

## Original Article

# Correlation between ultrasound bladder parameters with severity of symptoms and response to treatment in patients with benign prostatic hyperplasia under medical treatment

Mostafa Mazaheri<sup>1</sup>, Farhad Tadayon<sup>2,3</sup>, Saeid Khanbabapour<sup>4</sup>, Ashkan Omid<sup>5</sup>, Hanieh Salehi<sup>6</sup>, Reza Kazemi<sup>2,3</sup>

<sup>1</sup>Department of Urology, School of Medicine, Isfahan University of Medical Sciences, Isfahan, Iran; <sup>2</sup>Assistant Professor, Department of Urology, School of Medicine, Isfahan University of Medical Sciences, Isfahan, Iran; <sup>3</sup>Isfahan Research Center of Kidney Transplantation, Department of Urology, Al-Zahra Research Institute, Isfahan University of Medical Sciences, Isfahan, Iran; <sup>4</sup>Department of Radiology, School of Medicine, Isfahan University of Medical Sciences, Isfahan, Iran; <sup>5</sup>School of Medicine, Islamic Azad University Tehran Faculty of Medicine, Tehran, Iran; <sup>6</sup>School of Medicine, Isfahan University of Medical Sciences, Isfahan, Iran

Received January 12, 2021; Accepted April 15, 2021; Epub June 15, 2021; Published June 30, 2021

**Abstract:** Background: Benign prostatic hyperplasia (BPH) is the most common benign mass in men, there are not standard parameter for diagnosis of BPH based on ultrasound bladder parameter, so the aim of the study was correlation between ultrasound bladder parameters with severity of symptoms and response to treatment in patients with benign prostatic hyperplasia under medical treatment. Methods: This prospective cross-sectional study was performed on 100 men over 40 years of age with a diagnosis of BPH referred to the urology clinics of Al-Zahra and Khorshid hospitals, Isfahan, Iran in 2018-2020. The International Prostate Symptom Score (IPSS), bladder wall thickness, bladder weight, Intravesical prostatic protrusion (IPP) and response to treatment were examined before and after treatment. Patients underwent standard drug treatment with a Tamsulosin 0.4 mg daily and finasteride 5 mg daily for BPH and followed for a period of 3-6 months. Results: There were significant differences between severity of symptoms before treatment with age, bladder wall thickness, bladder weight and IPP ( $P < 0.001$ ). The symptoms of 76 patients were recovered and 24 patients not changed After treatment, so the patients were compared based on outcomes to treat, all patients with mild symptoms, 28 patients with moderate symptoms and 18 patients with severe symptoms were recovered, so the treatment outcome was significant based on symptoms ( $P < 0.001$ ). The means of age, bladder wall thickness and bladder weight in recovered group was significantly lower than not changed group ( $P < 0.001$ ). Also the frequency of IPP in the recovered group was significantly lower than not changed group ( $P < 0.001$ ). Conclusion: The use of ultrasound parameters has a high value in determining the response to treatment in BPH patients and the diagnostic value of IPSS, IPP, bladder wall thickness and bladder weight were important determined response to treatment and severity of disease. Also relation between bladder weight with response to treatment and severity of disease were evaluated for first time in the current study.

**Keywords:** Ultrasound, bladder, benign prostatic hyperplasia, medication

## Introduction

Benign prostatic hyperplasia (BPH) is the most common benign mass in men and there are correlation between age and incidence of BPH [1-3]. The prevalence of symptoms in patients with BPH were presented nearly 14 million men in the United States studies and about 300 million of international studies [4-6]. Some studies showed a significant association between ultrasound morphology of the bladder and clinical symptoms of BPH, while other studies disagree

with this results [7]. According to the results of some studies, bladder wall thickness and prostate volume in BPH patients can be very useful and helpful to diagnose and treatment of symptoms of BPH patients. It also seems that by morphological examination of the bladder and prostate in these patients, the prognosis of obstruction can be predicted and the necessary treatment can be performed before occurrences of symptoms [8]. There are many discrepancies between different studies on the association of bladder and prostate morpholo-

## Benign prostatic hyperplasia

gy with clinical symptoms and response to treatment in patients with BPH [9-12].

Therefore, there are not reliable document for bladder wall thickness and ultrasound weight of bladder to determine and diagnose bladder outlet obstruction and different results have been presented in different studies [8-11, 13-16]. In addition, there are very limited studies in this field in Iran. Therefore, this study was designed and performed to determine the relationship between ultrasound bladder parameter of the bladder and prostate with the severity of clinical symptoms due to BPH and response to drug treatment.

### Materials and methods

#### *Study design*

This prospective cross-sectional study was performed on 100 men with mean aged  $64.28 \pm 8.22$  years diagnosed BPH who referred to the urology clinics of Al-Zahra and Khorshid hospitals, Isfahan, Iran in 2018-2020. All protocols of present study have been approved by the ethical committee of Isfahan University of Medical Sciences (IR.MUI.MED.REC.1399.009) and all patients were satisfied to participate in the study. Also informed consent was signed by the patients before starting study.

Inclusion criteria included men patients with aged over 40 years with complaints of obstructive and irritating urinary symptoms who were diagnosed with BPH based on clinical symptoms and ultrasound. The not meeting criteria were included patients with urinary tract infection or inflammation of prostate, history of stone or tumor of bladder, increase in serum PSA or rectal examination of suspected prostate cancer, urinary tract stenosis, prostate cancer, history of pelvic radiotherapy, history of bladder neuropathy, treatment with Anti-androgenic drugs, bladder volume less than 50 cc, and history of bladder or prostate surgery. Exclusion criteria also included noting follow up during study, and the impossibility of examining the bladder morphology due to anatomical problems.

#### *Assessments*

Data assessment tools in this study included a data collection checklist for each patient that includes demographic information (name and

last name, phone number, age, undergoing disease, smoking history, family history, treatment information and response to treatment), clinical examination, transabdominal and ultrasound findings and clinical symptoms were performed for the patients. Symptoms of BPH were identified and recorded for each patient using the International Prostate Symptom Score (IPSS) [17].

IPSS is an international scoring of prostate symptoms developed for the initial evaluation of lower urinary symptoms. This rating includes 7 questions about urinary frequency, enuresis, low flow of urine, straining when urinating, disconnection and connection of urine flow, feeling of not emptying the bladder and urgency to urinate. Each question is given a score between 0-5 according to the patient's answer and the total score is determined. Scoring system was including 0-7 Mild; 8-19 moderate and 20-35 severe symptoms. Also patients were divided in three groups (mild, moderate and severe) based on IPSS score.

The patients were then examined by a single radiologist under a trans-abdominal ultrasound of the bladder and prostate when the bladder volume was between 200 and 400 cc, and the morphology of the bladder and prostate was determined for each patient and the results were recorded. The purpose of bladder morphology in this study was to determine bladder wall thickness based on millimeters, specific weight of bladder muscle which is estimated based on the formula (bladder wall volume  $\times$  weight of bladder muscles) that bladder wall volume is from volume fraction and prostatic morphology based on intravesical prostatic protrusion (IPP) [18].

#### *Treatment and follow up*

Finally, patients underwent standard drug treatment with an alpha-blocker (Tamsulosin 0.4 mg daily) and finasteride 5 mg daily if have medical indication for BPH (PSA greater than 1.5 or prostate volume greater than 40 cc) and followed for a period of 3-6 months. So based on recovery of symptoms after treatment patients were divided into recovered symptoms and not changed symptoms after treatment.

#### *Statistical analysis*

The data of study were enrolled analyzed with SPSS software version 24. The qualitative vari-

# Benign prostatic hyperplasia

**Table 1.** Variables of study based on severity of symptoms before treatment

Variables	Severity of symptoms before treatment based on IPSS			P-value
	Mild (n=30)	Moderate (n=35)	Severe (n=35)	
Age (mean ± SD)	58.63±7.31	65.34±7.26	68.05±7.38	<0.001*
Bladder wall thickness (mm) (mean ± SD)	3.60±0.41	4.81±0.52	4.81±0.73	<0.001*
Bladder weight (gram) (mean ± SD)	39.46±5.50	62.94±15.28	95.37±9.97	<0.001*
IPP	0	19 (54.3%)	20 (57.1%)	<0.001**

\*One-Way ANOVA, \*\*Chi Square, IPP: Intravesical prostatic protrusion, IPSS: International Prostate Symptom Score.

**Table 2.** Variables of study based on treatment outcome

Variables		Changing the symptoms after treatment		P-value
		Recovered	Not changed	
Severity of symptoms before treatment based on IPSS	Mild	30 (39.5%)	0	<0.001*
	Moderate	28 (36.8%)	7 (29.2%)	
	Severe	18 (23.7%)	17 (70.8%)	
Age		63.22±8.32	67.62±7.05	0.02**
Bladder wall thickness		4.07±0.73	4.67±0.63	<0.001**
Bladder weight		58.09±21.16	96.25±12.36	<0.001**
Intravesical prostatic protrusion (IPP)		20 (26.3%)	19 (79.2%)	<0.001***

IPP: Intravesical prostatic protrusion, IPSS: International Prostate Symptom Score. \*Chi Square, \*\*Independent t test, \*\*\*Fisher's exact test.

ables were showed based frequency and percentage and quantitative variables were showed based on mean and SD. The relationship between qualitative variables were analyzed based on Chi square and Fisher's exact test and relationship between quantitative and qualitative variables were analyzed based on Independent and One-way ANOVA and Pearson correlation was used to correlate between quantitative variables. Also P under 0.05 was considered significant.

## Results

### Before treatment

In the current study, there were significant differences between severity of symptoms before treatment with age, bladder wall thickness, bladder weight and IPP (P<0.001) (**Table 1**). Based on Pearson correlation, there was direct significant correlation between age with bladder wall thickness (r=0.51, P<0.001) and bladder weight (r=0.46, P<0.001).

### Outcomes

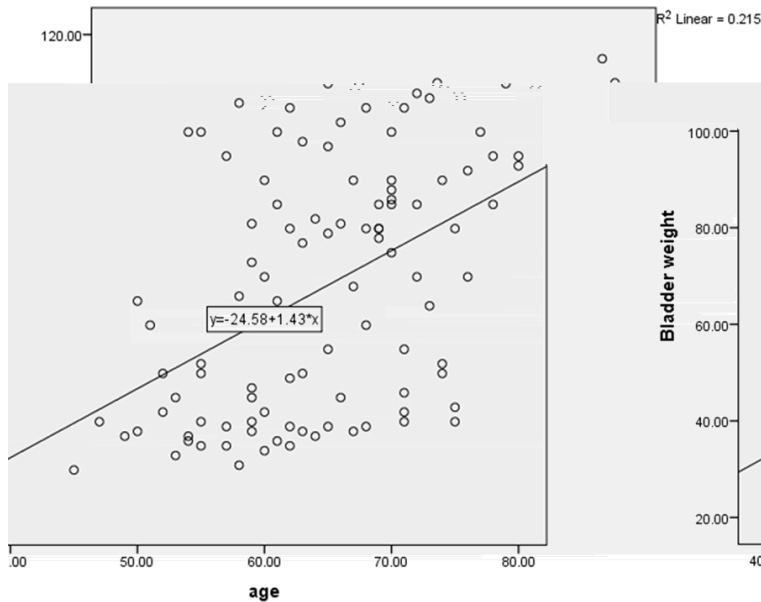
The symptoms of 76 patients were recovered and 24 patients not changed After treatment,

so the patients were compared based on outcomes to treat, so there was significant relationship between the treatment outcome and severity of symptoms before treatment (P<0.001). The means of age, bladder wall thickness and bladder weight in recovered group was significantly lower than not changed group (P<0.001). Also the frequency of IPP in the recovered group was significantly lower than not changed group (P<0.001) (**Table 2**). There was positive significant correlation between age with bladder wall thickness (r=0.51, P<0.001) and bladder weight (r=0.46, P<0.001) (**Figure 1**).

## Discussion

Based on current study results, the patients with mild to moderate symptoms response to treatment was better than patient with severe symptoms. Also there was an inverse significant relationship between age and response to treatment. On the other hand, in patients with lower bladder wall thickness and bladder weight, the response to treatment were better than patients with higher bladder wall thickness and bladder weight and finally, patients with the low IPP, response to treatment was better than high IPP.

## Benign prostatic hyperplasia



**Figure 1.** Correlation between age and bladder weight.

In a study conducted by Selcen et al. that aimed to determine the bladder wall thickness and bladder weight in healthy adults by ultrasound. The results of this study showed that the normal amount of bladder wall thickness in ultrasound was  $2.0 \pm 0.4$  mm and the normal amount of ultrasound bladder weight was  $44.6 \pm 8.3$  g [19]. In our study, bladder wall thickness and bladder weight were  $4.21 \pm 0.75$  mm and  $67.25 \pm 25.36$  g, respectively, so the amount of bladder thickness and bladder weight in BPH patients in our study were significantly higher than the normal level reported in above study. Another study by Sironi in 2002 examined changes of the bladder wall during treatment with Tamsulosin in patients with BPH. In this study, changes in the bladder wall and improvement in the symptoms of bladder outflow obstruction following tamsulosin use were more noticeable than before the treatment period [14]. In our study, the severity of patients' symptoms based on IPSS system in patients after drug treatment with tamsulosin and finasteride was significantly reduced.

Miyashita et al. conducted patients with BPH had a significant relationship between the incidence of acute urinary obstruction with the age, prostate volume and bladder wall thickness [9]. In the current study, there was also a significant relationship between severity of disease with age, bladder wall thickness and bladder weight.

In Thekumpadam et al. study of ultrasound bladder parameter in BPH patients treated with drugs, the results of this study showed that there were significant relationships between IPSS, unflow, age, prostate volume, IPP, bladder wall thickness, prostatic urethral angle before and after treatment. Of the 100 patients studied, 70% had complete recovery and 30% had no improvement in treatment. Bladder ultrasound parameters were suitable tools for measuring response to treatment in BPH patients. Also, resistive index and bladder wall thickness were two important parameters that had a significant relationship with response to treatment

in BPH patients. Also, the most important increasing in prostatic urethral angle and IPP were valuable parameters for not improving the symptoms of patients with BPH [20]. In our study, the results were similar to the above study. Ultrasound parameters and study variables were significantly related and also 76 patients out of 100 patients fully recovered, in addition bladder wall thickness, age, IPSS, IPP, and bladder weight were important tools to determine the recovery of patients after treatment and response to treatment.

Another study by Akino et al. showed that ultrasound of bladder wall thickness could be as effective tool as uroflowmetry and PVR measurements to determine the severity of bladder outlet obstruction and deciding on surgical procedures and effective treatment [10]. In other study that examined the bladder wall thickness to diagnose bladder outlet obstruction in 180 patients (mean aged 62 years) with non-neurological urinary incontinence and bladder wall thickness, the bladder wall thickness in all patients were between 1.1 to 4.5 mm. There was no significant difference between the mean bladder wall thickness between patients with and without bladder outlet obstruction. Therefore, the thickness of the bladder wall could not predict bladder outlet obstruction [8]. In our results bladder wall thickness was predicting marker for response to treatment and was a well ultrasound marker for patients BPH.

## Conclusion

Therefore, according to the results of this study and other studies, the use of ultrasound parameters has a high value in determining the response to treatment in BPH patients and the diagnostic value of IPSS, IPP, bladder wall thickness and bladder weight were important determined response to treatment and severity of disease. In the current study for first time, correlation bladder weight with severity of disease and response to treatment in patients with BPH were evaluated. One of the limitations of this study were not evaluating other variables effect on the response to treatment and low sample size, so due to the limitations of this study, more studies are needed in this field.

## Acknowledgements

The present study was approved in the Isfahan University of Medical Sciences and registry number is IR.MUI.MED.REC.1399.009 with URL (<https://ethics.research.ac.ir/ProposalCertificateEn.php?id=126809&Print=true&NoPrintHeader=true&NoPrintFooter=true&NoPrintPageBorder=true&LetterPrint=true>).

## Disclosure of conflict of interest

None.

**Address correspondence to:** Reza Kazemi, Assistant Professor, Department of Urology, School of Medicine, Isfahan University of Medical Sciences, Isfahan, Iran; Isfahan Research Center of Kidney Transplantation, Department of Urology, Al-Zahra Research Institute, Isfahan University of Medical Sciences, Isfahan, Iran. Tel: +98 913 086 1885; E-mail: reza-kazemi@med.mui.ac.ir

## References

- [1] Tanagho EA and Aninch JWM. Smith's general urology. ResearchGate 2008.
- [2] Alavi A, Izadpanahi MH, Haghshenas L, Faridzad R, Eslami MJ and Ghadimi K. Comparing urine levels of BLCA-4 nuclear matrix protein in patients with bladder cancer and non-bladder cancer. *Int J Physiol Pathophysiol Pharmacol* 2019; 11: 289.
- [3] Fahim M, Zadeh AR, Shoureshi P, Ghadimi K, Cheshmavar M, Sheikhinia N and Afzali M. Alcohol and multiple sclerosis: an immune system-based review. *Int J Physiol Pathophysiol Pharmacol* 2020; 12: 58.
- [4] Stamey TA, Caldwell M, McNEAL JE, Nolley R, Hemenez M and Downs J. The prostate specific antigen era in the United States is over for prostate cancer: what happened in the last 20 years? *J Urol* 2004; 172: 1297-1301.
- [5] Hakenberg OW, Linne C, Manseck A and Wirth MP. Bladder wall thickness in normal adults and men with mild lower urinary tract symptoms and benign prostatic enlargement. *Neurourol Urodyn* 2000; 19: 585-593.
- [6] Canepa G, Capponi G, Campodonico F and Maffezzini M. The influence of TUR or open prostatectomy on ultrasound estimated bladder weight (UEBW): a prospective study on 26 patients. *Neurourol Urodyn* 2003; 22: 41-41.
- [7] Brkljačić B, Kuzmić AC and Dmitrović R. Ultrasound-estimated bladder weight in healthy children. *Eur Radiol* 2004; 14: 1596-1599.
- [8] Blatt AH, Titus J and Chan L. Ultrasound measurement of bladder wall thickness in the assessment of voiding dysfunction. *J Urol* 2008; 179: 2275-2279.
- [9] Miyashita H, Kojima M and Miki T. Ultrasonic measurement of bladder weight as a possible predictor of acute urinary retention in men with lower urinary tract symptoms suggestive of benign prostatic hyperplasia. *Ultrasound Med Biol* 2002; 28: 985-990.
- [10] Akino H, Maekawa M, Nakai M, Shioyama R, Ishida H, Oyama N, Miwa Y and Yokoyama O. Ultrasound-estimated bladder weight predicts risk of surgery for benign prostatic hyperplasia in men using  $\alpha$ -adrenoceptor blocker for LUTS. *Urology* 2008; 72: 817-820.
- [11] Bright E, Oelke M, Tubaro A and Abrams P. Ultrasound estimated bladder weight and measurement of bladder wall thickness-useful noninvasive methods for assessing the lower urinary tract? *J Urol* 2010; 184: 1847-1854.
- [12] Hosseini J, Fallah-Karkan M, Rahavian A, Soleimanzadeh F, Salimi H, Ghadimi K and Fahim M. Feasibility, complication and long-term follow-up of the newly nelaton based urethral dilation method, retrospective study. *Am J Clin Exp Urol* 2019; 7: 378.
- [13] Lee HN, Lee YS, Han DH and Lee KS. Change of ultrasound estimated bladder weight and bladder wall thickness after treatment of bladder outlet obstruction with dutasteride. *LUTS* 2017; 9: 67-74.
- [14] Sironi D, Levorato CA, Deiana G, Borgonovo G, Belussi D, Ranieri A and Lembo A. Decrease of ultrasound estimated bladder weight during tamsulosin treatment in patients with benign prostatic enlargement. *Arch Ital Urol Androl* 2002; 74: 90-94.
- [15] Aganovic D, Hasanbegovic M, Prcic A, Kulovac B and Hadziosmanovic O. Which is a better indicator of bladder outlet obstruction in patients with benign prostatic enlargement-intravesical protrusion of prostate or bladder wall thickness? *Med Arch* 2012; 66: 324.

## Benign prostatic hyperplasia

- [16] Shuang W, Wang D, Zhang X, Liu C, Cao X, Wang J, Gao J, Ren Z and Lü Y. Analysis of the diagnostic criteria of bladder outlet obstruction in benign prostatic hyperplasia. *Natl J Androl* 2004; 10: 743-746.
- [17] Araki I and Kuno S. Assessment of voiding dysfunction in Parkinson's disease by the international prostate symptom score. *J Neurol Neurosurg Psychiatry* 2000; 68: 429-433.
- [18] Simon C, Cho CC, Hung EH, Zou J, Yuen BT, Shi L, Chiu PK, Yee SC and Ng AC. Thickness-to-height ratio of intravesical prostatic protrusion predicts the clinical outcome and morbidity of prostatic artery embolization for benign prostatic hyperplasia. *J Vasc Interv Radiol* 2019; 30: 1807-1816.
- [19] Kanyilmaz S, Calis FA, Cinar Y and Akkoc Y. Bladder wall thickness and ultrasound estimated bladder weight in healthy adults with portative ultrasound device. *J Res Med Sci* 2013; 18: 103.
- [20] Puthenveetil RT, Baishya D, Barua S and Sarma D. Implication of ultrasound bladder parameters on treatment response in patients with benign prostatic hyperplasia under medical management. *Asian J Urol* 2015; 2: 233-237.