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Original Article

Radiology Section

Role of Shear Wave Elastography in Assessing the Severity of Bladder Outlet Obstruction in Patients with Benign Prostatic Hyperplasia: A Cross-sectional Study

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ABSTRACT

Introduction: Benign Prostatic Hyperplasia (BPH) is a disease prevalent in ageing men. The BPH causes Bladder Outlet Obstruction (BOO) which may even lead to hydronephrosis and renal insufficiency. Therefore, diagnosis of severity of BOO is necessary in the treatment of patients with BPH.

Aim: To assess the accuracy of various ultrasound parameters {volume of prostate, Resistive Index (RI) of capsular arteries of prostate and stiffness of prostate} in the prediction of severity of BOO in patients with BPH.

Materials and Methods: The cross-sectional study was conducted between November 2020 and January 2021 in the Department of Radiology at at Government Kilpauk Medical College, Chennai, Tamil Nadu, India. Total 55 males between 40 to 80 years of age with symptoms of lower urinary tract obstruction participated. Multi-parametric Transrectal Ultrasound (TRUS) examination of the prostate including Grey scale, Colour Doppler Sonography (CD) and Shear Wave Elastography (SWE) were performed on patients with BPH who had undergone urodynamic evaluation. Volume of the prostate gland, RI of capsular arteries and stiffness or elastic modulus of the prostate gland were measured in the TRUS examination and compared with uroflowmetry which was used as a standard. Receiver Operating Characteristic (ROC) curve was used to assess diagnostic performance of the three ultrasound parameters. The thresholds maximising the Youden index were calculated, and corresponding sensitivity, specificity, positive predictive value, negative predictive value and accuracy are reported.

Results: Among the 55 males in the study the mean age of study population was 59.6 years and standard deviation of 7.9. Mean International Prostate Symptom Score among the population was 18.9±4.9. Mean volume of prostate was 33.66±7.166 cc. Mean RI was 0.75±0.11. Mean stiffness of prostate calculated was 40.9±11.3 Kpa. The stiffness or elastic modulus of the prostate was the most strongly correlated indicator with the severity of BOO (R^2=0.77, p-value <0.001), and had the largest area under the ROC curve 0.942 (95% CI was 0.844-0.987) with a significant p-value of <0.0001 while RI and volume of the prostate gland had an Area Under the Receiver Operating Characteristic Curve (AUROC) of 0.810 (95% CI was 0.64-0.87) and 0.779 (95% CI was 0.64-0.88), respectively. The diagnostic cut-off values for stiffness of prostate, RI of capsular arteries and volume of prostate were 31.6 kPa, 0.68 and 28 mL, respectively.

Conclusion: The stiffness of the prostate measured on SWE is a promising indicator in the assessment of the severity of BOO.

Keywords: Bladder obstruction, Elastic modulus, Prostatic stiffness, Transrectal ultrasound, Urodynamics

INTRODUCTION

Benign enlargement of prostate is termed as Benign Prostatic Hyperplasia (BPH), which is often associated with Lower Urinary Tract Symptoms (LUTS) such as dysuria, feeling of incomplete emptying, straining, nocturia and urgency. The BPH, one of the most common diseases in ageing men, increases after the age of 40 years, with a prevalence of 8-60% at age 90 years [1]. Important criteria for the diagnosis of BPH are enlarged prostatic volume >20 cc, a maximum urinary flow rate (Qmax) <10 mL, and an International Prostate Symptom Score (IPSS) >7 [2].

Prostate is supplied by the capsular and urethral branches of the prostatic arteries. Capsular arteries supply peripheral two-thirds and the rest of the gland is supplied by the urethral branches. The capsular arteries course along the postero-lateral border of the prostate and perforate the capsule to enter the peripheral zone. The urethral arteries run along the prostatic urethra after they enter into the prostate at the bladder neck. In BPH, when the prostatic enlarges the blood flow between the peripheral zone and transitional zone in the prostate are compressed causing increase in Resistive Index (RI) of the capsular arteries [3].

Irregular proliferation of connective tissues, smooth muscles and glandular epithelial cells can be demonstrated in histopathological examination in the transitional zone of the prostate resulting in the increased stiffness of prostate in BPH [4-6]. The clinical progression of BPH symptoms not only depends on total prostate volume but also their regular proliferation of various connective tissues within the gland. Elastography can be used to detect the variation in stiffness of the gland and thereby the severity of Bladder Outlet Obstruction (BOO).

The tissue elasticity can be calculated by measuring the velocity of shear waves. The elastogram is displayed over the B-mode image in a colour-coded scale. The SWE generates an absolute value of tissue stiffness in kilopascal. Many prostate studies using SWE have focused mainly on the differential diagnosis of benign and malignant lesions [7-10]. In present study, the stiffness measured by SWE was used to categorise the severity of BOO in patients with BPH.

MATERIALS AND METHODS

This cross-sectional study was conducted in the Department of Radiology, Government Kilpauk Medical College, Chennai, Tamil Nadu, India, between November 2020 and January 2021. The study was done following approval from Institutional Ethics Committee (ECR J385 Inst TN 2020).

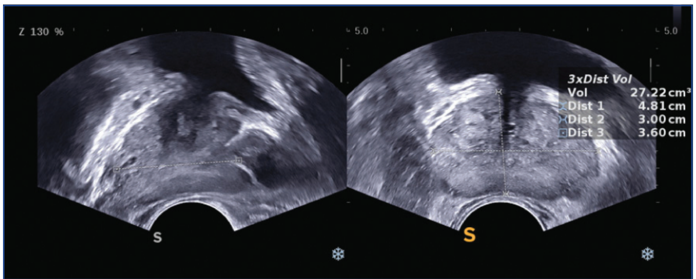
Inclusion and Exclusion criteria: The number of patients with LUTS who presented to Ultrasound (USG) Department during the stated period of study (between 40-80 years of age) were included in the study. Patients with Prostate Specific Antigen (PSA) values >10 ng/mL, history of transurethral resection, known cases of carcinoma prostate and patients with urethral stenosis, a prostatic depth more than 8 cm from the skin, uncontrolled diabetes mellitus, neurologic diseases were excluded from the study.

The patients were assessed for the severity of complaints of LUTS using International Prostate Symptom Score (IPSS) as a part of the routine work up [11]. A total of 55 males between 40 to 80 years of age with symptoms of lower urinary tract obstruction were included in the study.

Study Procedure

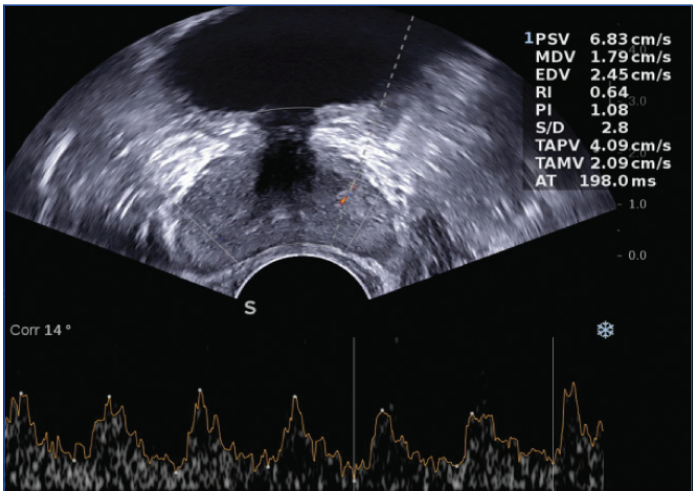
All patients underwent Transrectal Ultrasound (TRUS) examination in Aixplorer Supersonic Ultrasound machine. Multiple parameters were measured including volume of prostate gland on Grey scale, RI of capsular arteries on Colour Doppler and Young's modulus for stiffness in kilopascals using Shear Wave Elastography (SWE).

The TRUS procedure was explained to the patients and consent was obtained from all patients. Scanning was done in the left lateral position with their knees bent towards the chest. After adequate local anaesthetic application, the endo-cavitary probe (3-12 HZ) was inserted into the rectum and prostate was visualised. Grey scale examination of the prostate was done in the axial and sagittal planes and Volume of Prostate (PV) was calculated using ellipsoid formula Height×Width×Length×0.52 [Table/Fig-1].



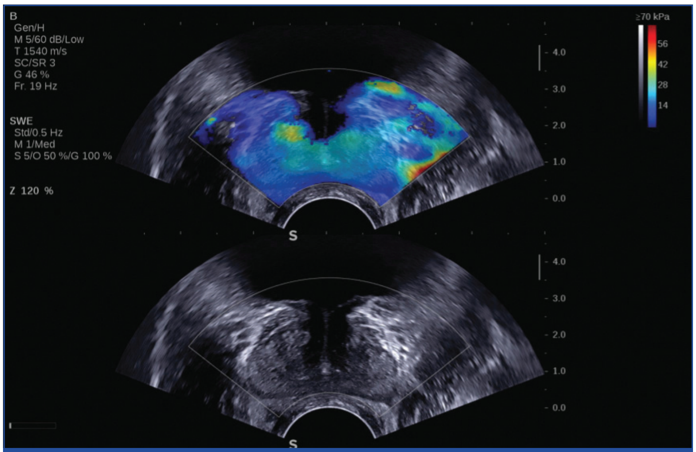
[Table/Fig-1]: Measurement of prostate volume on grey scale examination on axial and sagittal planes.

Low flow power doppler settings were used for optimal visualisation of capsular arteries with minimal background noise. Intraprostatic capsular arteries were identified between the transitional and peripheral zone. Blood flow in the capsular arterieswas recorded followed by spectral waveform analysis. When the doppler spectral waveform analysis became stable for atleast five pulses the RI was automatically calculated [Table/Fig-2].

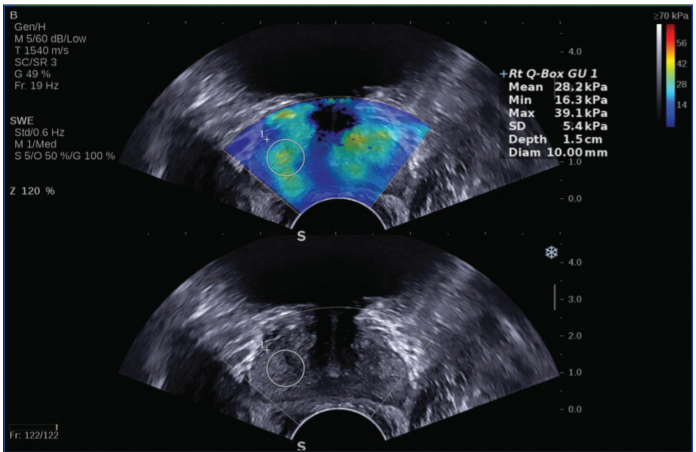


[Table/Fig-2]: Measurement of Resistive Index (RI) of left capsular artery on Colour Doppler (CD) sonography.

The SWE was turned on and stiffness of the prostate gland was obtained at three levels i.e., apex, mid zone and base in both right and left lobes of the gland. Mean value of stiffness was obtained from the average of the values obtained from six zones. Optimised settings with maximised penetration, elasticity scale set to 70 kPa were used. The Q box in which the elastogram is calculated was set to 10 mm. The probe was kept in a steady-state position for a few seconds until stabilisation of the colour map, and the images were stored. The softer tissue displayed blue colour while stiffer tissue displayed red colour. Then, the box was moved a few millimeters to encompass the rest of the gland in three levels at the base, mid zone and apex and elastograms were stored. During SWE, minimal pressure was put on the gland through the probe, to avoid creating false areas of increased stiffness in the gland [Table/Fig-3,4].



[Table/Fig-3]: Measurement of stiffness or elastic modulus of prostate using Shear Wave Elastography (SWE) showing normal appearance, the entire gland evenly shaded in blue.



[Table/Fig-4]: The use of colour coded map to identify areas of increased stiffness in Shear Wave Elastography (SWE). In this image, the areas of increased stiffness show green and yellow colour where as the normal gland displays blue.

Then these patients underwent uroflow dynamic evaluation byurologist who was blind to the TRUS and SWE. The urodynamic flow rate was plotted on the Schaefer nomogram and Q max value was obtained for each of them. The results obtained from uroflowmetry were used to categorise the patients with obstruction into three grades (I, II, III) as mild (Qmax >15 mL/s), moderate (Qmax 10-15 mL/s) and severe (Qmax <10 mL/s) [12].

STATISTICAL ANALYSIS

Quantitative values are presented as the mean ± standard deviation. Regression analysis was used to compare features among the different BOO groups. A ROC curve was used to assess diagnostic performance. The thresholds maximising the Youden index were calculated, and corresponding sensitivity and specificity are reported. A p-value <0.001 was considered statistically significant and all interval estimations given in this paper are 95% Confidence Intervals (CI). Statistical analysis were performed by using statistics analysis software MedCalc (Version 20.006).

RESULTS

Among the 55 males in the study, the mean age of study population was 59.6 years and standard deviation of 7.9. Mean International

Prostate Symptom Score (IPSS) score among the population was 18.9±4.9. Mean volume of prostate was 33.66±7.166 cc. Mean RI was 0.75±0.11. Mean stiffness of prostate calculated was 40.9±11.3 Kpa.

Based on the urodynamic Schaefer nomogram, the number of patients with grade I, II, III of bladder outlet obstruction was 12, 25, and 18, respectively. The characteristics of various BOO groups is summarised in [Table/Fig-5].

Prostate Volume (Grey scale), RI (Doppler) and stiffness (Elastography) were compared with uroflowmetry using regression analysis and correlation coefficient of -0.54,-0.47 and -0.88 were obtained respectively. Stiffness calculated in SWE was the feature most strongly correlated with BOO stage witha coefficient of determination (R2) of 0.77 with a significant p-value of <0.0001 [Table/Fig-6].

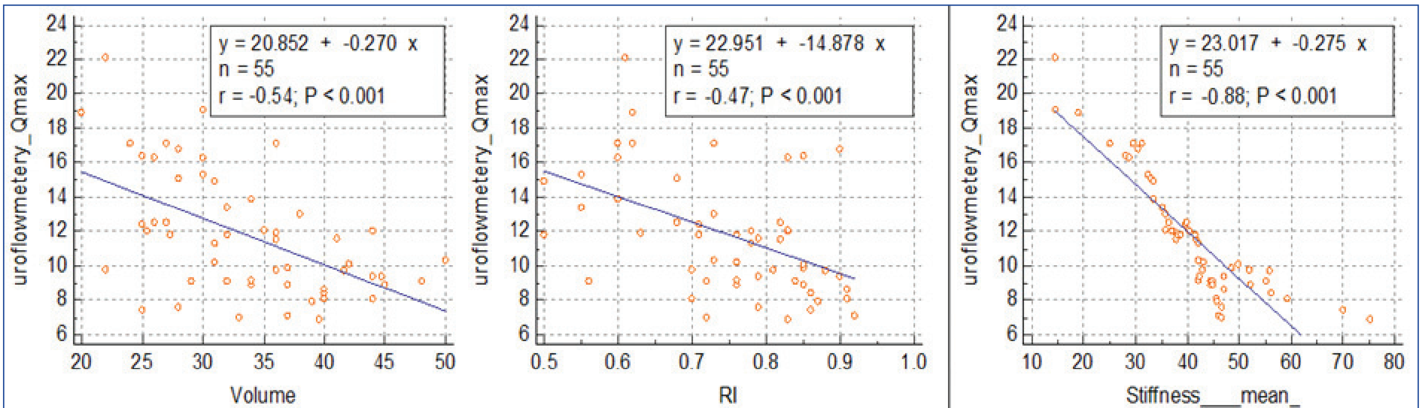
The AUCs for volume of the prostate gland, RI of capsular arteries and stiffness of prostate is shown in [Table/Fig-7,8]. The comparison AUCs revealed that stiffness of prostate calculated in SWE had the best AUC for BOO, 0.942 (95% CI: 0.844-0.987).

DISCUSSION

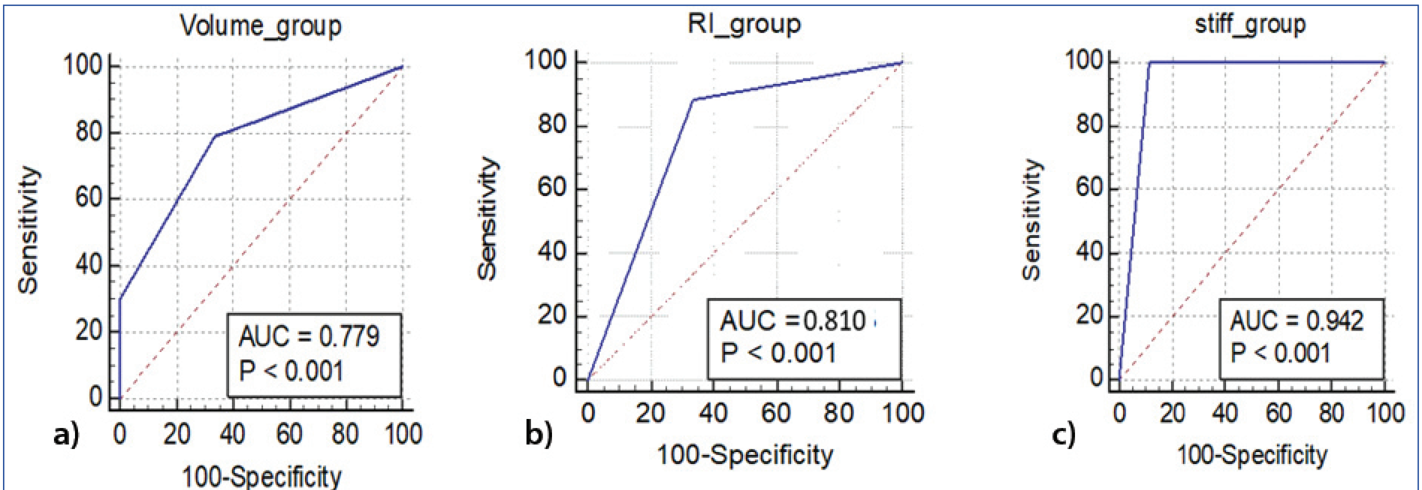
The various diagnostic features and grading the severity of BOO have been studied. The IPSS questionnaire is useful for assessment of symptoms in patients with BPH but its reliability remains far from optimal [13]. A relationship between prostate volume and BOO stage has been reported [14,15]. However, volume of the prostate gland is not always associated with BOO stage was found [16]. Previous studies have also suggested the use of parameters like intravesical prostatic protrusion, prostatic urethra angle and prostatic circle area ratio for evaluation of BOO [17-19]. However, none of these factors are well-recognised non invasive diagnostic indicators of BOO. Another parameter, RI of prostate capsular arteries was used to evaluate BOO, on the basis that there is an increase in inner prostatic pressure in BOO [10]. Zhang M et al., and Rouvière O et al., in their studies have proved that the elastic modulus of prostate in shear wave velocity based methods was comparable to the results of detrusor pressure on urodynamic study and prostatectomy specimen respectively [20,21].

BOO severity stages-number of patients	Volume		Resistive index		Stiffness		Qmax	
	Range (mL)	Mean±SD (mL)	Range	Mean±SD	Range (Kpa)	Mean±SD (Kpa)	Range (mL/s)	Mean±SD (mL/s)
I-12	20-27	24.5±2.1	0.5-0.62	0.57±0.04	14.5-32.4	26.3±6.6	22.1-15.3	16.8±1.2
II-25	27.3-36	32.0±2.9	0.63-0.82	0.74±0.04	33.4-44.1	39.6±3.3	15.1-10.7	11.5±1.4
III-18	37-50	41.9±3.6	0.83-0.92	0.86±0.02	44.8-75.3	52.4±8.5	9.4-6.9	8.3±0.83

[Table/Fig-5]: Summary of characteristics of the various Bladder Outlet Obstruction (BOO) groups.



[Table/Fig-6]: Linear regression scatter plot that shows the line of best-fit between uroflowmetry and various ultrasound parameters prostate volume, RI of capsular arteries and stiffness calculated by SWE and and correlation coefficient (r) of -0.54, -0.47 and -0.88 were obtained, respectively.



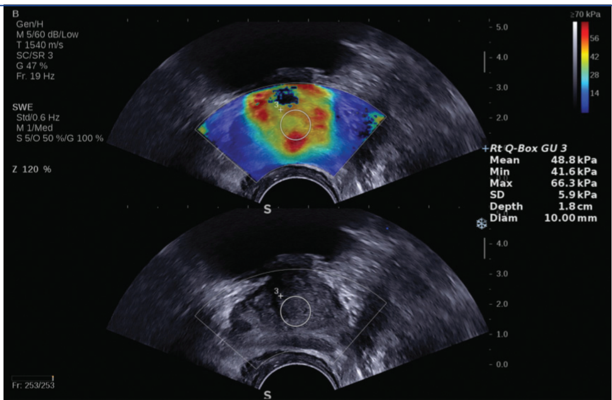
[Table/Fig-7]: Analysis of Receiver Operating Characteristic (ROC) curves plotted for various parameters a) Volume; b) RI; c) Stiffness against uroflowmetry.

TRUS parameter	AUC	95% CI	Sensitivity	Specificity	PPV	NPV	Accuracy	p-value
Volume of prostate gland*	0.779	0.64-0.88	79.07%	66.67%	79	91	84	<0.0001
Resistive index of capsular arteries†	0.810	0.64-0.87	88.03 %	66.67%	83	58	87	0.0003
Stiffness of prostate‡	0.942	0.84-0.98	100%	88.37%	88	100	92	<0.0001

[Table/Fig-8]: Summary of Receiver Operating Characteristic (ROC) curves of features predicting severity of BOO.
*Volume of prostate gland 28 mL was the cut-off value to define BOO; †Resistive Index (RI) of capsular arteries 0.68 was the cut off value to define BOO; ‡Stiffness of prostate 31.6 kPa was the cut off value to define BOO, p-value <0.0001 is considered statistically significant

In the present study, we used the prostate elastic modulus, which was determined with SWE, to accurately assess the severity of BOO in patients with BPH along with previously studied parameters, the total prostate volume and RI of prostate capsular arteries. The most important finding in our study was that the elastic modulus of the prostate was the indicator most strongly correlated with BOO stage and had the highest AUC which suggests that stiffness of the prostate may be used as a non invasive indicator of BOO.

The mechanism underlying the relationship between stiffness and BOO has not yet been clarified. The composition of prostatic tissue changed in patients with BPH suggested that there is increase in proportions of connective tissue and smooth muscle cells in the hyperplastic prostate when compared with the healthy prostate [6]. Because different tissues have different elastic moduli, the change in composition of prostatic components might induce changes in stiffness. During micturition, the distension pressure on the urethra compresses the surrounding prostatic tissue. Also, compared with stiff prostate tissue, soft prostate tissue is more deformed at the same pressure, indicating a higher distension range, resulting in more compliance of the urethra and therefore less obstruction of urine flow. In contrast, a stiff prostate causes the urethra to be non complaint or less compliant, resulting in more severe BOO. The present study results indicated that elastic moduli of the prostate could be a non invasive indicator of BOO. Patients with a small prostate and normal RI of capsular artery with a stiff prostate was diagnosed as having severe BOO [Table/Fig-9].



[Table/Fig-9]: Increased stiffness in a small prostate (Volume 25.7cc) A portion of the central gland displays a mosaic pattern of red and yellow indicating stiffer tissue.

If only volume of the prostate gland is used for the analysis, then normal or mildly enlarged prostate could not be diagnosed as BOO. The RI of prostate capsular arteries might be affected by several factors including age, atherosclerosis, and haemodynamic status, which might affect the results. In the present study based on the stiffness of the prostate the severity of BOO was diagnosed more accurately which was confirmed using the urodynamic pressure flow Schaefer nomogram.

Limitation(s)

Sample size should be increased in the future. Second, the detection zone could not cover the entire prostate in the large prostate, which was restricted by the attenuation of the shear waves and could have affected the results. Third, control group of normal volunteers was not included in the present study.

CONCLUSION(S)

The present study developed a new application for prostate SWE. The stiffness or elastic modulus of the prostate is a reliable indicator in the assessment of the severity of BOO in patients with BPH.

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