RESEARCH ARTICLE

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The Diagnostic Value of Bladder-Wall Thickness and ARFI Elastography of Bladder Wall amongst Patients with BPH

ABSTRACT

Objective: The present study identified bladder-wall thickness and, through the use of ARFI elastography, bladder-wall elasticity values amongst patients with benign prostate hyperplasia (BPH), then examined their relationship with the disease diagnosis and progression.

Methods: The study included 60 patients with BPH (patient group) and 50 healthy volunteers (control group). All members of the patient and control groups were measured for bladder-wall thickness (BWT) and bladder-wall mean shear-wave velocity (BW mean SWV) values, as well as for uroflowmetry parameters. The patient group was divided into the sub-groups of mild-medium and severe BPH, according to the International Prostate Symptom Score (IPSS). The patient and control groups and their sub-groups were compared amongst themselves.

Results: Whilst the BPH group indicated a mean wall thickness of 6.3±2 mm (range: 3-12 mm), the control group yielded a result of 2.8±0.7 mm (range: 2-5 mm), which led to the conclusion that there was a significant difference between these groups ($p<0.01$). The BWmeanSWV value was 1.39±0.5 m/s (range: 0.60-2.65 m/s) for the BPH group and 1.01±0.2 m/s (range: 0.60-1.50 m/s) for the control group, and this also indicated the presence of a significant difference between the groups ($p<0.01$). According to the IPSS, BWT was observed to be significantly higher in the severe sub-group when compared to the mild-medium BPH group [(5.07±1 mm; range: 3-7 mm), (6.8±2 mm; range: 4-12 mm), $p<0.01$).

Conclusions: When compared to the control group, patients with BPH showed significantly higher BWT and BWmeanSWV values; these two parameters may provide an additional method in the diagnosis of bladder outlet obstruction secondary to BPH. BWT, increasing in parallel with the severity of BPH, may be utilised in the follow-up for BPH progression.

Keywords: Bladder-Wall Thickness, Bladder-Wall Shear-Wave Velocity, ARFI Elastography, Benign Prostate Hyperplasia.

Benin Prostat Hiperplazili Hastalarda Mesane Duvar Kalınlığı ve Mesane Duvar ARFI Elastografinin Tanı Değeri

ÖZET

Amaç: Çalışmamızda benign prostat hiperplazili (BPH) hastalarda mesane duvar kalınlığı ve ARFI elastografi yöntemi ile mesane duvarı elastisite değerlerini saptayıp, hastalığın tanısı ve progresyonu ile ilişkisini araştırdık.

Gereç ve Yöntem: Çalışmaya 60 BPH'lı hasta (Hasta grubu) ile 50 sağlıklı gönüllü (Kontrol grubu) dahil edildi. Hasta ve kontrol grubunun tamamında mesane duvar kalınlığı (MDK), mesane duvarı MDmeanSWV değerleri ve uroflovmetre parametreleri ölçüldü. Hasta grup; International Prostate Symptom Skoru'na (IPSS) göre hafif-orta ve şiddetli BPH subgruplarına ayrıldı. Hasta–kontrol gurubu ve subgruplar kendi aralarında karşılaştırıldı.

Bulgular: BPH'lı grup mesane duvar kalınlığı 6.3±2 mm (3-12 mm) iken kontrol grubunda 2.8±0.7 mm (2-5 mm) olup her iki grup arasında anlamlı fark mevcuttu ($p<0.001$). MDmeanSWV değeri BPH'lı grupta 1.39±0.5 m/s (0.60-2.65 m/s) iken, kontrol grubunda 1.01±0.2 m/s(0.60-1.50) olup her iki grup arasında anlamlı fark mevcuttu($p<0.001$).

IPSS ye göre şiddetli BPH'lı grup, hafif-orta BPH grup ile karşılaştırıldığında MDK, şiddetli subgrupta anlamlı şekilde daha yüksek bulundu [sırasıyla; 5.07±1 (3-7), 6.8±2 (4-12), $p<0.01$].

Sonuç: Kontrol grubuna göre BPH'lı hastalarda MDK ile birlikte MDmeanSWV elastografi değerleri belirgin yüksektir, bu iki parametre BPH'ya sekonder gelişen mesane çıkış obstrüksiyon tanısında ilave bir yöntem olabilir. BPH şiddeti ile paralel artış gösteren MDK, BPH progresyonunun takibinde kullanılabilir.

Anahtar Kelimeler: Mesane Duvarı Kalınlığı, Mesane Duvarı Shear-Wave Velositesi, ARFI Elastografi, Benign Prostat Hiperplazisi.

INTRODUCTION

More than 50% of cases of benign prostate hyperplasia (BPH), a disease with an incidence rising in parallel with age, are observed amongst older male patients. 28% of patients of the age of 70 or above exhibit medium-to-severe lower urinary tract symptoms (1-3). The bladder outlet obstruction caused by BPH increases the detrusor pressure and causes the urinary flow rate to decrease during voiding (4). Infravesical obstruction in patients with BPH causes detrusor hypertrophy, which in turn leads to the emergence of irritative urinary symptoms. Bladder outlet obstruction was reported to be non-symptomatic in 52% of patients with BPH (5-6).

According to studies conducted on animals with obstruction of the bladder, there was a significant increase in the bladder-wall thickness due to smooth muscle cell hypertrophy, as well as fibrocystic hyperplasia and collagen accumulation on the bladder wall. These findings were also identified in human patients with bladder outlet obstruction (7-8). Trabecular formation in the bladder and bladder hypertrophy findings can be established through cystoscopy or cystography. However, these techniques do not provide objective or quantitative means for measuring the degree of bladder hypertrophy. Furthermore, the most reliable functional method in the diagnosis of bladder outlet obstruction is the evaluation of urodynamic pressure flow. However, it includes such complications as bleeding and infection and is a time-consuming and costly method (9).

Uroflowmetry is an urodynamic test that enables the non-invasive evaluation of the properties of urinary flow during urination (10). Prostate-induced bladder outlet obstruction causes a lower flow rate, and uroflowmetry provides us with a more objective criterion when compared to the symptoms of the disease in BPH diagnosis (11). The International Prostate Symptom Score (IPSS) is quite useful during the follow-up for disease progression in the identification of treatment modalities by providing a better understanding of BPH-related disease symptoms. IPSS>7 are accepted as important criteria in the diagnosis of BPH (12).

Bladder elasticity emerges secondary to the presence of a higher ratio of connective tissue in the bladder wall than that in the smooth muscle. When compared to the smooth muscle, the bladder becomes more rigid in direct proportion with the increase of the quantity of connective tissue, and can expand to a much lesser degree during filling (13-14-15). Cystometry, considered to be the gold standard in the evaluation of bladder compliance, is an uncomfortable method for patients and poses a risk of infection at the same time. Acoustic radiation force impulse (ARFI) imaging is a new, non-invasive and low-cost method for evaluating tissue elasticity. Integrated into the ultrasound technique, ARFI imaging enables the quantitative and qualitative evaluation of tissue elasticity. The measurement of shear-wave velocity (SWV) in the tissue where the region of interest (ROI) is situated indicates higher SWV and higher rigidity, thereby allowing the identification of the mechanical properties of the tissue (16).

We first identified bladder-wall thickness (BWT) and, through the use of ARFI elastography, differences in bladder elasticity amongst patients with BPH and volunteers, and then we examined the relationship between the severity of BPH and BWT, BWmeanSWV values.

MATERIAL AND METHODS

Patients: The study included 105 patients with BPH that presented at the urology department with lower urinary tract symptoms between August 2014 and May 2015. Fourthy-five of these patients were excluded from the study due to the presence of exclusion criteria such as uncontrolled diabetes mellitus, neurological diseases affecting urinary function, bladder and prostate cancers, history of lower urinary tract surgery, urinary tract infection or urethral stricture. The study included 60 male patients with BPH and 50 healthy volunteer. Age - matched healthy male volunteers, who are free of any systemic disorder and without any urinary tract complaints formed the control group.

The study was approved by the ethics board of Dicle University. Consent forms were collected from the patients and the healthy volunteers.

Imaging: Individuals were subjected to B-mode ultrasonography (US) and ARFI elastography imaging through the use of an Acuson S2000 ultrasound system (Siemens Solutions, Mountain View, CA, USA) and a convex probe (4 C1, frequency range: 1–4 MHz). The B-mode US examination was undertaken by a radiologist with 16 years of experience in this field, and the evaluation of the ARFI elastography measurements (Virtual Touch™ Tissue Quantification) was done by the same radiologist (B.A.) with 2 years of experience in this field. The first step was to measure the prostate volume in the BPH and control groups using B-mode US. The prostate volume was calculated using the following formula: $\pi/6 \times$ (transverse diameter $\times$ anteroposterior diameter $\times$ cephalocaudal diameter) (17).

Afterward, BWT was measured on the anterior and right and left lateral bladder walls, and the average of all three measurements was recorded as the wall thickness. The Region of Interest (ROI) was placed onto the bladder wall and the measured SWV value was obtained in metres/second. A total of eight valid SWV measurements were taken for each measurement of the anterior, posterior, right and left bladder wall with full bladder (Figure 1).

IPSS and Uroflowmetry: The urinary symptoms of patients were evaluated based on the International Prostate Symptom Score. The total

IPSS score was subcategorised into voiding and storage symptom sub-scores (18). The IPSS requires men to quantitative seven symptoms using a score ranging from 1 to 5 on the basis of their experience in the past 30 days. The IPSS also includes one question that assesses how bothersome their symptoms have been. The answer to this question becomes very important when considering whether to commence treatment for patients with BPH/LUTS. Each severe symptom can be assessed with a maximum score of 5, thus the maximum possible score is 35. A score of zero indicates the absence of any BPH symptoms. A symptom score between 1 and 7 is considered mildly symptomatic, 8-19 is moderately symptomatic, and 20-35 is severely symptomatic. The question about the bothersome nature of the symptoms is scored separately as 0-6 (19). The BPH group was divided into two sub-groups for the identification of disease severity: severe BPH with IPSS≥20 and mild-moderate BPH with IPSS<20.

Uroflowmetry measurements, including the maximum urinary flow rate (Qmax), average urinary flow rate (Qave) and post-voiding residue (PVR), were conducted in the standing position with the use of Bluetooth uroflowmetry (Urodyn+, MMS, Flowmaster, NL). Those with a voided volume of <125 mL were not included. Qmax and PVR measurements were repeated. PVR measurements were undertaken with a bladder scanner (Login C3, Premium, GE, China). Two sub-groups were formed with <10 and ≥10, according to Qmax, and then subjected to comparison (20).

Statistical Analysis: SPSS 16.0 (Statistical Package for the Social Sciences version 16.0 for Windows, SPSS Inc., Chicago, IL, USA) was used for the statistical analysis. The Kolmogorov-Smirnov test was used for the distribution of data. Data were expressed as mean ± standard deviation. For the evaluation of the continuous variables, we used Student's t-test for parametric data and the Mann-Whitney U test for nonparametric data; the categorical valuables were analyzed with the chi-square test. The relation between the parameters was analyzed with the Spearman and Pearson correlation test. For detecting the effect of parameters on BWmeanSWV values used logistic regression test. In order to predict the severity of BPH, we calculated the areas under the ROC curves for the prostate shear wave speed. A value of $p<0.05$ was accepted as significant.

RESULTS

Out of the total of 110 patients included in the study, 60 formed the group of BPH patients and 50 formed the control group. The mean age of the control group was 57.1±8 years (range: 50-63 years), whilst the mean age of the BPH group was 60.5±6 years (range: 50-73) years), there was no significant difference between the two groups (p = 0,07). Prostate volume was 66.1±27 ml (range: 21-131 ml) in the BPH group and 19.9±5 ml (range: 10-31 ml) in the control group, indicating a significant difference between the two groups. Whilst the BPH group indicated a mean wall-thickness of 6.3±2 mm (range: 3-12 mm), the control group yielded the result of 2.8±0.7 mm (range: 2-5 mm), which led to the conclusion that there was a significant difference between these groups ($p<0.01$). The BWmeanSWV value was 1.39±0.5 m/s (range: 0.60-2.65 m/s) for the BPH group and 1.01±0.2 m/s (range: 0.60-1.50 m/s) for the control group, and this also indicated the presence of a significant difference between the groups ($p<0.01$) (Figures 2-3).

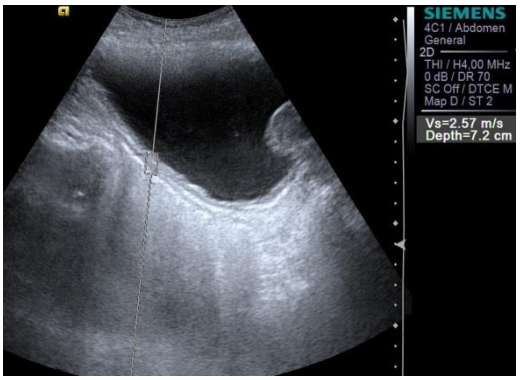

Figure 1. Bladder-wall SWV measurement

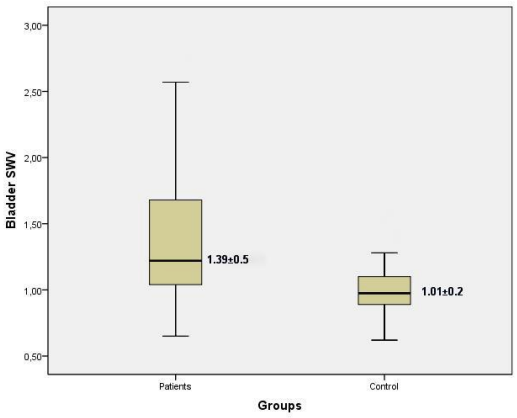

Figure 2. Comparison of BWmeanSWV value between patients with BPH and the healthy control group

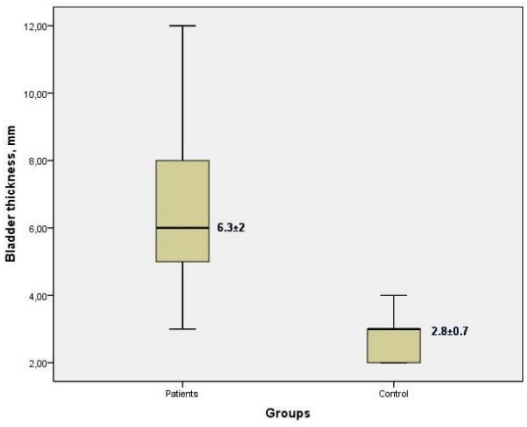

Figure 3. Comparison of bladder-wall thickness between patients with BPH and the healthy control group

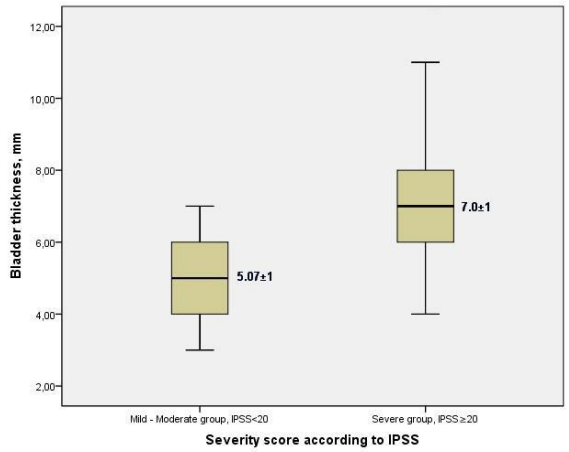

Figure 4. Comparison of BW thickness between mild-medium and severe BPH sub-groups according to IPSS

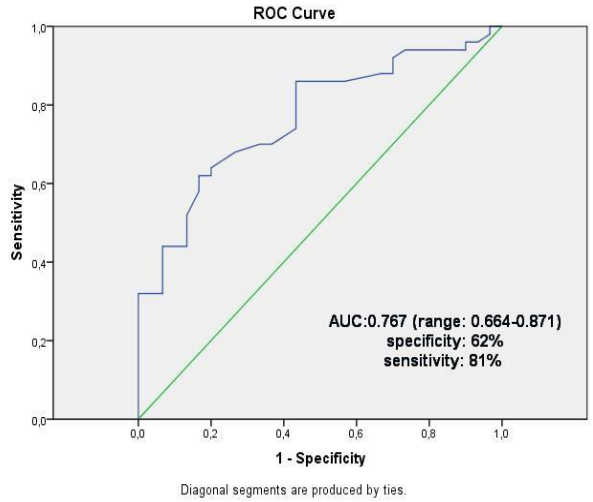

Figure 5. Diagnostic performance of BWmeanSWV value in patients with BPH

The correlation analysis undertaken with age, BWT, IPSS score and uroflowmetry parameters through BWmeanSWV identified a significant positive correlation between BWT and IPSS [(r=0.482, p<0.01), (r=247, p=0.04), respectively]. Furthermore, a weak negative correlation was identified in Qmax (r=-0.219, p=0.04) (Table 1).

The logistic regression test gave way to the identification of a significant relation between BWmeanSWV and BWT, with no indication of any other parameter affecting BWmeanSWV (Table 2).

The BPH group was divided into two sub-groups for the identification of disease severity, i.e., severe BPH with IPSS≥20 and mild-moderate BPH with IPSS<20. When the severe BPH group was compared with the mild-moderate BPH group, BWT was found to be significantly higher in the severe sub-group (7.0±1 mm; range: 3-7 mm) (5.07±1 mm; range: 4-12 mm) (p<0.01) (Figure 4). However, BWmeanSWV values were slightly higher in the severe BPH group than in the mild-moderate BPH group, and no statistically significant difference could be identified (1.38±0.4; range: 0.8-2.1) (1.41±0.5; range: 0.6-2.6) (p=0.9).

The comparison between two sub-groups formed with values of <10 and ≥10, based on Qmax, showed a significantly higher BWT in the Qmax<10 sub-group than in the Qmax≥10 sub-group (p<0.01). BWmeanSWV was slightly higher in the Qmax<10 sub-group than in the Qmax≥10 sub-group, with no statistically significant difference identified (Table 3).

The ROC analysis undertaken to assess the diagnostic value of BWmeanSWV for BPH calculated AUC as 0.767 (range: 0.664-0.871), specificity as 62%, and sensitivity as 81% (Figure 5).

Table 1. Correlation analysis of BWmeanSWV value in patients with BPH with age, bladder-wall thickness, maximum flow rate and IPSS

	r	**P***
Age, year	0.352	0.3
Bladder thickness, mm	0.482	< 0.01
Qmax,mL/s	-0.219	= 0.04
IPSS	0.247	0.04

Pearson correlation test * ;IPSS: International Prostate Symptom Score; ; Qmax: Maximum urinary flow rate

Table 2. Detecting the effect of age, Prostate volüme, Bladder thickness parameters on the on BWmeanSWV values by logistic regression test.

Model		Unstandardized Coefficients		Standardized Coefficient[a]s	t	Sig.*
		B	Std. Error	Beta		
1	(Constant)	.675	.151		4.475	.000
	Age. year	.001	.003	.054	.405	.687
	Prostate volüme, mL	-.001	.002	-.058	-.390	.698
	Bladder thickness, mm	.120	.033	.532	3.590	.001

a. Dependent Variable: Bladder SWV,* logistic regression test

Table 3. Comparison of bladder-wall thickness, BWmeanSWV and uroflowmetry parameters between groups with Qmax scores < 10 and Qmax ≥ 10

Parameters		n	Values*	Range	*P***
Age,year	Qmax scores < 10	30	65.9±9	47-87	
	Qmax scores ≥ 10	20	64.4±7	52-76	0.3
BWmeanSWV,m/s	Qmax scores < 10	30	1.4±0.5	0.65-2.65	0.1
	Qmax scores ≥ 10	20	1.2±0.3	0.84-2.15	
Bladder thickness, mm	Qmax scores < 10	30	7.2±2	4-12	
	Qmax scores ≥ 10	20	5.1±1	3-7	< 0.01
Voiding volüme,mL	Qmax scores < 10	30	114±71	13-275	
	Qmax scores ≥ 10	20	223±189	65-931	< 0.01
Voiding time,s	Qmax scores < 10	30	54.8±32	12-138	0.8
	Qmax scores ≥ 10	20	56±33	13-138	
PVR,mL	Qmax scores < 10	30	81.4±63	0-226	0.3
	Qmax scores ≥ 10	20	65±52	0-190	

Values are mean±SD *; Mann-Whitney U test**;BPH: Benign prostate hypertrophy; BWmeanSWV: bladder-wall mean shear-wave velocity; IPSS: International Prostate Symptom Score; PVR: post-void residual

DISCUSSION

BWT was higher in the BPH group than in the control group. Pathological conditions causing bladder outlet obstruction, including BPH, do affect the bladder-wall thickness (21-23). Histologically, smooth muscle cells were reported to lead to the development of hypertrophy, hyperplasia and collagen accumulation between muscle cells. Such muscle hypertrophy weakens the detrusor muscle further (21-24). There are other factors affecting the bladder wall, including age, sex and bladder fullness (8). We minimised the variation in bladder fullness by undertaking the measurements on those with bladder volumes ≥200 ml so that such variations would not affect the BWT measurement. The comparison between mild-medium BPH and severe BPH sub-groups under IPSS showed a significantly higher value for BWT in the severe BPH sub-group. Azab *et al.* identified a positive correlation between BWT and IPSS in patients with BPH (25). Similarly, Parks *et al.* reported a positive correlation between IPSS and BWT (26).

We identified a significantly higher BW mean SWV value in the BPH group in its comparison with the control group. Bladder-wall rigidity escalates along with the increase in connective tissue accumulation brought along by smooth muscle cell hypertrophy induced by bladder outlet obstructions, such as BPH, in the bladder wall. Collagen accumulation appears in the distances between expanded muscle cells caused by the decrease in intermediate cell junctions (13-15,27). The identification of higher bladder-wall elasticity in patients with BPH than in those in the control group may be based upon these histopathological changes. However, we conducted a multi-variance analysis under the notion that age could be an influential factor for bladder rigidity; this established that patient age did not affect the BWmeanSWV value. We determined a positive correlation between BWmeanSWV and IPSS and Qmax in the correlation analysis. Nevertheless, the comparison of BWmeanSWV value between mild-medium BPH and severe BPH groups, calculated according to IPSS, did not provide us with any statistically significant difference between the two groups, even though the BWmean SWV value was slightly higher in the severe BPH group. Studies undertaken with more comprehensive patient series are needed to identify whether BWmeanSWV can be used in the follow-up for disease progression. As a relatively non-invasive method, when compared to the invasive method of cystometry in the evaluation of bladder compliance, US-based ARFI elastography also enables evaluation of the mechanical properties of the bladder wall. Numeric values obtained through ARFI-elastography provide quantitative information that is useful for the evaluation of bladder elasticity.

The present study had certain limitations. As the correlation between the bladder wall elastic module and bladder outlet obstruction could not be clarified, there is a need for further studies as precursors based on the provision of SWV values in the identification of bladder elasticity.

CONCLUSION

When compared to the control group, patients with BPH show significantly higher BWT and BWmeanSWV values, and these two parameters may provide an additional method in the diagnosis of bladder outlet obstruction secondary to BPH. BWT, increasing in parallel with the severity of BPH, may be utilised in the follow-up of BPH progression.

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Conflict of Interest: The authors declare that they have no competing interests.

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