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Intravesical Prostatic Protrusion in Men in Olmsted County, Minnesota

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Abstract

Purpose—Ultrasonically measured intravesical prostatic protrusion may be a promising noninvasive method of assessing bladder outlet obstruction. Previous investigations of this technique focused on patients with acute urinary retention and symptomatic men identified in urology clinics, which may not reflect the distribution of intravesical prostatic protrusion in community dwelling men.

Materials and Methods—In 2006 a total of 322 white men residing in Olmsted County, Minnesota underwent transrectal ultrasound examination which permitted direct measurement of intravesical prostatic protrusion. Cross-sectional associations between lower urinary tract symptoms/benign prostatic enlargement and intravesical prostatic protrusion were measured. Rapid increases in lower urinary tract symptoms/benign prostatic enlargement measures as predictors of severe intravesical prostatic protrusion were also assessed.

Results—Overall 10% of these men had an intravesical prostatic protrusion of 10 mm or greater. Greater intravesical prostatic protrusion was weakly correlated with greater prostate volume (r_s = 0.28), higher obstructive symptoms (r_s = 0.18) and lower peak urinary flow rate (r_s = −0.18). Men

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Study received institutional review board approval.

with the most rapidly growing prostate before intravesical prostatic protrusion measurement were 3 times more likely to have an intravesical prostatic protrusion of 10 mm or greater. Men with an intravesical prostatic protrusion of 10 mm or greater were more likely to use medications for lower urinary tract symptoms/benign prostatic enlargement compared to those with an intravesical prostatic protrusion less than 10 mm (adjusted OR 2.95, 95% CI 1.23–7.06).

Conclusions—These population based data provide reference ranges for future studies of intravesical prostatic protrusion as a predictor of adverse urological outcomes. Intravesical prostatic protrusion is significantly correlated with greater prostate volume, higher obstructive symptoms and lower peak urinary flow rate, suggesting that it may have clinical usefulness in predicting the need for treatment.

Keywords

urinary tract; prostate; urinary retention; organ size; prostatic hyperplasia

Benign prostatic enlargement is a common problem for aging men[1] that has been associated with increased risk of LUTS,[2] AUR,[3] and medical and surgical treatment.[4] Several studies have suggested that it is not BPE alone that causes LUTS, but rather the extent to which the prostate protrudes into the bladder. These studies suggest that ultrasonically measured IPP is correlated with BPE,[5,6] and that it may be a useful, noninvasive predictor of urodynamically ascertained BOO[5,7–9] as well as a predictor of TWOC success for men with AUR.[6,10] Chia et al found that 75% of men with significant BOO had IPP greater than 10 mm, whereas only 8% of men with nonsignificant BOO had IPP greater than 10 mm.[7] Lim[5] and Nose[9] et al found correlations between IPP and BOO of 0.51 and 0.62, respectively. In a series of 100 consecutive men with an initial episode of AUR only 33% of men with an IPP greater than 10 mm had a successful TWOC, while 64% of men with IPP from 1 to 5 mm had a successful TWOC.[10]

While these studies provide initial support for the use of ultrasonic IPP measurement in managing BOO and successful TWOC, they have been limited to clinical series of patients, and do not reflect the full spectrum of BPE and IPP. Studying only a limited range of disease may overestimate sensitivity and specificity.[11] To more fully understand the usefulness of IPP measurement it is necessary to investigate the distribution of IPP and associations with urological outcomes in the general community. Therefore, data from the Olmsted County Study of Urinary Symptoms and Health Status Among Men were used to describe IPP in a population based sample of men, and to assess associations between IPP and LUTS, prostate volume, post-void residual and peak urinary flow rate.

Materials and Methods

Study Population

Many of the details of the study have been previously published.[12,13] A randomly sampled, population based group of white men 40 to 79 years old residing in Olmsted County, Minnesota in 1990 was identified through the Rochester Epidemiology Project.[14] Men who had a history of prostate or bladder surgery, urethral surgery or stricture, or medical or other neurological condition that could affect normal urinary function were excluded from study. After excluding men with preexisting conditions from analysis 3,874 were asked to join the study and 2,115 agreed to participate (55%). A comparison of medical records of participants and nonparticipants indicated few differences except for a history of urological diagnosis, with responders having a slightly greater prevalence of diagnosis of kidney stones, urinary tract infections or benign prostatic hyperplasia.[15]

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Participants completed a previously validated baseline questionnaire that assessed lower urinary tract symptom severity from questions similar to the American Urological Association Symptom Index and associated bother. All participants also voided into a portable urometer to measure peak urinary flow rate. A 25% random subsample was invited to participate in a detailed in-clinic urological examination including transrectal sonographic imaging to determine prostate volume and serum PSA. Of 537 men 475 (88%) agreed to participate in this more intensive examination.

The cohort was actively followed on a biennial basis for 16 years using a protocol similar to that of the initial examination. During the second and third round of visits men who did not participate in the followup were replaced by 332 men randomly selected from the community after being screened for the exclusion criteria used at baseline. Of the replacement men 158 were added to the clinic subset. Since that time the study has been maintained as a closed cohort. However, in the 8th biennial round (2004) a random sample of 133 men who had previously been receiving questionnaires was added to the in-clinic subset. The study was reviewed and approved by the institutional review boards of Mayo Clinic and Olmsted Medical Center.

Measurement of IPP

IPP measurements were incorporated into the in-clinic examination during the 9th biennial round of the study (2006). IPP was measured from images of the prostate obtained from transrectal ultrasound using the midline sagittal image by drawing a line from the anterior to posterior intersections of the bladder base and tip of the intravesical prostatic protrusion (fig. 1). A cut point of IPP 10 mm or greater, which has been previously shown to be predictive of BOO and successful TWOC, was used for categorical analyses.[6,7,10] Other cut points were also examined.

Measurement of LUTS/BPE

Methods for determining prostate volume and LUTS measures have been previously described. Prostate volume was measured by transrectal ultrasound (type 8551 7.0 MHz endosonic multiplane transducer, Bruel and Kjaer, Naerum, Denmark).[3,16] LUTS and associated bother were measured by a previously validated questionnaire with questions similar to the American Urological Association Symptom Index.[13,17] Serum PSA was determined with the Tandem-R PSA assay (Hybritech Inc, San Diego, California). The serum samples were obtained before any prostatic manipulations including digital rectal examination and transrectal ultrasound.[18] Peak urinary flow rates were measured electronically using a Dantec 1000 urometer (Dantec Medical, Santa Clara, California).[19]

Measurement of Treatment

Information on the use of medical and surgical LUTS/BPE treatments and prostate cancer diagnoses was obtained through self-report, and through passive followup of the community medical records.

Statistical Analyses

Descriptive statistics of the measurements at the 2006 followup visit were tabulated. Spearman rank correlation coefficients were used to describe the cross-sectional relationships between IPP and LUTS/BPE measures. Linear mixed effects regression models were used to estimate annual longitudinal changes in each LUTS/BPE measure by regressing each measure on the time from initial measurement and 10-year age groups. An interaction term was included to allow for different slopes across age groups. An overall annual change (slope) for each man was determined by combining the average longitudinal changes (fixed effects) with the individual changes (random effects). Similarly fixed and random effects allowed the determination of an overall baseline intercept for each age decade and allowed for offsets for each individual. Observations after treatment for BPE and diagnosis of prostate cancer were censored. Because of skewed distributions a log transformation was applied to peak urinary flow rate, PSA and total prostate volume measurements before slope determination. Logistic regression models were used to examine associations between severe IPP (IPP 10 mm or greater) and rapid changes in LUTS/BPE measures. Other cut points were also examined. Logistic regression models were used to examine the cross-sectional association between LUTS/BPE medication use and LUTS/BPE measures. Multivariable logistic regression models were used to simultaneously adjust for all variables in the model. All analyses were done using SAS® version 8.2.

Results

A total of 349 men (median age 65.6 years) participated in the in-clinic examination in 2006. Transrectal ultrasonic IPP measurements were available for 322 of 349 men (92%), with a median (IQR) of 0 mm (0 to 5) (table 1). For these men 194 (60%) had no protrusion, 96 (30%) had an IPP of 1 to 9 mm and 32 (10%) had an IPP of 10 mm or greater (fig. 2).

There was no significant correlation between IPP and age ($r_s = 0.08$, $p = 0.17$). However, larger IPP was significantly but weakly correlated with increasing symptoms, bother, prostate volume, PSA and decreasing peak flow rate (all $p < 0.05$, table 2). The correlations were modest. However, the strongest correlation was between IPP and prostate volume ($r_s = 0.28$, $p < 0.0001$). Among the individual symptoms the highest correlations were between IPP and the obstructive symptoms of incomplete emptying, stopping and starting, straining and weak stream, with correlations of 0.13, 0.14, 0.12 and 0.21, respectively (all $p < 0.05$).

There was a trend for men with more rapid increases in prostate volume to be more likely to have had IPP measurements of 10 mm or greater compared to those with less rapid increases in prostate volume (table 3). Men with more rapid increases in obstructive symptom score and those with more rapid decreases in peak urinary flow rate were more likely to have an IPP of 10 mm or greater. However, these trends were only marginally significant.

As a test of whether IPP might be a clinically useful predictor of BPE severity, we examined the cross-sectional association between IPP and LUTS/BPE medical treatment. At the 2006 followup visit 70 men (22%) reported that they were taking an oral or herbal medication for LUTS/BPE symptoms. Of these men approximately 59% were taking an α-blocker, 20% were taking an herbal medication (such as saw palmetto), 9% were taking a combination of an α-blocker and a 5α-reductase inhibitor, 1 was taking an antimuscarinic medication, and 11% were taking a combination of an α-blocker, a 5α-reductase inhibitor, an herbal medication or an antimuscarinic medication. Men with an IPP of 10 mm or greater were more than 3 times more likely to use LUTS/BPE medications compared to men with an IPP less than 10 mm, with an odds ratio of 3.25 (95% CI 1.53–6.93) (table 4). After adjusting the association between IPP and medication use for age, LUTS/BPE measures, and bother score, the odds ratio remained significant and was only slightly attenuated.

Discussion

These data indicate that increasing IPP was weakly but significantly associated with increasing prostate volume, obstructive symptoms, PSA and decreasing peak urinary flow rate. Additionally, men with IPP 10 mm or greater were more than 3 times more likely to be taking LUTS/BPE related medications.

These IPP data from community based men may serve as useful reference ranges for future studies incorporating this measure. Previous IPP use has been confined to patients with severe BPE symptoms who were having an evaluation which included invasive urodynamics or men with an episode of acute urinary retention.[5–10] IPP measures were much higher in these men compared to those in our study population, as these previous reports suggested that 33% to 60% of men may have IPP measures greater than 10 mm compared to the 10% of men in our study population. Additionally, Mariappan et al observed a correlation of 0.59 between IPP and prostate volume in a sample of men presenting with AUR,[6] and Lim et al found a correlation of 0.61 between IPP and prostate volume in a group of men presenting with LUTS.[5] In this study the highest correlation was between IPP and prostate volume. However, the correlation of 0.28 in a community based sample was much lower than that observed in clinical cohorts.

Longitudinal data of LUTS/BPE measures years before IPP measurement allow the assessment of predictors of severe prostatic protrusion. In this study men with the most rapidly growing prostate were more likely to have an IPP of 10 mm or greater, which has been used as a cut point indicative of severe protrusion, BOO and unsuccessful TWOC.[6,7,10] Previous work from our group indicated that men with the most rapidly growing prostate were twice as likely to have rapidly increasing symptoms, which could partially explain the stronger associations seen in the symptomatic men recruited into the previous studies.[20] While only marginally significant, men with more rapidly increasing obstructive symptoms and decreasing peak flow rate were more likely to have an IPP of 10 mm or greater, which supports the idea that severe protrusion may be a predictor of BOO and unsuccessful TWOC.

If IPP is a useful clinical measure of disease severity, one also should see an association between IPP and medication use. We have previously shown that increased symptoms, decreased peak urinary flow rate and an enlarged prostate independently predicted future treatment for this community cohort.[4] In this study cross-sectionally men with severe IPP were 3 times more likely to be using a LUTS/BPE medication. Interestingly severe IPP and increased symptoms remained independently associated with current medication use after adjustment for age, total prostate volume, peak urinary flow rate and bother score. This finding raises a question of significant interest to clinical urologists treating BPE. What is there about an IPP of 10 mm or greater per se that leads to medical treatment, even after accounting for total prostate volume and reported bother?

Strengths of this study include the ability to survey IPP in a population based cohort of men, resulting in baseline reference ranges for future studies using IPP as a predictor of adverse urological outcomes. Additionally, longitudinal data of LUTS/BPE measures years before IPP measurement allow the assessment of predictors of severe prostatic protrusion. However, there are some potential limitations to consider as well. The IPP measures were available at a single point. Therefore, it is not possible to determine when IPP first developed or to assess temporality. Measurement of IPP from archival transrectal ultrasound images obtained in earlier rounds may allow us to determine the rate of IPP change over time as well as the associated temporal development of symptoms and treatment. Additionally, generalizability may be limited as all participants in this cohort study were white with a predominantly northwestern European ethnic background, and were 54 to 90 years old. These findings may not be applicable to other ethnic populations and age groups.

Of the men in this analysis 15 of 322 (4.7%) had received treatment, and 89 of the 418 (16.3%) in-clinic men who did not participate during this round had been treated or diagnosed with cancer. This could bias our estimates of IPP toward the null if these men were also likely to have enlarged IPPs.

Finally the effect of bladder volume and ultrasound test-retest on IPP measurements was not assessed in this sample. In a sample of 22 symptomatic men undergoing transurethral resection of the prostate Yuen et al found that IPP measured via abdominal ultrasound decreased with increasing bladder volume and recommended IPP measurement at a bladder volume between 100 and 200 ml.[21] If this effect is also applicable to men without indications for transurethral resection of the prostate, any measurements obtained from men with larger bladder volumes would tend to bias the results toward no association. However, the men in our study voided before the ultrasound appointment with 83% having less than 200 ml and 88% having less than 250 ml post-void residual.

Conclusions

These population based data provide reference ranges for future studies examining IPP and the use of IPP as a predictor of urological outcomes. Additionally, these results indicate that IPP is significantly correlated with greater prostate volume, higher obstructive symptoms and lower peak urinary flow rates, suggesting that it may have clinical usefulness in predicting the need for treatment.

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Abbreviations and Acronyms

AUR	acute urinary retention
BOO	bladder outlet obstruction
BPE	benign prostatic enlargement
IPP	intravesical prostatic protrusion
LUTS	lower urinary tract symptoms
PSA	prostate specific antigen
TWOC	trial without catheter

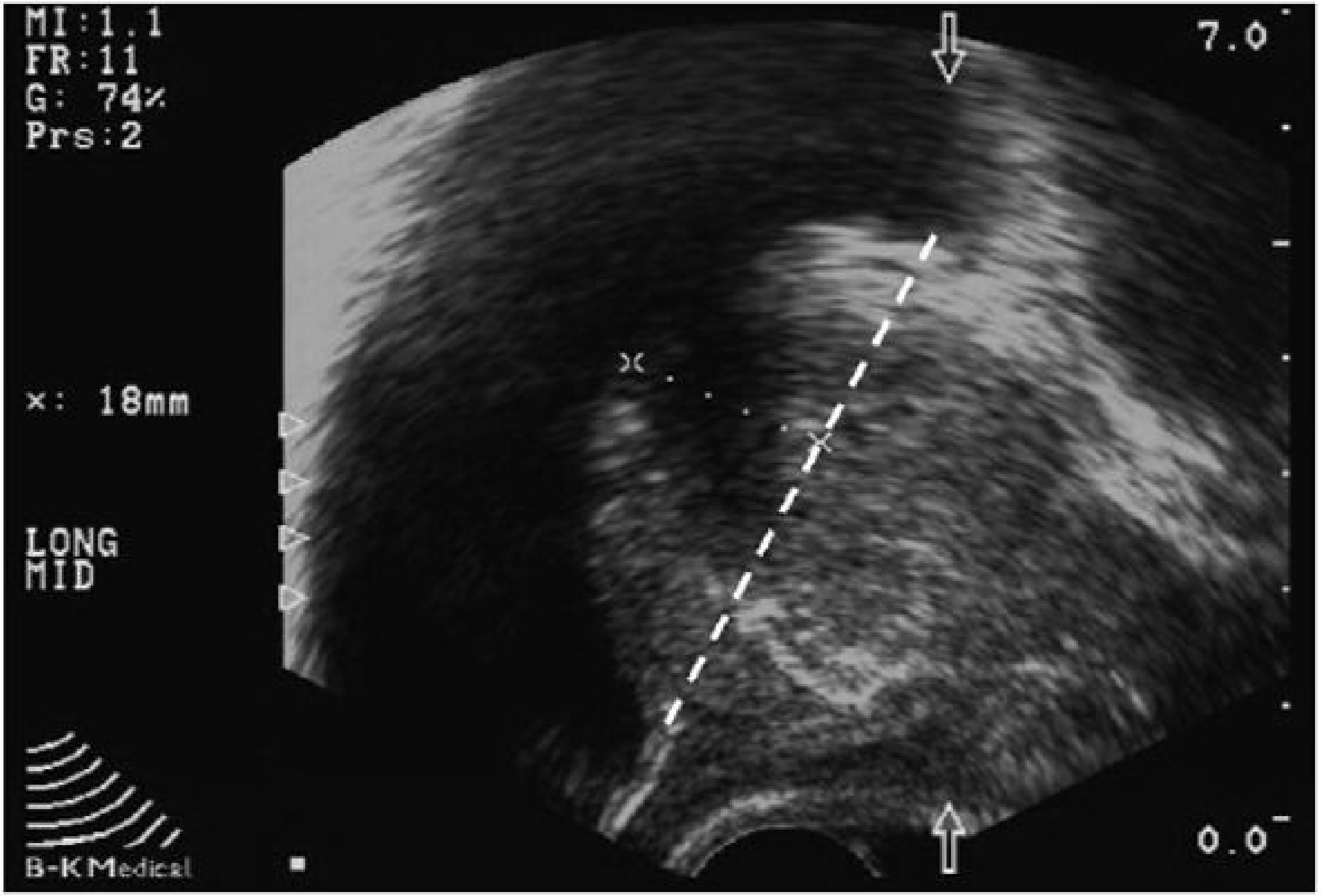

Figure 1.
Measurement of IPP via transrectal ultrasonic imaging

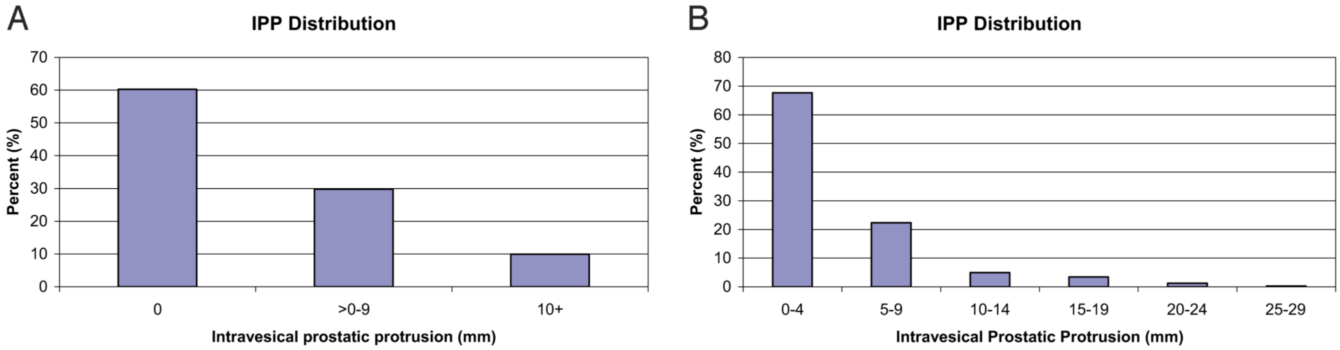

Figure 2.
Distribution of IPP size (mm) examining various cut points

Table 1

Descriptive patient characteristics

	No. Pts	Median (25th, 75th percentiles)
Age	322	65.7 (60.5, 71.2)
Symptom score:	322	8.0 (4.0, 12.0)
Irritative	322	4.0 (2.0, 6.0)
Obstructive	322	4.0 (1.0, 7.0)
Bother	322	3.0 (0.0, 8.0)
Peak urinary flow rate (ml/sec)	319	16.4 (11.3, 23.1)
Total prostate vol (ml)	321	31.2 (26.2, 42.7)
Total PSA (ng/ml)	322	1.2 (0.7, 2.2)
Post-void residual vol (ml)	322	38.0 (19.0, 104.0)

Table 2
Spearman correlations between IPP and LUTS/BPE measures

	Unadjusted R, p
Age	0.08, 0.17
Symptom score	0.15, 0.01
Irritative symptom score:	0.07, 0.21
Daytime frequency	0.09, 0.11
Nocturia	0.04, 0.45
Urgency	0.05, 0.36
Obstructive symptom score:	0.18, 0.001
Incomplete emptying	0.13, 0.02
Stopping/starting	0.14, 0.01
Straining	0.12, 0.03
Weak stream	0.21, 0.0002
Bother score	0.12, 0.04
Peak urinary flow rate (ml/sec)	−0.18, 0.001
Total prostate vol (ml)	0.28, <0.0001
Total PSA (ng/ml)	0.14, 0.01
Post-void residual vol (ml)	0.11, 0.05

Table 3
Association between changes (slopes) in LUTS/BPE measures and IPP severity

Percentiles	OR (95% CI)	p for Trend
Symptom score slope:		
0–25	1.00 —	0.0957
25–50	1.23 (0.36–4.21)	
50–75	2.39 (0.79–7.22)	
75–100	2.17 (0.71–6.67)	
Irritative score slope:		
0–25	1.00 —	0.1358
25–50	2.08 (0.60–7.21)	
50–75	2.99 (0.91–9.81)	
75–100	2.41 (0.71–8.17)	
Obstructive score slope:		
0–25	1.00 —	0.0694
25–50	1.42 (0.43–4.67)	
50–75	1.64 (0.51–5.26)	
75–100	2.65 (0.89–7.90)	
Bother score slope:		
0–25	1.00 —	0.5047
25–50	0.30 (0.08–1.17)	
50–75	1.24 (0.48–3.18)	
75–100	1.00 (0.38–2.67)	
Peak flow rate slope:		
75–100	1.00 —	0.0488
50–75	6.48 (0.75–55.70)	
25–50	4.23 (0.46–39.16)	
0–25	9.00 (1.09–74.57)	
Prostate vol slope:		
0–25	1.00 —	0.0061
25–50	3.11 (0.31–30.91)	
50–75	6.61 (0.77–56.86)	
75–100	10.56 (1.29–86.51)	

Table 4
Association between LUTS/BPE medication use and IPP

	Unadjusted OR (95% CI)	Adjusted OR (95% CI)*
IPP (mm):		
Less than 10	1.00	1.00
10 or Greater	3.25 (1.53–6.93)	2.95 (1.23–7.06)
Age:		
50–59	1.00	1.00
60–69	0.89 (0.42–1.88)	0.94 (0.42–2.15)
70+	2.18 (1.03–4.64)	1.52 (0.66–3.51)
Symptom score:		
7 or Less	1.00	1.00
Greater than 7	6.00 (3.01–11.95)	3.37 (1.43–7.98)
Bother score:		
3 or Less	1.00	1.00
Greater than 3	3.86 (2.17–6.88)	1.95 (0.94–4.05)
Peak flow rate (ml/sec):		
12 or Greater	1.00	1.00
Less than 12	2.33 (1.33–4.07)	1.38 (0.74–2.57)
Prostate vol (ml):		
30 or Less	1.00	1.00
Greater than 30	2.28 (1.29–4.02)	1.56 (0.82–3.00)

*Odds ratios adjusted for all variables in the table.