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Original article

Significant intravesical prostatic protrusion and prostatic calcification predict unfavorable outcomes of medical treatment for male lower urinary tract symptoms

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ABSTRACT

Objective: To evaluate the impact of intravesical prostatic protrusion (IPP) and prostatic calcification on medical treatment for male lower urinary tract symptoms (LUTS).
Materials and methods: Men over the age of 40 years with total International Prostate Symptom Score (IPSS) ≥ 8 were recruited from January to August 2013. The maximal flow rate, postvoiding residual (PVR) urine volume, total prostate volume (TPV), transitional zone volume (TZV), transitional zone index (TZI), and grades of IPP and prostate calcification were recorded. All patients received α-blocker monotherapy, and Global Response Assessment (GRA) was used to determine treatment response 1 month after the treatment. The primary end point was to compare the treatment results in patients with and without significant IPP or prostate calcification. Univariate and multivariate logistic regression analyses were performed to determine whether IPP and prostatic calcification are predictors of improved outcome (GRA ≥ 1).
Results: We enrolled 112 men with a mean age of 65.5 (range, 42–89) years. IPP was significantly positively correlated with TPV, TZV, TZI, and PVR. Prostatic calcification was significantly negatively correlated with total IPSS, IPSS Voiding, and IPSS Storage. After 1-month treatment with α-blockers, the average total IPSS decreased from 18.2 ± 7.4 to 13.1 ± 4.5. Sixty-nine patients (61.6%) reported improved outcomes. Patients with large prostate volumes (TPV ≥ 40 mL) and small prostate volumes (TPV < 40 mL) had similar improved outcome rates (56.5% and 65.1%, respectively). Patients with significant IPP (Grades II and III) had significantly lower improved outcome rates (36.8%) than those without significant IPP (74.3%). Patients with prostatic calcification also had a significantly lower rate of improved outcome (47.9%) than those who did not (71.9%). Multivariate logistic regression analyses showed that IPP and prostatic calcification are predictors of unfavorable outcome (GRA < 1) after adjusting for age, TPV, and total IPSS.
Conclusion: Significant IPP and prostatic calcification are unfavorable predictors of successful α-blocker treatment for benign prostatic hyperplasia-induced male LUTS.

1. Introduction

Benign prostatic hyperplasia (BPH) affects over 50% of men by 60 years of age, resulting in millions of dollars in health-care expenditures for the treatment of lower urinary tract symptoms (LUTS) and urinary obstruction.[1] The use of α-blockers is the first-line treatment for patients with bothersome LUTS caused by BPH, but some patients are dissatisfied with initial medical treatment. Patients with more severe symptoms and larger prostate volumes have a higher risk of medical treatment failure. The International Prostate Symptom Score (IPSS) and total prostate volume (TPV) are useful predictors of medical treatment maintenance.[2]

Intravesical prostatic protrusion (IPP) is a morphological change in the prostate. Patients with significant IPP are more likely to have decreased peak urinary flow rates and to present with acute urinary retention (AUR).[3] IPP can also be used to predict the success of a

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voiding trial following AUR,[4] and patients with significant IPP have more severe bladder outlet obstruction (BOO) and impaired detrusor function.[5] Lee et al[6] found that a higher IPP grade is associated with a higher risk of clinical progression in LUTS. Male overactive bladder may be correlated with IPP,[7] and the degree of IPP can also be associated with storage symptoms.[8] Further, significant IPP may be an independent predictor of improved postoperative outcomes.[9]

Multiple small calcifications are often incidental findings on prostate ultrasounds and an indicator of the aging process rather than pathologic findings. Larger numbers of prostatic calcifications have been reported to be related to underlying inflammation.[10] However, the role of prostatic calcification in male LUTS has not been investigated. The objective of this study was to evaluate the impact of IPP and prostatic calcification on medical treatment for LUTS.

2. Materials and methods

Men over the age of 40 years with a total IPSS ≥8 were recruited from January 2013 to August 2013. The IPSS Voiding (IPSS-V) and Storage (IPSS-S) subscores were recorded separately according to the validated Chinese version of the IPSS. Each patient's baseline maximal flow rate (Q_{max}), postvoiding residual (PVR) urine volume, voided volume, and serum prostate-specific antigen (PSA) levels were obtained. Patients were excluded if they had a PSA >10 ng/mL, a history of urinary retention, urodynamically proven detrusor hypoactivity, active urinary tract infection, urinary stone, documented genitourinary cancer, previous transurethral surgery, or had taken α-blockers, antimuscarinic agents, or 5α-reductase inhibitors within the previous 6 months.

All men underwent transrectal ultrasound of the prostate with a 6.5-MHz probe (SSD-5000; Aloka, Chiba, Japan) by a single physician. TPV, transitional zone volume (TZV), and transitional zone index (TZI) were calculated. IPP and prostatic calcification were also recorded. The IPP score was defined by the distance between the tip of the protrusion and the bladder neck. An IPP ≤5 mm was classified as Grade I, 5–10 mm as Grade II, and >10 mm as Grade III.

All patients received α-blocker monotherapy (tamsulosin 0.2 mg once daily) for 12 weeks. Each patient was assessed at 4 weeks and 12 weeks after the treatment. Patients rated their symptoms after treatment compared with their symptoms at baseline using a validated Global Response Assessment (GRA) questionnaire, a 7-point scale ranging from markedly worse (−3) to markedly improved (+3).[11,12] Patients with a GRA score ≥ 1 at 4 weeks after the treatment were considered as having improved outcome and were maintained on their current medication. Patients with a GRA score <1 were then either administered combined therapy or switched to another medication at the discretion of the investigator. The primary end point of the study was to evaluate the correlation of IPP and prostatic calcification with outcomes 4 weeks after the treatment. The secondary end point was to evaluate the correlation of IPP and prostatic calcification with other parameters.

Continuous variables are represented as the mean ± standard deviation, and numbers and percentage (%) represent categorical data. The Chi-square test was used for categorical variables. Spearman rank test was used to assess the correlation between the parameters. Univariate and multivariate logistic regression analyses were performed to determine whether IPP and prostatic calcification are predictors of treatment response. A p value <0.05 was taken to be significant. Statistical analysis was performed using SPSS 17.0 statistical software (SPSS Inc., Chicago, IL, USA).

Table 1
Baseline characteristics of patients.

	Mean	SD
Age (y)	65.5	10.9
TPV (mL)	42.0	24.4
TZV (mL)	17.1	12.9
TZI	0.39	0.13
Q_{max} (mL/s)	14.5	15.5
PVR (mL)	29.1	27.5
Total IPSS	18.2	7.4
IPSS-V	10.6	5.2
IPSS-S	7.5	3.4
IPP		
Grade I		74 (66.1%)
Grade II		21 (18.8%)
Grade III		17 (15.2%)
Calcification		
Yes		48 (42.9%)
No		64 (57.1%)

IPP = intravesical prostatic protrusion; IPSS = International Prostate Symptom Score; IPSS-S = IPSS Storage subscore; IPSS-V = IPSS Voiding subscore; PVR = postvoid residual; Q_{max} = maximal flow rate; TPV = total prostate volume; TZI = transitional zone index; TZV = transitional zone volume; SD = standard deviation.

3. Results

A total of 112 men with a mean age of 65.5 (range, 42–89) years were enrolled in the study. Table 1 summarizes the baseline characteristics. The mean prostatic volume was 42.1 mL. Of these, 74 (66.1%), 21 (18.8%), and 17 (15.2%) patients had Grade I, Grade II, and Grade III IPP, respectively. Thirty-eight (33.9%) patients had significant IPP (Grade II and Grade III). Forty-eight patients (42.9%) had prostatic calcification whereas 64 patients (57.1%) did not.

When we evaluated the correlation between IPP and other parameters using the Spearman rank correlation test, IPP was significantly positively correlated with TPV ($\gamma = 0.44$), TZV ($\gamma = 0.43$), TZI ($\gamma = 0.22$), and PVR ($\gamma = 0.30$: Table 2). Prostatic calcification was significantly negatively correlated with total IPSS ($\gamma = 0.49$), IPSS-V ($\gamma = -0.41$), and IPSS-S ($\gamma = -0.43$; Table 3).

After 1 month of α-blocker treatment, the average total IPSS decreased from 18.2 ± 7.4 to 13.1 ± 4.5. Sixty-nine patients (61.6%) reported an improved outcome (GRA ≥ 1), whereas 43 (38.4%) patients reported no improvement (GRA < 1; Table 4). Patients with large prostate volumes (TPV ≥ 40 mL) and small prostate volumes (TPV < 40 mL) had similar rates of improved outcome (56.5% and 65.1%, respectively). In contrast to TPV, patients with significant IPP (Grade II and Grade III) had significantly lower rates of improved outcome (36.8%) than those without significant IPP (74.3%). In addition, patients with prostatic calcification also had significantly

Table 2
Association between IPP and other parameters.

	Association coefficient (γ)*	p
Age	0.11	0.23
TPV	0.44	0.00*
TZV	0.43	0.00*
TZI	0.22	0.02*
Calcifications	−0.11	0.27
Q_{max}	−0.12	0.36
PVR	0.30	0.02*
Total IPSS	0.01	0.95
IPSS-V	−0.71	0.64
IPSS-S	0.12	0.44

*$p < 0.05$ using Spearman rank correlation.
IPP = intravesical prostatic protrusion; IPSS = International Prostate Symptom Score; IPSS-S = IPSS Storage subscore; IPSS-V = IPSS Voiding subscore; PVR = postvoid residual; Q_{max} = maximal flow rate; TPV = total prostate volume; TZI = transitional zone index; TZV = transitional zone volume.

Table 3
Association between prostatic calcification and other parameters.

	Association coefficient (γ)*	p
Age	0.12	0.20
TPV	0.06	0.43
TZV	−0.03	0.75
TZI	−0.20	0.21
Q_{max}	−0.12	0.34
PVR	0.10	0.42
Total IPSS	−0.48	0.00*
IPSS-V	−0.41	0.01*
IPSS-S	−0.43	0.00*

*$p < 0.05$ using spearman rank correlation.
IPSS = International Prostate Symptom Score; IPSS-S = IPSS Storage subscore; IPSS-V = IPSS Voiding subscore; PVR = postvoid residual; TPV = total prostate volume; TZI = transitional zone index; TZV = transitional zone volume.

lower rates of improved outcome (47.9%) than those without prostatic calcification (71.9%; Table 4). Multivariate logistic regression analyses showed that both IPP and prostatic calcification are predictors of unfavorable medical treatment outcomes (GRA < 1), after adjusting for age, TPV, and total IPSS ($p = 0.019$ and $p = 0.024$, respectively).

4. Discussion

The α-blockers represent the first-line treatment for patients with bothersome LUTS caused by BPH, but some patients have less-than-satisfactory results with their initial medical treatment. Our results show that significant IPP and prostatic calcification are unfavorable predictors of successful medical treatment with α-blockers for male LUTS caused by BPH.

IPP assessed by transabdominal ultrasonography has been reported to be a better and more reliable predictor of BOO than prostate volume.[13] Transabdominal ultrasound measurement of prostatic volume correlates well with the transrectal measurement.[14] Our study shows that patients with significant IPP tend to have larger prostate volumes, TZV, TZI, and PVR, but not IPSS. Prostate calcification is associated with IPSS instead of IPP. With regard to prostate calcification, our results are similar to those of previous studies.[15] The prevalence of prostate calcification was high in patients complaining of LUTS.[16]

Other sonographic characteristics were found to be associated with LUTS, including prostatic urethral angle, resistive index of the capsular artery, presumed circle area ratio, prostatic urethral angle, intraprostatic protrusion, and detrusor wall thickness.[17,18] In our study, prostate calcifications were associated with LUTS, but not IPP. Lee et al[19] described two morphologic types of IPP: trilobar and bilobar enlargement. Prostate volume, BOO index, and bladder compliance index were significantly lower in the bilobar adenoma group than in the trilobar adenoma group. However, none of them could play the urodynamic studies role in BOO diagnosis.[18]

Table 4
Comparisons of treatment outcomes between patients with and without large prostate (TPV ≥ 40 mL), significant IPP (Grade II and Grade III), and prostatic calcification.

	GRA ≥ 1	GRA < 1	p
Total patients, n (%)	69 (61.6%)	43 (38.4%)	
TPV ≥ 40 mL	26 (56.5%)	20 (43.5%)	0.43
TPV < 40 mL	43 (65.1%)	23 (34.9%)	
Significant IPP (Grade II and Grade III)	55 (74.3%)	29 (25.7%)	0.001*
No significant IPP	14 (36.8%)	24 (63.2%)	
Prostatic calcification	23 (47.9%)	25 (52.1%)	0.017*
No prostatic calcification	46 (71.9%)	18 (28.1%)	

*$p < 0.05$ using Chi-square test.
GRA = Global Response Assessment; IPP = intravesical prostatic protrusion; TPV = total prostate volume.

The existing literature has demonstrated that significant IPP contributes to decreased Q_{max} and BOO index on urodynamics.[3,13] Significant IPP also tends to predict AUR and a higher risk of medical treatment failure.[2] Our study revealed that α-blockers may be more effective in improving symptom scores in patients with mild IPP than in those with moderate or severe IPP.[10,13] Significant IPP can be regarded as a more severe form of BOO. Male patients with moderate to severe LUTS tend to have overactive bladder symptoms, which is correlated with IPP.[7] To the best of our knowledge, this is the first study to demonstrate that prostate calcification can serve as an unfavorable predictor for male LUTS.

The major limitation of our study was the lack of a placebo group, making it impossible to eliminate the placebo effect on treatment response. Another limitation is the small sample size. In addition, although regression analysis showed that both IPP and prostate calcification were significant predictors of unfavorable outcomes after medical treatment for male LUTS, regression to the mean of the extreme variable may be another factor that limits the significance of our results.

5. Conclusion

Prostatic calcification is associated with LUTS. Patients with significant IPP and prostatic calcification had an unfavorable response to α-blockers.

Conflicts of interest

The authors have no conflicts of interest to disclose.

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References

1. Bechis SK, Otsetov AG, Ge R, Olumi AF. Personalized medicine for management of benign prostatic hyperplasia. *J Urol* 2014;**25**:304–8.
2. Hong SJ, Ko WJ, Kim SI, Chung BH. Identification of baseline clinical factors which predict medical treatment failure of benign prostatic hyperplasia: an observational cohort study. *Eur Urol* 2003;**44**:94–9. discussion 99–100.
3. Doo CK, Uh HS. Anatomic configuration of prostate obtained by noninvasive ultrasonography can predict clinical voiding parameters for determining BOO in men with LUTS. *Urology* 2009;**73**:232–6.
4. Tan YH, Foo KT. Intravesical prostatic protrusion predicts the outcome of a trial without catheter following acute urine retention. *J Urol* 2003;**170**:2339–41.
5. Keqin Z, Zhishun X, Jing Z, Haixin W, Dongqing Z, Benkang S. Clinical significance of intravesical prostatic protrusion in patients with benign prostatic enlargement. *Urology* 2007;**70**:1096–9.
6. Lee LS, Sim HG, Lim KB, Wang D, Foo KT. Intravesical prostatic protrusion predicts clinical progression of benign prostatic enlargement in patients receiving medical treatment. *Int J Urol* 2010;**17**:69–74.
7. Kim KH, Kim YS. Correlation of male overactive bladder with intravesical prostatic protrusion. *Korean J Urol* 2010;**51**:843–6.
8. Wee JH, Choi YS, Bae WJ, Kim SJ, Cho HJ, Hong SH, et al. Influence of intravesical prostatic protrusion on preoperative lower urinary tract symptoms and outcomes after 120 w high performance system laser treatment in men with benign prostatic hyperplasia. *Korean J Urol* 2012;**53**:472–7.
9. Lee JW, Ryu JH, Yoo TK, Byun SS, Jeong YJ, Jung TY. Relationship between intravesical prostatic protrusion and postoperative outcomes in patients with benign prostatic hyperplasia. *Korean J Urol* 2012;**53**:478–82.
10. Geramoutsos I, Gyftopoulos K, Perimenis P, Thanou V, Liagka D, Siamblis D, et al. Clinical correlation of prostatic lithiasis with chronic pelvic pain syndromes in young adults. *Eur Urol* 2004;**45**:333–7. discussion 337–8.
11. Liao CH, Lin VC, Chung SD, Kuo HC. Therapeutic effect of α-blockers and antimuscarinics in male lower urinary tract symptoms based on the International Prostate Symptom Score subscore ratio. *Int J Clin Pract* 2012;**66**:139–45.
12. Liao CH, Kuo YC, Kuo HC. Predictors of successful first-line antimuscarinic monotherapy in men with enlarged prostate and predominant storage symptoms. *Urology* 2013;**81**:1030–3.
13. Chia SJ, Heng CT, Chan SP, Foo KT. Correlation of intravesical prostatic protrusion with bladder outlet obstruction. *BJU Int* 2003;**91**:371–4.

14. Yuen JS, Ngiap JT, Cheng CW, Foo KT. Effects of bladder volume on transabdominal ultrasound measurements of intravesical prostatic protrusion and volume. *Int J Urol* 2002;**9**:225–9.
15. Yang HJ, Huang KH, Wang CW, Chang HC, Yang TK. Prostate calcification worsen lower urinary tract symptoms in middle-aged men. *Urology* 2013;**81**:1320–4.
16. Hong CG, Yoon BI, Choe HS, Ha US, Sohn DW, Cho YH. The prevalence and characteristic differences in prostatic calcification between health promotion center and urology department outpatients. *Korean J Urol* 2012;**53**:330–4.
17. Bang WJ, Kim HW, Lee JY, Lee DH, Hah YS, Lee HH, et al. Prostatic urethral angulation associated with urinary flow rate and urinary symptom scores in men with lower urinary tract symptoms. *Urology* 2012;**80**:1333–7.
18. Abdi H, Kazzazi A, Bazargani ST, Djavan B, Telegrafi S. Imaging in benign prostatic hyperplasia: what is new? *Curr Opin Urol* 2013;**23**:11–6.
19. Lee SW, Cho JM, Kang JY, Yoo TK. Clinical and urodynamic significance of morphological differences in intravesical prostatic protrusion. *Korean J Urol* 2010;**51**:694–9.