

Is intravesical prostatic protrusion a risk factor for hydronephrosis and renal insufficiency in benign prostate hyperplasia patients?

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Abstract

Background: Some patients with benign prostatic hyperplasia (BPH) and lower urinary tract symptoms hesitate to undergo surgical treatment until acute urinary retention (AUR) occurs. Some of these patients have been found to have hydronephrosis or even renal insufficiency. This study aimed to analyze the risk factors for hydronephrosis in patients with AUR who needed to receive transurethral resection of the prostate (TURP).

Methods: We retrospectively analyzed 91 patients from January 2014 to June 2015, who had BPH and received TURP for AUR. Patients with urolithiasis, prostate cancer, bladder cancer, gross hematuria, previous bladder radiation therapy, or urinary tract surgery were excluded. Parameters of intravesical prostatic protrusion (IPP), serum prostatic specific antigen (PSA), total prostate volume (PV), age, body mass index (BMI), hypertension (HTN), diabetes mellitus (DM), coronary artery disease (CAD), and serum creatinine (Cr) were compared between the hydronephrosis and non-hydronephrosis groups.

Results: There were significant differences in IPP ($p < 0.001$) and Serum Cr ($p < 0.001$) between the hydronephrosis and non-hydronephrosis groups. For IPP, the cut-off values of the highest risk of hydronephrosis was 1.95 cm. There were no significant differences in age, BMI, DM, HTN, CAD, total PV, and PSA between the two groups. IPP was not correlated with total PV ($p = 0.423$). Most of the patients with hydronephrosis had renal function improvement after TURP.

Conclusion: IPP was a significant risk factor for hydronephrosis in BPH patients. If the patients' IPP exceeded 1.95 cm, they had a higher risk of having hydronephrosis when AUR occurred. Hydronephrosis is a risk factor for renal insufficiency, and Serum Cr levels decreased significantly in the patients of our study.

Keywords: Hydronephrosis; Prostatic hyperplasia; Renal insufficiency; Transurethral resection of prostate

1. INTRODUCTION

The prevalence of benign prostatic hyperplasia (BPH) with lower urinary tract symptoms (LUTS) is associated with increasing age. Transurethral resection of the prostate (TURP) is considered the gold standard surgical treatment for LUTS secondary to BPH. The number of TURPs performed has declined and the timing of surgical treatment for patients with BPH is delayed significantly over the last three decades owing to pharmaceutical therapy.¹

Many complications have been reported in patients with BPH, including urinary tract infections, bladder stones, bladder diverticula, vesicoureteral reflux, hydronephrosis, renal insufficiency, and urinary retention. Among which hydronephrosis, renal insufficiency, and urinary retention are the most prevalent.² These complications are regarded as being absolute or relative indications for the surgical removal of the prostatic transition

zone. Surgical treatment may relieve the aforementioned complications if performed early enough.

TURP is indicated for patients with bothersome moderate or severe LUTS who request active treatment or who either fail or do not want medical therapy.³ Among indications for TURP, urinary retention is still by far the most common condition.¹ In the real life, when life expectancy is steadily increasing, many patients with BPH and LUTS hesitate to receive surgical treatment and prefer medical control until the occurrence of acute urinary retention (AUR). These patients appear to be able to tolerate bothersome LUTS, even those refractory to medical control. However, some of these patients may also have hydronephrosis or renal insufficiency with the progression of BPH.⁴ Most of whom are unaware of these problems until the incidental finding of AUR.

One of the mechanism of hydronephrosis has been postulated that bladder muscle hypertrophy induced anatomic obstruction of the uretero-vesical junction (UVJ) or functional compression of the UVJ due to increase of ureteral resistance through the ureteral tunnel when there is bladder overdistension. It remains to be evaluated what kind of factor would increase the risk of hydronephrosis and even further induce renal insufficiency in men with BPH.⁵

Therefore, the aim of this study is to analyze whether patients who needed TURP for AUR tended to have hydronephrosis and renal insufficiency. We also present serum Cr and hydronephrosis condition before and after TURP. This is the first article that presents these data completely.

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2. METHODS

We retrospectively evaluated 184 patients with BPH who received TURP for AUR at Taipei Veterans General Hospital from January 2014 to June 2015. Before analysis, patients with urolithiasis, prostate cancer, bladder cancer, bladder radiation therapy, previous urinary tract surgery, or gross hematuria when AUR occurred were excluded. The patients with systemic inflammatory response syndrome were also excluded. The rationale was to exclude other risk factors for AUR rather than BPH-related factors. We divided the patients into two groups: those with or without hydronephrosis before TURP. Hydronephrosis was evaluated by abdominal sonography within 1 month before TURP. Parameters of intravesical prostatic protrusion (IPP), serum prostatic specific antigen (PSA), total prostate volume (PV), age, body mass index (BMI), hypertension (HTN), diabetes mellitus (DM), coronary artery disease (CAD), and serum creatinine (Cr) were analyzed between these two groups. The lowest serum Cr level within 1 month after surgery was recorded. Total PV was measured by using sonography with the ellipsoid formula: width × height × length × 0.52.

In this study, we measured IPP by sonography within 1 month before TURP. IPP was defined as the distance between the tip of the prostate median lobe and bladder neck in the mid sagittal plane.

2.1. Statistical analysis

The statistical analysis was performed by using IBM SPSS ver. 20.0 (IBM Co., Armonk, NY, USA). χ^2 tests, Fisher's exact test, *t*-test, Wilcoxon scores, and receiver operating characteristic curve were used.

3. RESULTS

Of the 184 patients, 93 patients were excluded due to urolithiasis, prostate cancer, bladder cancer, or gross hematuria. Totally, 91 patients were enrolled. The average age was 75.6 ± 11.4 years (mean ± SD). BMI was 24.5 ± 3.4. The patient number of DM was 19, HTN was 54, and CAD was 12 people. Serum Cr before TURP was 1.83 ± 2.2 mg/dL; PV was 94.4 ± 51.9 cc; PSA was 7.46 ± 6.6 ng/mL and IPP was 1.86 ± 0.77 cm.

We divided these 91 patients into two groups by the hydronephrosis in sonography within 1 month before TURP was performed. There were 24 patients in hydronephrosis group and 67 patients in another. Table 1 shows that there were significant differences in IPP ($p < 0.001$) and Cr ($p < 0.001$) between the hydronephrosis and non-hydronephrosis groups. There were no significant differences in age, BMI, DM, HTN, CAD, pre-TURP, PSA, UFR between the two groups. IPP was not correlated with total PV ($p = 0.423$).

Table 1
Hydronephrosis and non-hydronephrosis groups analysis

	Hydronephrosis	Non-hydronephrosis	<i>p</i>
No., <i>n</i>	24	67	...
Age, <i>y</i>	75.2 ± 11.7	75.8 ± 11.5	0.93*
BMI	23.3 ± 3.5	24.9 ± 3.4	0.06*
DM, <i>n</i>	3	16	0.20**
HTN, <i>n</i>	15	39	0.94**
CAD, <i>n</i>	2	10	0.37**
Cr before TURP, mg/dL	3.49 ± 4.09	1.40 ± 1.13	<0.001*
Prostate volume, cc	101.79 ± 60.83	121.46 ± 240.67	0.36*
IPP, cm	2.36 ± 0.72	1.70 ± 0.71	<0.0001*
PSA, ng/mL	7.73 ± 6.03	7.30 ± 6.95	0.78*

Data are presented as *n* or mean ± SD (range).

BMI = body mass index; CAD = coronary artery disease; Cr = creatinine; DM = diabetes mellitus; HTN = hypertension; IPP = intravesical prostatic protrusion; PSA = prostatic specific antigen; TURP = transurethral resection of the prostate.

*Mann-Whitney test.

**Fisher's exact test.

Table 2

The difference of serum creatinine before and after TURP

	Hydronephrosis	Non-hydronephrosis	<i>p</i>
F/u No., <i>n</i>	22	16	...
Age, <i>y</i>	75.7 ± 11.5	81.3 ± 11.5	0.21*
BMI	23.4 ± 3.6	24.3 ± 3.3	0.48*
Cr before TURP, mg/dL	3.44 ± 3.70	1.71 ± 0.87	0.04*
Cr after TURP, mg/dL	1.32 ± 0.44	1.55 ± 0.93	0.94*
Difference value of Cr, mg/dL ^a	2.12 ± 3.58	0.16 ± 0.34	<0.0001*

Data are presented as *n* or mean ± SD (range).

Cr = creatinine; TURP = transurethral resection of the prostate.

^aDifference value of Cr (mg/dL) = Cr before TURP (mg/dL) – Cr after TURP (mg/dL).

*Mann-Whitney test.

Table 2 showed the difference in serum Cr levels before and after TURP. In our retrospective study, most of non-hydronephrosis patient did not have post-TURP serum Cr record due to normal preoperative serum Cr. There were 22 patients and 16 patients followed serum Cr value before and after TURP, respectively. In hydronephrosis group, serum Cr was 3.44 ± 3.70 mg/dL before TURP and 1.32 ± 0.44 mg/dL after TURP. In non-hydronephrosis group, serum Cr was 1.71 ± 0.87 mg/dL before TURP and 1.55 ± 0.93 mg/dL after TURP. Most of the hydronephrosis patients had renal function improvement except one patient who had chronic kidney disease and complicated urinary tract infection after the operation. Difference value of serum Cr (Cr before TURP – Cr after TURP) showed statistically significant decreased serum Cr in hydronephrosis patients compared with non-hydronephrosis patients ($p < 0.0001$).

There were only seven patients who repeated sonography after TURP. Six patients showed hydronephrosis with renal insufficiency before operation. Postoperative sonography showed that only one of them had no hydronephrosis improvement. Serum Cr on this patient still improved from 1.95 to 1.35 mg/dL and his IPP was 3.5 cm. All other post TURP hydronephrosis improved patients showed serum Cr improvement.

In a total of 63 patients, 23 patients' sonography before the operation were with foley catheter inserted. Four patients had hydronephrosis and 19 patients did not. There was no statistically significant ($p = 0.541$) relationship of foley insertion and hydronephrosis before the operation in our data base. In 23 foley-inserted patients, nine patient's serum Cr > 1.3 mg/dL before TURP and 14 were not. There was also no statistically significant ($p = 0.597$) relationship. Normal serum Cr range was 0.7-1.3 mg/dL in men.

As shown in the Fig. 1, we used ROC curve to analyze the correlation of IPP with hydronephrosis, the cut-off point of IPP was determined as 1.95 cm. AUC (area under curve) = 0.751 and Youden's index (sensitivity + specificity – 1) was 0.376. The sensitivity and specificity was 72.0% and 65.6%, respectively. The odds ratio was 4.909 (95% CI, 1.781 to 13.533).

4. DISCUSSION

Many patients with BPH hesitate to receive surgical treatment even when LUTS cannot be controlled by medications, and some of them suffer from renal insufficiency during disease progression. In this study, we aimed to determine whether patients who needed TURP for AUR tended to have hydronephrosis or renal insufficiency.

4.1. Renal insufficiency

The mechanism of renal insufficiency is thought to be induced by urine reflux or urinary tract infections. In our study, the serum Cr level was statistically higher in the hydronephrosis group, with a level before TURP as 3.49 ± 4.09 mg/dL in the hydronephrosis group and 1.40 ± 1.13 mg/dL in the non-hydronephrosis group, respectively ($p < 0.001$).

Table 2 shows that the average serum Cr level improved in both groups. In the hydronephrosis group, the serum Cr level

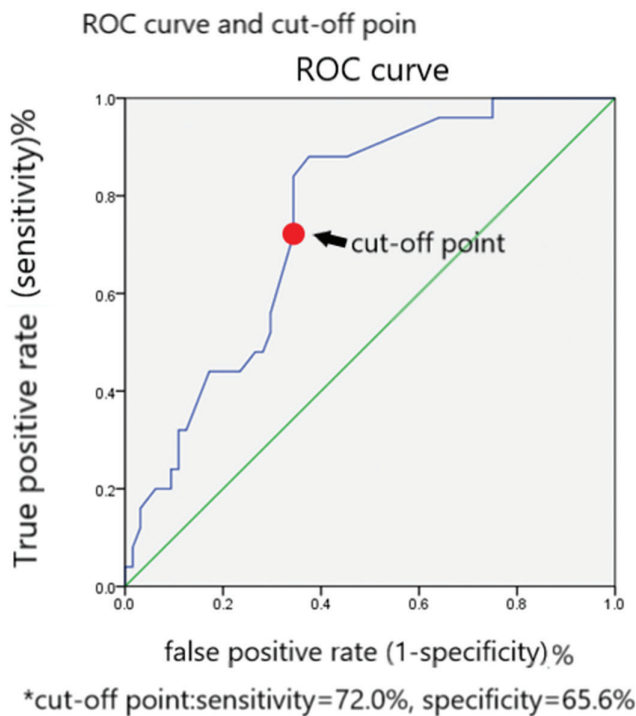


Fig. 1 ROC curve and cut-off point : the correlation of IPP and hydronephrosis.

was significantly lower than in the non-hydronephrosis group. Difference value of serum Cr (Cr before TURP – Cr after TURP) showed statistically significant decrease in serum Cr level in hydronephrosis patients compared with that of the non-hydronephrosis patients ($p < 0.0001$).

This suggests that surgical treatment that relieved bladder outlet obstruction could improve the renal insufficiency. However, due to the retrospective design, some patients without hydronephrosis did not have post-TURP serum Cr record. Serum Cr level was not routinely rechecked if a normal preoperative serum Cr level was noted. Post-TURP abdominal sonography was also not routinely performed. There were only seven patients who repeated sonography after TURP. Six patients showed hydronephrosis with renal insufficiency before operation. All patients' serum Cr levels were decreased after operation but the sample size was too small to get significant result.

Rule et al. reported renal function deterioration could be found in symptomatic men (IPSS > 7 , odds ratio 2.91) with low maximum urinary flow rate ($Q_{max} < 15$ mL/sec, odds ratio 2.96) and PVR > 100 mL (odds ratio 2.28).⁶ Gerber et al. reported that 11% of male patients with LUTS had renal insufficiency,² and that serum Cr concentration was not associated with symptom score or quality of life. The authors concluded that diabetes mellitus and hypertension were the most likely causes of the elevation of Cr concentration. Patients with renal insufficiency have higher intravesical pressures compared to those without renal insufficiency.⁷ Furthermore, men with decreased bladder compliance are more likely to develop renal insufficiency (78%) compared to those with normal bladder compliance (36%),⁸ and low bladder compliance is directly related to BPO.⁹ It remains to be evaluated why men with BPO develop low bladder compliance, whether more severe BPO increases the risk of renal insufficiency, and the role that time plays.

4.2. Intravesical prostatic protrusion

In our study, the mean length of the IPP was 2.36 ± 0.72 cm in the hydronephrosis group and 1.70 ± 0.71 cm in the non-hydronephrosis group. The statistically significant association between these two groups shows that IPP was a risk factor for hydronephrosis.

The degree of IPP was defined as the shortest diameter between the bladder neck and the tip of the IPP on a sagittal image as described by Mariappan et al.¹⁰ Their data base was 121 men. They classified IPP into three grades: grade I, an IPP of < 5 mm; grade II, an IPP of 5 to 10 mm; and grade III, an IPP of > 10 mm. Grade I, protrusion is 0 to 4.9 mm; grade II, 5 to 10 mm; and grade III > 10 mm. All IPP lengths in the patients with BPH with hydronephrosis were grade III in this study. In the non-hydronephrosis group, 11 patients had IPP grade II and 56 patients had grade III.

In our study, the cut-off value of IPP that yielded the highest risk of hydronephrosis was 1.95 mm. IPP was well correlated with obstruction condition of BPH in urodynamic testing.¹¹ The result can help patient–physician communication with treatment strategy including TURP or to follow medication. In the future, adding a grade IV, maybe IPP > 2 cm, is to emphasize the risk of hydronephrosis and renal insufficiency. Our study was a retrospective study of 91 patients. The idea of grade IV needs more prospective studies and more patient numbers to support the new grading system.

IPP may also be correlated with PV, detrusor overactivity, bladder compliance, detrusor pressure at maximum urinary flow, bladder outlet obstruction index and post-void residual (PVR), and negatively correlated with Q_{max} .¹¹ Several studies have reported that IPP may predict successful outcomes of trial without catheter after AUR.^{10,12} More studies are needed to evaluate IPP as a noninvasive alternative to pressure flow studies in the assessment of male LUTS.

The values of PV and IPP are listed in Table 1. IPP was not correlated with total PV ($p = 0.423$) in our study. The relationship between PV and BPO has been extensively investigated, and a weak correlation has generally been accepted. A reasonable explanation is that not only the size but also the shape of the prostate adenoma causes urinary tract obstruction. The severity of LUTS suggestive of BPH was poorly correlated with BPO.^{13,14} It had also been shown that IPP is strongly correlated with BPO, and in the current study 21% of the prostates with grade 1 IPP were obstructed, compared to 94% of those with grade 3 IPP. This finding is consistent with a previous study, and suggests¹⁵ that IPP may be a better predictor of BPO than PV.¹⁶

4.3. Acute retention of urine

All of our patients had AUR, which can often present as a urological emergency with a sudden inability to urinate often with the symptom of lower abdominal pain.^{17,18} Although the etiologies of AUR are variable, BPH accounts for most episodes with the prevalence rate estimated to be as high as 53%.¹⁹ For this reason, the prevalence of AUR in the ageing population is likely to increase.

4.4. Hydronephrosis

Two mechanisms have been proposed for hydronephrosis: First, anatomic obstruction of the ureterovesical junction due to bladder muscle hypertrophy as a result of BPO; Second, functional compression of the ureterovesical junction, leading to an increase in ureteral resistance through the ureteral tunnel due to bladder over-distension. Many other possible causes for hydronephrosis have also been proposed.²⁰ One trial enrolled 27 patients with hydronephrosis and found that 52% of these patients had bladder storage pressures ($P_{det} > 40$ cmH₂O at maximum bladder capacity).⁷ In addition, higher and sustained storage pressures were related to renal insufficiency in the patients with hydronephrosis, indicating that vesical pressure during the filling phase may play a role in upper urinary tract complications. This may also be one of the mechanisms for the relationship between bladder outlet obstruction and upper urinary tract complications.⁵

With the improvement of medication, the timings of TURPs have been prolonged in this aging society. Urinary retention is still by far the most common indication that motivate patient to receive TURP. In our study, we indicated the risk of hydronephrosis and renal insufficiency in these patients. Young et al. reported

that there has been also a significant rise in the percentage of high pressure chronic retention in patients who need TURP for BPH-related AUR. More and more of these bladder dysfunction patients either have persistent storage LUTS or eventually require long-term catheterization or intermittent self-catheterization. The result raises the question of what is the long-term real life impact of medical therapy in BPH patients. We need much more study in strategy of medical and surgical treatments in men with LUTS secondary to BPH who eventually require surgery.

4.5. Limitations

There are some limitations to this study. First, it was conducted at a single institution and was retrospective. Therefore, certain selection bias is likely to have affected our data. For example, we did not query whether the physicians chose to obtain blood tests or not from their patients. In some patients, postoperative Cr data were not available. Second, ultrasonography was not performed by the same operator, and there were no definite criteria for diagnosing hydronephrosis based on bedside ultrasound. Dilatation of the renal pelvis is a subjective determination tool that may be too difficult to define patients with mild hydronephrosis. In addition, the time duration to AUR before Foley placement was unavailable in most of the patients. It is possible that this may be a factor that helps to distinguish which patients are at risk of hydronephrosis or elevated Cr. Further studies should also investigate this issue. A larger study with more complete baseline and follow-up data collection using the same well-trained ultrasonographers may improve the study results.

In conclusion, IPP was a significant risk factor for hydronephrosis in BPH patients. If the patients' IPP exceeded 1.95 cm, they had a higher risk of having hydronephrosis when AUR occurred. IPP was not correlated with total PV. Hydronephrosis is a risk factor for renal insufficiency, and Serum Cr decreased significantly in our study. The result can help patient-physician communication with treatment strategy including TURP or keep medication.

REFERENCES

- Young MJ, Elmussareh M, Morrison T, Wilson JR. The changing practice of transurethral resection of the prostate. *Ann R Coll Surg Engl* 2018;100:326–9.
- Gerber GS, Goldfischer ER, Karrison TG, Bales GT. Serum creatinine measurements in men with lower urinary tract symptoms secondary to benign prostatic hyperplasia. *Urology* 1997;49:697–702.
- Nickel JC, Méndez-Probst CE, Whelan TF, Paterson RF, Razvi H. 2010 Update: guidelines for the management of benign prostatic hyperplasia. *Can Urol Assoc J* 2010;4:310–6.
- Lee JH, Kwon H, Park YW, Cho IC, Min SK. Relationship of estimated glomerular filtration rate with lower urinary tract symptoms/benign prostatic hyperplasia measures in middle-aged men with moderate to severe lower urinary tract symptoms. *Urology* 2013;82:1381–5.
- Oelke M, Kirschner-Hermanns R, Thiruchelvam N, Heesakkers J. Can we identify men who will have complications from benign prostatic obstruction (bpo)? Ici-rs 2011. *Neurourol Urodyn* 2012; 31:322–6.
- Rule AD, Jacobson DJ, Roberts RO, Girman CJ, McGree ME, Lieber MM, et al. The association between benign prostatic hyperplasia and chronic kidney disease in community-dwelling men. *Kidney Int* 2005;67:2376–82.
- Ghobish AG. Storage detrusor pressure in bilateral hydronephrosis. *Eur Urol* 2001;39:571–4.
- Comiter CV, Sullivan MP, Schacterle RS, Cohen LH, Valla SV. Urodynamics risk factors for renal dysfunction in men with obstructive and nonobstructive voiding dysfunction. *J Urol* 1997;158:181–5.
- Madersbacher S, Pycha A, Klingler CH, Mian C, Djavan B, Stulnig T, et al. Interrelationships of bladder compliance with age, detrusor instability, and obstruction in elderly men with lower urinary tract symptoms. *Neurourol Urodyn* 1999;18:3–15.
- Mariappan P, Brown DJ, McNeill AS. Intravesical prostatic protrusion is better than prostate volume in predicting the outcome of trial without catheter in white men presenting with acute urinary retention: a prospective clinical study. *J Urol* 2007;178:573–7.
- 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.
- 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.
- Netto Junior NR, D'Ancona CA, de Lima ML. Correlation between the international prostatic symptom score and a pressure-flow study in the evaluation of symptomatic benign prostatic hyperplasia. *J Urol* 1996;155:200–2.
- el Din KE, Kiemeny LA, de Wildt MJ, Rosier PF, Debruyne FM, de la Rosette JJ. The correlation between bladder outlet obstruction and lower urinary tract symptoms as measured by the international prostate symptom score. *J Urol* 1996;156:1020–5.
- Chia SJ, Heng CT, Chan SP, Foo KT. Correlation of intravesical prostatic protrusion with bladder outlet obstruction. *BJU Int* 2003;91:371–4.
- Wang D, Huang H, Law YM, Foo KT. Relationships between prostatic volume and intravesical prostatic protrusion on transabdominal ultrasound and benign prostatic obstruction in patients with lower urinary tract symptoms. *Ann Acad Med Singapore* 2015;44:60–5.
- Emberton M, Anson K. Acute urinary retention in men: an age old problem. *BMJ* 1999;318:921–5.
- Choong S, Emberton M. Acute urinary retention. *BJU Int* 2000;85:186–201.
- Chen JS, Chang CH, Yang WH, Kao YH. Acute urinary retention increases the risk of complications after transurethral resection of the prostate: a population-based study. *BJU Int* 2012;110:E896–901.
- Sutaria PM, Staskin DR. Hydronephrosis and renal deterioration in the elderly due to abnormalities of the lower urinary tract and ureterovesical junction. *Int Urol Nephrol* 2000;32:119–26.