.05$.

3. RESULTS

The main clinical and demographic characteristics of the patients are given in Table 1. The IPP mean value was 11.8mm (± 11.2), with the BWT mean value of 5.2 mm (± 1). 17 patients (15.3%) had the IPP <5 mm, 30 patients (27%) had the IPP in the range of 5-10 mm, and 64 patients (57.7%) had the IPP >10 mm. At the same time, according to the BOOI <20, 20 patients (18%) was out of obstruction, while 37 (33.3%) and 54 patients (48.6%) were in non-classified and obstruction zone, respectively, (BOOI 20-40 and >40). According to the BOOI obstruction levels, the Kruskal Wallis test showed a significant difference in the IPP size (Figure 1). The IPP mean value in the zone out of obstruction was 8.8 (± 4.1) mm, in the non-classified zone the IPP was 9.9 (± 5) mm, and in the zone of clear obstruction 14.3 (± 7.6) mm ($p = 0.0005$). The patients were then

Clinical and demographics characteristics	Arithmetic mean (SD), Median	Range
Age (years)	65.4 (7.5); 67	48-82
PSA (ng/ml)	2.3 (1.5); 1.9	0.2-6.3
PV(cc)	47.4 (22); 41	25-120
I-PSS	18.2 (5.8); 19	6-31
Q_{max} free (ml/sec)	9.1 (4.4); 8.1	2.1-25
BWT (mm)	5.2 (1); 5.4	2.2-6.8
PVR (ml)	50.1 (52.3); 31	0-250
IPP (mm)	11.76 (6.6); 11.2	1-32

PSA-Prostate specific antigen, PV-prostate volume, I-PSS International prostatic symptom score, Q_{max} free-maximum urinary flow, BWT-bladder wall thickness, PVR-post void residual urine IPP –intravesical protrusion of prostate

Table 1. Basic clinical and demographics characteristic of the BPE group

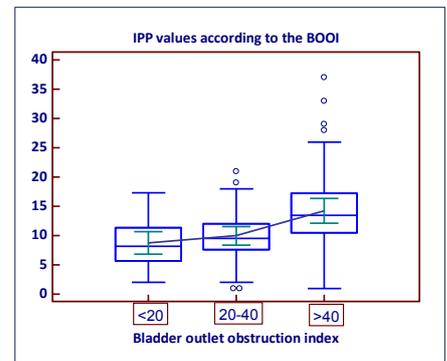


Figure 1. IPP values according to the bladder outlet obstruction index

dichotomised in groups with the cut-off value of IPP >10 mm. The mean BOOI for the group with IPP<10 mm was 35.6 (24.9), while the mean BOOI for the group with IPP>10 mm was 49.8 (29); T test 6.1 ($p = 0.0009$). Furthermore, there was a statistically significant linear regression between these two factors (Figure 2).

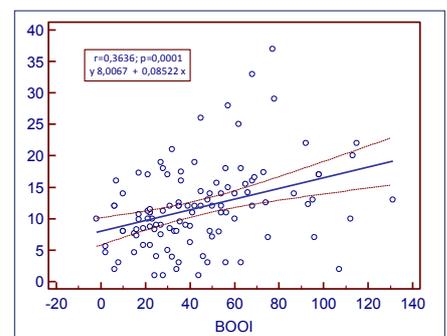


Figure 2. Linear regression for IPP and bladder outlet obstruction index (BOOI)

Pearson Corr. coef.	IPP (mm)		BWT (mm)	
	r	p	r	p
Age	0.08	0.38	0.23	0.02
IPSS	0.05	0.6	0.17	0.08
PV (cc)	0.61	0.0000	0.25	0.007
PSA (mg/ml)	0.478	0.0000	0.4	0.0000
Q _{max} free (ml/sec)	-0.27	0.004	-0.18	0.06
PVR (ml)	0.14	0.14	0.08	0.37
Cyst.Cap (ml)	0.19	0.048	-0.07	0.49
BC (ml/cmH2O)	-0.11	0.24	-0.03	0.78
DO	0.08	0.43*	0.04	0.6*
P _{muo} (cm/H2O)	0.19	0.04	0.06	0.5
P _{det} Q _{max} (cm/H2O)	0.37	0.0001	0.1	0.29
DCD (sec)	0.212	0.03	-0.016	0.8
BVE	-0.2	0.03	-0.19	0.04
BCI	0.21	0.02	0.01	0.9
BOOI	0.36	0.0001	0.15	0.12

* Spearman (rho) corr.coefficient. IPP-intravesical protrusion of prostate, BWT-bladder wall thickness, PV-prostate volume, Q_{max}-peak urinary flow, PVR-post void residual urine, Cyst.Cap.-cystometric capacity, BC-bladder compliance, DO-detrusor overactivity, P_{muo}- minimal urethral opening pressure, P_{det}Q_{max}-detrusor pressure at Q_{max}, DCD-detrusor contraction duration, BVE-bladder voiding efficiency, BCI-bladder contractility index

Table 2. Correlation analysis of IPP and BWT with clinical and urodynamic parameters

A correlation analysis of IPP with clinical and urodynamic parameters showed a good and statistically significant correlation with the prostate volume, serum PSA, while there was no correlation with IPS score (or its obstructive and irritative subgroups). Out of the urodynamic parameters the IPP shows a statistically significant correlation with Q_{max} free, cystometric capacity, P_{det} Q_{max}, BVE, BCI and pressure at minimal urethral opening (P_{muo}) (Table 2). Spearman rank correlation coefficient showed a significant correlation between the IPP and ICS nomogram and Schaefer obstruction class (LinPURR) with the values of rho=0.33 (p=0.0005) and rho=0.39 (p<0.0001), respectively. There is a good correlation of IPP with BWT (r=0.45; p=.0000), although the BWT does not show significant correlations with clinical and urodynamic parameters, except with the patient age, PSA, and shows a weak statistically inverted correlation with BVE (Table 2.). Detrusor overactivity (DO) does not show a correlation with the IPP or with the BWT.

Trichotomising the patients according to the IPP size, the ANOVA test showed significant differences in the prostate volume, Q_{max}, BWT, PSA and P_{det} Q_{max}, with a significant obstruction increment towards the IPP transition levels. While the mean BOOI for the groups with IPP<5mm and IPP 5-10 mm

in the non-classified region is 35.5 and 35.8, the mean BOOI of 50.4 is indicative of an advanced obstruction for the group of patients with IPP>10 mm (p=0.03) (Table 3). Even though the differences in postvoid residual urine are not statistically significant, there is a growth trend from the mean volume of 45 and 36 ml for the first two groups towards a larger quantity of residual urine in the third group (56.6 ml). Detrusor overactivity does not show an incidence increase towards the IPP transition values.

The determination of the discriminant validity of IPP according to the obstruction (BOOI>40) led to the calculation of the area under ROC curve for the IPP in obstruction prediction of 0.71 (95% CI 0.615 to 0.791); p=0.0001, (Sensitivity 59.6, Specificity 81.4, +LR 3.2, -LR 0.5, PPV 73.8, and NPV 69.6).

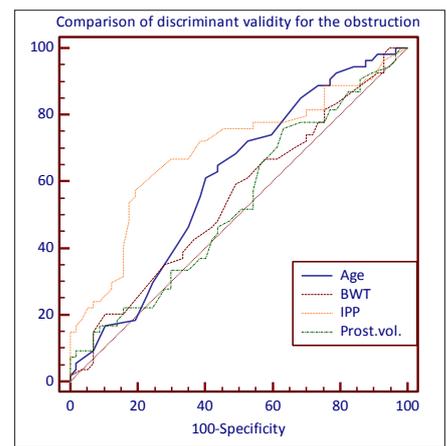


Figure 3. Comparison of ROC curves

The value of 5 mm was taken as the cut-off value according to the obstruction for BWT. 33 patients (57.9%) outside obstruction had the value of BWT >5mm, and 36 patients (66.7%) within the obstruction region, so that the area under the curve (AUC) for BWT is 0.61 with sensitivity 64.5 and specificity 59.2, similarly to the discriminant value of age with the area of 0.60. Prostate volume shows the weakest discrimination with regard to obstruction (Figure 3).

The applied stepwise logistic regression analysis for bladder outlet

No pat. 111	IPP <5mm (17) Mean (SD), Med. (range)	IPP 5-10 mm(30) Mean (SD), Med. (range)	IPP > 10 mm (64) Mean (SD), Med. (range)	Anova (F) p
Age	63.5 (7.2) 66 (48-72)	64.3 (8.5) 64.5 (48-75)	66.4 (7) 67 (52-82)	1.5 0.2
IPS Score	16.5 (6.8) 15 (6-31)	19.1 (5.4) 20 (10-27)	182. (5.6) 19 (8-28)	1.1 0.3
P V(cc)	29.7 (9.7) 26 (20-56)	41.7 (16.4) 38 (24-111)	54.8 (23.3) 49 (24-120)	8.3 <0.001
Q _{max} (ml/sec.)	11.9 (6) 10.5 (4.3-25)	8.9 (3.2) 9.2 (4.6-17)	8.5 (4.1) 7.7 (2.1-18.9)	4.4 0.016
BWT (mm)	4 (0.7) 4 (2.2-4.8)	4.9 (1) 4.8 (2.2-6.6)	5.6 (0.8) 5.9 (2.4-6.8)	25.3 <0.001
PSA (ng/ml)	1.3 (1) 1 (0.2-3.4)	2 (1.2) 1.8 (0.4-4.8)	2.8 (1.7) 2.5 (0.4-6.3)	8.3 <0.001
PVR (ml)	45.3 (59.8) 20 (10-185)	36.7 (46) 25 (2-250)	56.6 (52.6) 37.5 (0-212)	1.5 0.23
DO	5 (29.4%)	10 (34%)	24 (37.6%)	0.44 0.8*
Cyst. Cap. (ml)	259.7 (64.4) 257 (152-356)	230.4 (60) 228.5 (121-390)	257 (66.8) 253 (112-462)	2 0.14
BC (ml/cmH2O)	31.8 (14.3) 35 (11-56)	34.4 (15.3) 40 (10-56)	31.7 (15) 34.5 (4-67)	0.35 0.7
P _{det} Q _{max} (cmH2O)	53.8 (13.9) 54 (35-79)	51.9 (24) 45.5 (17-130)	66.5 (25.5) 62 (23-148)	4.7 0.01
P _{muo} (cmH2O)	31.5 (12.6) 29 (14-57)	24.7 (12.2) 23 (4-49)	40.4 (42) 29.5 (3.4-126)	2.4 0.09
BOOI	35.5 (25.2) 32 (2-107)	35.8 (25) 29 (2-112)	50.4 (29) 45 (-2-131)	3.7 0.03

* Chi2 test. PV-prostate volume, Q_{max}-peak urinary flow, BWT-bladder wall thickness, PVR-post void residual urine, Cyst. Cap.-cystometric capacity, BC-bladder compliance, DO-detrusor overactivity, P_{det}Q_{max}-detrusor pressure at Q_{max}, P_{muo}- minimal urethral opening pressure, DCD-detrusor contraction duration, BOOI-bladder outlet obstruction index

Table 3. Differences of clinical and urodynamic variables according to the grades of IPP

obstruction (as a dependent variable) showed that statistically most significant variables are the IPP ($p=0.01$, OR 1.1), Q_{\max} free ($p=0.01$, OR 1.1) and age ($p=0.03$, OR 0.3), with log likelihood of -28.8 , ($p<0.0001$). The significance level for the Hosmer & Lemeshow test is high ($p=0.6$; >0.1), indicating a good logistic regression model fit. The area under the ROC curve for these variables is 0.78 (95% CI 0.695 to 0.856). Saved predicted probabilities and their use as a new variables increase AUC to 0.88. The variables excluded from this model were BWT, BCI, PVR and prostate volume.

4. DISCUSSION

Benign prostatic hyperplasia affects the expression of lower urinary tract symptoms. Nevertheless there are no significant correlations between the symptoms and clinical and urodynamic parameters characterising mechanical obstruction (10). Owing to this, non-invasive prostate measurements are made in order to further explain morphofunctional correlations, trying to develop a new precise method that could replace the standard urodynamic studies, thus reducing the costs, increasing availability and reducing patients' discomfort. Since the bladder outlet obstruction (BOO) is a dynamic event caused both by mechanical obstruction and by bladder functioning, there is the rationale for including the anatomic evaluation of the prostate and bladder as part of the assessment (5).

It has become known that the prostatic configuration together with the expressed IPP can influence normal urination. The IPP seems to support intravesical obstruction through the "valve ball" mechanism, in which prostatic lateral and median lobes interfere with the complete opening of the vesical neck during urination, disrupting the funnelling effect of the bladder neck and causing dyskinetic movement of the bladder during voiding (11).

Literature reports a wide range of the confirmed IPP grade III; thus Reis et al. find the incidence for IPP gr. I of 28.5%, 12% grade II and 59.5% IPP gr. III (12), while Lieber et al. find only 10% of patients with IPP gr. III (13), and Kim finds the incidence gr. III of

IPP in 15% of patients (14). Chia et al. show that out of 125 patients who were diagnosed as having significant BOO (BOOI >40), 95 had grade III (76%) and 30 grade I–II IPP. Our study shows the incidence of IPP grade III of 57.7% within the observed sample, with the mean value of IPP amounting to 14.3 mm, in patients within the obstruction zone (BOOI >40). The mean value of BOOI for grade III of IPP amounted to 50.4 vs. 35.8 and 35.5 for grade II and grade I, respectively. Furthermore, the IPP correlates well with the obstruction determinants (the correlation coefficient for the BOO index and IPP is 0.37, $p<0.0001$, as well as a clearly demonstrated correlation with the ICS and Schafer nomogram). Chia et al., exploring the benefit of the intravesical prostatic protrusion in 200 patients, show that the IPP is a statistically significant predictor ($p<0.001$) of bladder outlet obstruction, and grade III IPP was associated with a higher BOO index than was grade I–II (BOOI 67.15 vs. 43.13, $p<0.001$) (5). Franco et al. find good correlations between intravesical prostatic protrusion and the bladder outlet obstruction index (Spearman's $\rho = 0.49$, $p=0.001$), and Schaefer obstruction class (Spearman's $\rho = 0.51$, $p = 0.001$) (15).

This study shows that the IPP has a good correlation with age, prostate volume (PV), maximum urinary flow, postvoid residual urine, and offers statistically significant correlations with the main urodynamic parameters typical of obstruction, but also of the bladder functioning (Pmuo, Pdet Q_{\max} , BVE and BCI; $p<0.05$). Han et al., examining mutual correlations of IPP with other clinical variables in 257 patients, show that the degree of IPP correlated positively with age ($r = 0.210$, $p < 0.01$), prostate volume ($r = 0.534$, $p < 0.01$) and PVR ($r = 0.314$, $p < 0.01$), while negatively with the Q_{\max} ($r = -0.364$, $p < 0.01$). There was no significant correlation between the degree of IPP and IPSS ($r = 0.064$, $p=0.299$) (16), just as our study shows no correlation of IPP and IPSS; ($r=0.05$, $p=0.6$). Kim et al. find only a statistically significant correlation between the IPP and IPSS, but with no difference between the obstructive and irritative domain of the question-

naire (17). Again, Kim (14) suggests that IPP, which reflects anatomical changes in the prostate, may be related to male symptoms of overactive bladder (OAB), defining the OAB in patients who complained of symptoms with 2 points or more for the 4th questionnaire related to urgency on the IPSS.

The IPP appears to be a very valuable and reproducible ultrasound feature, as part of the intravesical obstruction examination in patients with BPE. A high IPP grade can also be a strong outcome predictor after acute urinary retention (AUR) treated with trial without catheter (TWOC). Mariappan et al. shows that the TWOC is more likely to fail in patients with intravesical prostatic protrusion larger than 10 mm, because men with IPP 10 mm or less, compared to those with a larger intravesical prostatic protrusion, were 6 times more likely to have a successful trial without catheter (18). Furthermore, since intravesical prostatic protrusion significantly correlates with greater prostate volume, higher obstructive symptoms and lower peak urinary flow rate, it suggests that it may have clinical usefulness in predicting the need for treatment (13).

According to some researchers, bladder wall thickness (BWT) of 5 mm appears to be the best cut-off point for diagnosing BOO, carrying a high sensitivity and specificity (19). Franco et al. demonstrate that the detrusor wall thickness (DWT) is an excellent predictor of BOO, with AUC for DWT of 0.845, and a good correlation with the Schaefer obstruction class (Spearman's $\rho = 0.432$, $p = 0.02$) (15). Oelke et al. measured detrusor wall thickness and found that over 95% of patients with the detrusor thickness higher than 2 mm were in urodynamic obstruction (6). According to Kim et al. higher BWT grades showed significant differences with higher PV, serum PSA and IPSS ($p<0.05$). Furthermore, BWT >5 mm was associated with higher PVR and acute urinary retention (17). Our study did not show a strong discriminant power of BWT in relation to obstruction, as the AUC for BWT is only 0.61 (sensitivity 64.5 and specificity 59.2), and in addition to a good correlation with the IPP, there is only a statistically significant correlation with age

and serum PSA. Some researchers did not find a difference in the mean value of BWT between patients with normal UDS findings, intravesical obstruction or DO. The inconsistency in obtained results and a lack of technique standardization are limiting the use of BWT as a strong predictor of intravesical obstruction for the time being (12).

There is also the issue of the manner of ultrasound IPP determination. Some studies show an extended use of transrectal ultrasound (TRUS) in prostate measuring (13, 21.) Since the transrectal measuring causes a greater discomfort to patients, transabdominal ultrasound (TAUS) is shown to be equivalent to rectal ultrasound when the prostate is measured at the bladder volume above 100 ml (22). TAUS is now a common clinical method, non-invasive and easy to learn and evaluate. Using the same probe, the upper urinary tracts can be easily assessed at the same time. (5). Foo also concludes that the degree of IPP can be measured non-invasively in the midsagittal plane, and can be graded accordingly. Diagnosis of BPE in the clinic can be aided by simple, non-invasive, transabdominal ultrasound (23).

5. CONCLUSION

This study has demonstrated the use of assessing the intravesical prostatic protrusion in predicting intravesical obstruction in patients with BPE. It shows a good correlation of IPP with clinical and urodynamic variables, as well as high specificity and positive predictive value in terms of obstruction by the IPP grade increase, while the determination of the bladder wall thickness shows this parameter to be only a modest indicator of bladder outlet obstruction.

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