Original Article

Accuracy of transrectal strain elastography in detection of prostate cancer

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Abstract

Background: Elastography has emerged as a boon in aiding diagnosis of various neoplastic conditions. Strain elastography helps in differentiating hard lesions from the normal tissue on a real-time basis and targeting biopsies of the same described by other authors in various conditions. We assess a series of cases for the detection of prostate cancer using strain elastography of prostate.

Aims: The aim of this study was to assess the accuracy of transrectal strain elastography in diagnosis of prostate cancer.

Materials and Methods: This is an observational cross-sectional, prospective study. Transrectal strain elastography was performed using a C-10 3 v endocavity probe with elastography software and was compared against biopsy results on 25 adult male patients with raised prostate-specific antigen levels. Statistical significance of qualitative data across two study groups was tested using the Chi-square test or Fisher's exact test. The entire data were analyzed using SPSS version 16.0, Inc., Chicago, software for Microsoft Windows.

Results: Ten (40%) out of 25 patients demonstrated carcinoma prostate, 14 patients had benign prostatic hyperplasia, and 1 had prostatic abscess. Transrectal real-time elastography scores in patients with carcinoma patient were higher than those of benign conditions, i.e., 3 and 4 scores with accuracy of 92%, sensitivity of 85.7%, and specificity of 94.4%.

Conclusions: The overall accuracy of strain elastography was 92%, which enhanced the diagnostic yield in prostate carcinoma. Real-time strain elastography is a highly sensitive and specific technique for diagnosing prostatic carcinoma and guiding the prostate biopsy.

Keywords: Accuracy of elastography, prostate cancer detection, transrectal strain elastography, transrectal ultrasonography prostate

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INTRODUCTION

Prostate-specific antigen (PSA) levels are raised in prostatic cancer, prostatitis, and benign hyperplasia of the prostate. They are found in levels <4 ng/ml normally in the serum.[1] Carcinoma of prostate (PCa) may be suspected from abnormal PSA levels or digital rectal examination (DRE).[1] Further tests are then performed to reach a diagnosis. Transrectal ultrasonography (TRUS) is often initially performed to detect abnormalities of the prostate and surrounding tissues and to guide biopsy procedures.[2] The

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gold standard being ultrasonography (USG)-guided biopsy followed by histology.[3] Elastography has emerged as a forerunner to assess tissue differences in stiffness. Strain elastography estimates the tissue strain and can distinguish a hard focal lesion from a soft lesion providing an effective alternative to what has been historically qualitatively assessed by palpation.[4] Conventional B mode USG of prostate has a limited role in PCa detection. Even color or power Doppler has a low sensitivity and specificity (40%–50%) for its detection.[5-7] Prostate elastography provides high sensitivity and specificity for detecting PCa with high negative predictive values, thereby ensuring that few cancers will be missed.[8] In this study, we have assessed the accuracy of strain elastography of prostate by performing transrectal real-time strain elastography (TRTE) and comparing it with histopathological findings to reach to a better diagnostic yield.

MATERIALS AND METHODS

The study was approved by the Ethical Committee of the university. A written valid informed consent was obtained for every patient before performing the study. This was a prospective and cross-sectional study conducted on male patients of the age group between 50 and 84 years. The study was carried out over 2 years from August 2015 to 2017. The study group included 25 adult male patients referred to the Department of Radiodiagnosis and Imaging, of a tertiary care university hospital. They had raised serum PSA levels and clinically suspected to have PCa. All these patients underwent TRTE followed by prostate biopsy. Diagnoses were confirmed by histopathological examination of the specimen.

Elastography imaging

TRTE was performed using Philips iU22 ultrasound system with elastography software, and C10 3 v endocavity broadband curved array (C10-3 v) probe was used for B-mode biopsy and TRTE examinations.

The subjects were studied using the following protocol:

- Four hours fasting before the study
- The patient was placed in the left lateral position with bent knees and hip flexion
- Adequate amount of 2% lignocaine jelly was introduced in the anal canal and applied to the anal vergeto get good local anesthetic effect before inserting the C10 3 v probe
- The C10 3 v probe was covered with latex covering with adequate coupling agent in between and the probe was inserted in the rectum after initial milking to relax the anal sphincter
- The morphology of prostate gland, symmetry, and the capsule was initially assessed by grayscale ultrasound. Any focal lesion, asymmetry, capsular bulge, and diffuse alteration in gland echotexture were recorded. Color Doppler and power Doppler ultrasound modes were then used to detect any blood flow abnormality in the gland
- Strain elastography was then carried out. Each section was checked from the apex to base on both sides. The images were obtained in the transverse plane at up to 10 frames per second with focus at a depth of 1.5 cm from the surface of the probe. The region of interest of elastography was set at approximately 1 cm to the edge of the largest transverse image
- Manual compression and decompression of the prostatic tissue were carried out using the C10 3 v probe. Under the guidance of quality bar in the process of compression and decompression, the pressure and direction of manual vibration were adjusted until stable, repeatable images were obtained. The images were recorded for further interpretation and comparison
- Examination time for each patient was about 10–15 min.

Image interpretation and score assignment

Normal prostatic and soft tissues appeared red to green [Figure 1] on elastogram. The hard prostatic tissue appeared blue [Figures 2 and 3].

Elastographic score was assigned to each of the patient's elastogram. Elastography score – 1, 2, 3, 4, or 5 was assigned in accordance with values provided by Xu *et al.*:[8]

- A. Score 1: There was no blue area or star-like blue in outer glands

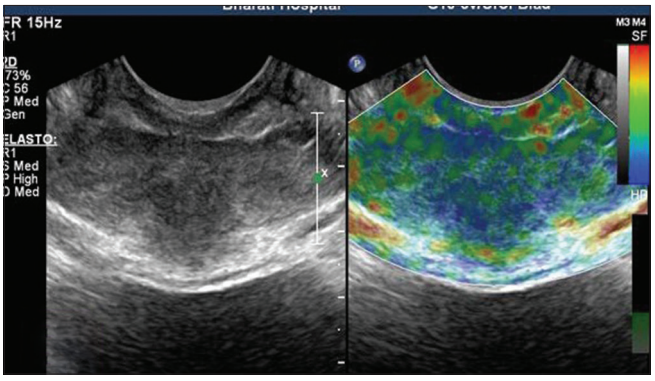


Figure 1: Transverse B-mode and elastography images in a 29-year-old control male with normal serum prostate-specific antigen level. B-mode ultrasound (right) shows normal prostate gland. Corresponding elastogram (left) shows no focal hardening of the peripheral zones of the prostate. Transrectal real-time strain elastography score 1 - there was no blue area or star-like blue in outer glands

- B. Score 2: The mosaic or a little symmetrical blue area in bilateral outer glands were seen, and the blue area is <5 mm in diameter
- C. Score 3: A little symmetrical blue area in bilateral outer glands, the diameter of blue area ≥5 mm
- D. Score 4: Asymmetric blue area in bilateral outer glands, the diameter of blue area ≥5 mm
- E. Score 5: Asymmetric blue area in bilateral outer glands, the blue area of more than 50%, and the blue area ≥50% of single outer gland area.

Prostatic biopsy

All patients underwent TRUS-guided 12 core prostate biopsy using 18G true cut biopsy gun under all aseptic precautions. All focal hard lesions suspected on elastogram were also targeted.

Statistical analysis

Data on qualitative characteristics are presented as *n* (% of cases). The statistical significance of difference of qualitative characteristics across two study groups was tested using the Chi-square test or Fisher's exact test. The diagnostic efficacy indices, such as sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy, were calculated for the test method against the gold standard of histopathology. Accuracy measure along with 95% confidence interval (CI) is also presented for each agreement analysis. To determine the extent and significance of agreement between the test methods and the gold standard, Cohen's Kappa Statistic was used.

$P < 0.05$ is considered to be statistically significant. All the hypotheses were formulated using two-tailed alternatives against each null hypothesis (hypothesis of no difference). The entire data were statistically analyzed using Statistical Package for Social Sciences (SPSS version 16.0, Inc., Chicago, IL, USA) for Microsoft Windows.

RESULTS

The most common age group involved, in this study, was between 61 and 70 years followed by the age group of 71–80 years [Table 1]. The mean ± standard deviation, median (minimum–maximum) age of the entire study group is 66.1 ± 7.55 and 65.0 (50.0–84.0) years, respectively.

Table 1: Age distribution in patients with raised prostate-specific antigen values (*n*=25)

Age group (years)	Number of patients (%)
41-50	1 (4.0)
51-60	4 (16.0)
61-70	13 (52.0)
71-80	6 (24.0)
81-90	1 (4.0)
Total	25 (100.0)

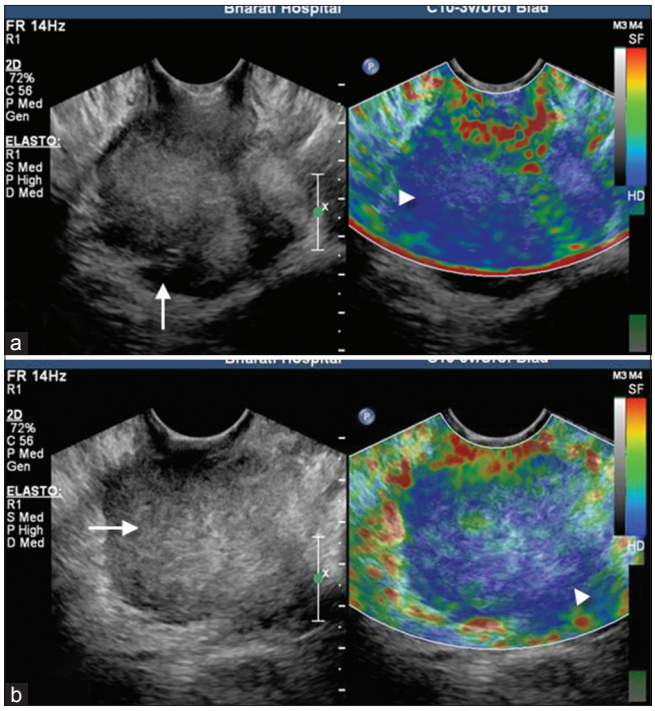


Figure 2: (a and b) Transverse B-mode and elastography images in a 75-year-old male. Digital rectal examination revealed Grade III hard prostate. Serum prostate-specific antigen was 148 ng/ml. B–mode image (right) shows prostatomegaly, heterogeneous echogenicity, and loss of normal zonal anatomy of prostate (arrow in a and b). Transrectal real-time strain elastography image (left) shows asymmetric blue area in bilateral outer glands, the diameter of blue area ≥5 mm (arrowhead in a and b). Biopsy revealed adenocarcinoma with Gleason Score (4 + 3) = 7

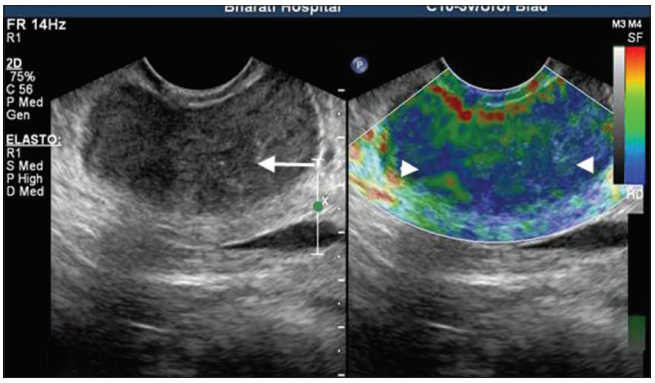


Figure 3: Transverse B-mode and elastography images in a 69-year-old male. Urgency and frequency of micturition with raised serum prostate-specific antigen prostate-specific antigen of 16 ng/ml. B-mode image (right) shows mild heterogeneous echotexture of the prostate (arrow). No focal hardening of the peripheral zones of the prostate on elastography (left). The mosaic or a little symmetrical blue area in bilateral outer glands, the blue area is <5 mm in diameter (arrowhead). Biopsy revealed benign hyperplasia of prostate with acute prostatitis

The most common serum PSA range, in our study, was between 11 and 50 ng/mL followed by values more than 100 ng/ml [Table 2].

In total, 10 of 25 patients (40%) were diagnosed with prostate cancer [Graph 1]. The Gleason score ranged from 4 to 7.

The TRTE scores of PCa and benign conditions were 3.20 ± 1.11 (range: 1–5) and 2.24 ± 1.01 (range: 1–4), respectively [Table 3]. The mean TRTE score of PCa was significantly higher than that of benign conditions ($P < 0.001$).

For screening of PCa, the sensitivity, specificity, PPV, and NPV of elastography compared to histopathology examination were 85.7%, 94.4%, 85.7%, and 94.4%, respectively. The overall accuracy (with 95% CI) of elastography against histopathology examination was 92.0% (81.4%–99.9%) [Graph 2 and Table 4].

Table 2: Distribution of serum prostate-specific antigen values in patients with suspected prostate cancer (*n*=25)

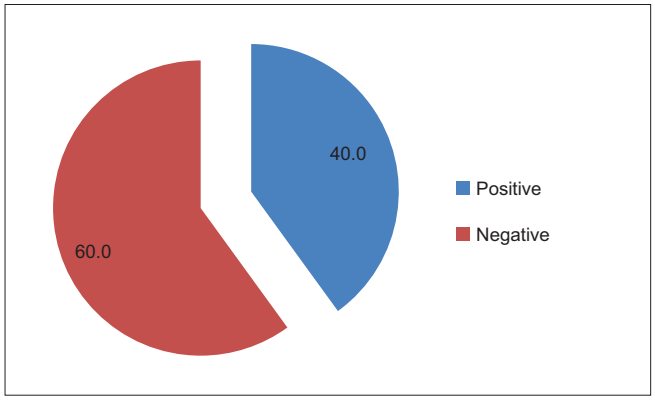
Serum PSA (ng/mL)	Number of patients (%)
4-10	2 (8.0)
11-50	19 (76.0)
51-100	1 (4.0)
>100	3 (12.0)
Total	25 (100.0)

PSA - Prostate-specific antigen

Table 3: Cross tabulation of elastography transrectal real-time strain elastography findings with biopsy (Gleason's score)

Gleason score (biopsy) versus TRTE cross-tabulation					
	Elastography score				Total
Biopsy score Gleason	1	2	3	4	
4	1	0	0	0	1
5	0	2	0	0	2
6	0	0	0	0	0
7	0	0	4	3	7
>7	0	0	0	0	0
Total	1	2	4	3	10

TRTE – Transrectal real-time strain elastography

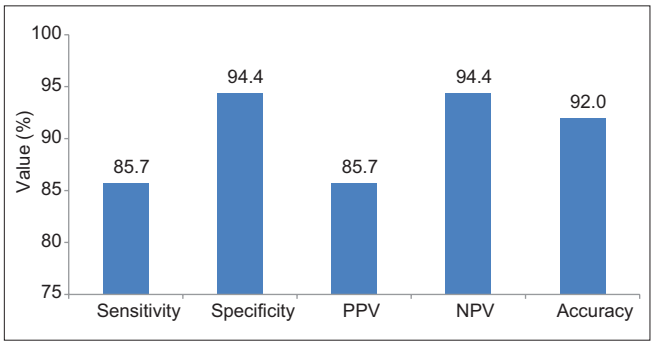


Graph 1: Distribution of patients (%) positive for carcinoma of prostate (biopsy proven)

DISCUSSION

Prostate cancer is one of the most common cancers in men in Western countries and stands the second position in male malignant tumors worldwide.[9] The incidence and prevalence of PCa have increased significantly since the last decade.[10,11] The diagnostic evaluation of PCa comprises of serum PSA level, DRE, and diagnostic imaging methods such as ultrasound and magnetic resonance imaging. Approximately 85% of PCa is multifocal and progresses along the prostate capsule, and it may not appear as a well-defined nodule such as other malignant tumors.[12] The ideal imaging technology should be both affordable and minimally invasive. Prostate biopsy is invasive, costly, and involves risk of complications. Therefore, the focus is required to improve prostate imaging that can be noninvasive and cost-effective. It can be achieved using real-time strain elastography. Elastography being noninvasive, easily available, cost-effective, and less time-consuming can be used as a screening tool in evaluation of PCa.[13-15]

In the nineties, Ophir *et al.* used elastography for biological tissues since then it has undergone many modifications,[16] and now TRTE is chiefly used to differentiate malignant hard lesions from soft lesions[15] and guiding transrectal prostate biopsies[8,17-19] as a new technique for better diagnostic yield in PCa. Patients with raised serum PSA levels, abnormal DRE with focal abnormal nodules on conventional ultrasound can be diagnosed by TRUS-guided biopsy targeting the nodule. However, for the patients with only elevated PSA levels without focal abnormalities, it remains unclear whether all quadrant biopsies are necessary. In such a group of patients by identifying hard tissue on elastogram, TRTE can increase the accuracy of biopsy, reduce the



Graph 2: The distribution of indices of diagnostic efficacy of elastography against histopathology examination as a Gold Standard (*n* = 25)

Table 4: The sensitivity and specificity analysis for the diagnosis of prostatic carcinoma based on elastography against the histopathology (Gleason score - gold standard) (*n*=25)

Elastography	Histopathology		Total, *n* (%)	Diagnostic efficacy indices (%)				
	Positive, *n* (%)	Negative, *n* (%)		Sensitivity	Specificity	PPV	NPV	Accuracy (95% CI)
Positive	6 (85.7)	1 (5.6)	7 (28.0)	85.7	94.4	85.7	94.4	92.0 (81.4-99.9)
Negative	1 (14.3)	17 (94.4)	18 (72.0)					
Total	7 (100)	18 (100)	25 (100)					

Values are *n* (% of cases). Cohen's Kappa value=0.802, *P*=0.001*** (statistically highly significant). PPV – Positive predictive value; NPV – Negative predictive value; CI – Confidence interval

number of biopsy cores, and eventually reducing the complication rate and pain to the patient. Cell density is greater in neoplastic tissue as compared to normal tissue which causes a change in tissue elasticity.[20] TRTE allows an assessment of tissue elasticity with color coding, in which, the scale ranged from red (soft) to blue (hard). Kamoi *et al.*,[21] initially, reported that the grading system of TRTE was valuable in the diagnosis of PCa, and this was successfully applied to breast lesions and thyroid nodules.[21,22] In the clinical application of TRTE-guided biopsy, hard areas with a diameter ≥5 mm in elasticity imaging were considered as malignant.[23,24] Many prostate cancers detected at biopsy were not visible at TRUS as many cases had isoechoic lesions.[21] Therefore, the TRTE score based on the symmetry, and elastic distribution of prostate helped in both diagnosis and focused biopsy guidance.

In this study, the mean TRTE score of PCa was significantly higher than that of benign conditions. The sensitivity, specificity, and overall accuracy of TRTE (with 95% CI) in diagnosis of PCa were 85.7%, 94.4%, and 92%, respectively. On the other hand, in the study of Kamoi *et al.*,[21] the sensitivity, specificity, and accuracy of the grading system of TRTE focused on prostate lesions were 68%, 81%, and 76%, respectively. The difference between the studies could be attributable to the large sample of the latter, namely *n* = 107 cases as compared to *n* = 25 in this study. Therefore, it may be valuable to introduce TRTE into routine clinical practice for the detection of the lesion and as a guide to biopsy. In the present study, TRTE detection rate of prostate cancer with a higher Gleason score was higher than that of lower Gleason score which compared favorably to studies of Kamoi *et al.*,[21] Aigner *et al.*,[18] and Spârchez.[11]

CONCLUSIONS

Our study has provided a higher level of confidence to use real-time strain elastography as an imaging tool to evaluate patients with raised serum PSA levels to enhance the diagnostic yield for the detection of prostate cancer. It can also be a good adjuvant to guide TRUS biopsy to avoid error.

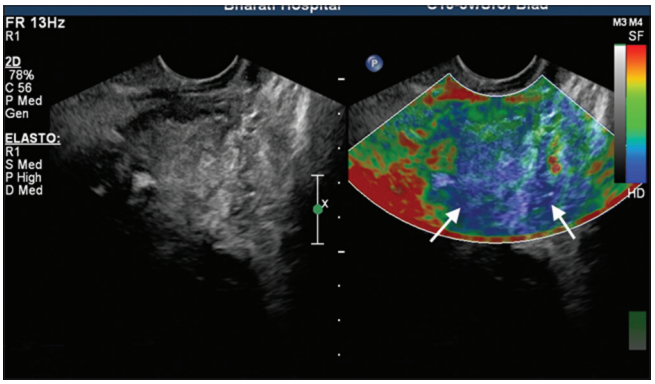


Figure 4: Transrectal real-time strain elastography can produce hard artifacts (arrow) with increasing depth of penetration

Limitations and pitfalls

The major limitation of TRTE is that the procedure of manually compressing the prostate gland is operator-dependent as brought out by the study of Miyagawa *et al.*[25]

Pelzer *et al.*[26] and Pallwein *et al.*[24] reported that TRTE could produce hard artifacts [Figure 4] with increasing depth of penetration.

The third limitation was that biopsy specimen cannot diagnose all the PCa due to the sampling error.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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