

Real Time Trans-Rectal Elastography of Prostate Correlation with Histopathology in a Suspected Case of Prostate Cancer

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ABSTRACT

Background

Early detection of prostate cancer, the second most common cancer in men worldwide, is the key for its successful treatment. Commonly used clinical criteria and imaging tools for detection of prostate cancer are less sensitive.

Objective

This study was aimed to find role of real time transrectal elastography of prostate for detection of prostate cancer.

Method

Study was conducted in 66 patients with clinical suspicion of prostate cancer, who were sent for ultrasound guided prostate biopsy. Transrectal ultrasound with real time elastography was performed in all the patients prior to the biopsy and looked for hard areas within the prostate. Then six-core tru-cut biopsy were taken in six zones of prostate, including the hard areas detected in the elastography. The histopathology report were correlated with the elastography findings.

Result

Median prostate specific antigen of the patients was 11.5 ng/ml with interquartile range of 8 to 23.5 ng/ml. Digital rectal examination showed hard nodular findings in 35 patients. Transrectal ultrasound showed 81 hypoechoic lesions in 31 patients. Elastography showed 127 hard areas in 31 patients. Histopathology showed 90 positive biopsy cores in 23 patients. Cancer detection rate of elastography was 82.6%. At 95% confidence interval, patients with elastography detected hard lesions had 19.4 times more likelihood to have prostate cancer. Sensitivity of elastography was high as compared to digital rectal examination and transrectal ultrasound alone.

Conclusion

Transrectal elastography had high sensitivity over clinical tools and transrectal ultrasonography for detection of prostate cancer.

KEY WORDS

Biopsy, Prostate cancer, Transrectal elastography

INTRODUCTION

Prostate cancer is the second most common cancer in men and fifth common cause of cancer deaths worldwide. It has indolent course and often asymptomatic at early stage, thus diagnosed at late age with 66 years as an average age at the time of diagnosis.¹ Early detection is key to successful treatment of prostate cancer and suspicion of prostate cancer is currently based on prostate specific antigen (PSA), Digital rectal examination (DRE) and transrectal ultrasound (TRUS). Detection rate of prostate cancer with PSA, DRE and TRUS are 30-35%, 20% and around 50% respectively.^{2,3} Magnetic resonance imaging (MRI) has been a promising method for detection of prostate cancer, however it is expensive and is not always available. Modification of TRUS with application of newer advances can be cheaper and made easily available.² Real time transrectal elastography (TRE) of prostate measures elastic properties and thus can be helpful in detecting malignant tissue in prostate as the malignant tissue owing to their more cell density are less elastic than normal prostate or benign lesions.⁴ Till date, no data of TRE study of prostate in Nepal is available. This study was aimed to find the role of TRE of prostate in suspected prostate cancers by correlating it with histopathology.

METHODS

This hospital based prospective study was done in 66 patients with clinical suspicion of prostate cancer sent to Radiology Department of Tribhuvan University Teaching Hospital for prostate biopsy during a period of October 2015 to September 2016. Purposive sampling technique was used to obtain sample size. Ethical clearance from Institute of Medicine and informed consent from the patients were obtained.

Sixty six patients with age > 40 years, serum PSA > 4 ng/ml, and abnormal DRE findings were included in the study. Prior to biopsy all the patients underwent TRUS using endocavity probe (C10-3v) of Philips iU22 machine. Suspicious hypoechoic lesions seen in periphery of prostate were recorded. Then real time elastography (TRE) was done in all the patients showing hypoechoic lesions in TRUS by inducing slight compression and decompression of the prostate with application of force by the transrectal probe. Prostate gland was scanned from base to apex in all six zones (base, mid gland and apex on either side) during the TRE and images of all the zones during compression were acquired. Color code in the ultrasound unit were red and green indicating soft areas and blue indicating hard area. Those areas showing blue color coding were recorded and correlated with suspicious hypoechoic lesions seen in TRUS.

Following TRUS and TRE, all the patients underwent TRUS guided six core biopsy (as it was our initial experience of TRUS biopsy) of prostate. Each core of biopsy was taken from bilateral apex, mid and base of prostate. Hypoechoic

lesions seen on TRUS and portion of the prostate showing blue color coding were included in the six core biopsy.

Histopathology report of all the patients were collected and correlation between serum PSA, DRE, TRUS, TRE and histopathology were done by Chi-square test, Odds ratio and ANOVA.

RESULTS

Sixty six patients with mean age of 68.9 ± 8.7 years and range of 66 to 88 years were included in the study. Range of serum PSA of the patients was 4 to 304 ng/ml with median serum PSA and interquartile range of 11.5 ng/ml and 8 to 23.5 ng/ml respectively. Thirty five patients had hard and nodular prostate on DRE. TRUS showed 81 suspicious hypoechoic lesions in 31 patients. TRE showed 127 blue color coded hard areas in prostate of 31 patients.

Histopathology showed 90 positive biopsy cores in 23 patients. Among these 23 patients, 55 suspicious hypoechoic lesions were seen in 19 patients in TRUS. However, only 42 hypoechoic sites in 14 patients showed true positivity (cancerous focus detection rate - 46.7%) when matching TRUS detected hypoechoic lesions with the biopsy sites. Thus, cancer detection rate of TRUS was 60.9%. Among the biopsy sites, maximum correlation was found in bases (66.7% in right base) and lowest correlation in apex (8.3% in left apex).

Table 1. Distribution of overall TRE and biopsy results. (n=66)

| TRE results | Biopsy results | | Total | Odds ratio (95% CI) |
|-------------|----------------|----------|-------|---------------------|
| | Negative | Positive | | |
| Negative | 32 | 3 | 35 | |
| Positive | 11 | 20 | 31 | 19.39 (4.81, 78.14) |
| Total | 43 | 23 | 66 | |

Twenty patients among 23 biopsy proven prostate cancer patients showed 95 hard areas on TRE. Overall sensitivity and specificity of TRE for detection of prostate cancer was 86.9% and 74.4%. However, among these 20 patients, 70 sites of 19 patients were matched with the biopsy positive sites. Thus, true positivity of TRE was 77.8% (cancerous focus detection rate) and cancer detection rate was 82.6%. Odds ratio between TRE and biopsy showed that at 95% confidence interval, patients with TRE detected hard lesions had 19.4 times more likelihood to have prostate cancer (Table 1). Among the biopsy sites, maximum correlation was found in left mid zone (93.3%) and lowest correlation was found in right mid zone (78.6%) (Table 2).

Among 35 patients with abnormal DRE findings, five had TRE hard findings in all sites and positive biopsy in all cores. All of these patients had PSA ≥ 100 ng/ml. Eighteen patients had TRE hard findings in at least one site and 12 patients had positive biopsy in at least one core. Sensitivity and specificity of DRE in prostate cancer detection was

Table 2. Correlation of Positive TRE with biopsy in accordance with sites (n=66)

| TRE positive (%) | Biopsy Positive (%) | | | | | |
|------------------|---------------------|----------------|------------|-----------|---------------|-----------|
| | Right base | Right mid zone | Right apex | Left base | Left mid zone | Left apex |
| Right base | 92.3 | 92.9 | 92.3 | 88.9 | 86.7 | 90.9 |
| Right mid zone | 84.6 | 78.6 | 76.9 | 83.3 | 86.7 | 81.8 |
| Right apex | 84.6 | 78.6 | 84.6 | 77.8 | 86.7 | 90.9 |
| Left base | 84.6 | 85.7 | 92.3 | 88.9 | 86.7 | 100 |
| Left mid zone | 92.3 | 100 | 100 | 94.4 | 93.3 | 100 |
| Left apex | 61.5 | 64.3 | 76.9 | 66.7 | 73.3 | 90.9 |

34.3% and 67.7% respectively. There was no significant correlation of DRE findings with TRE and biopsy findings ($p > 0.05$).

At 95% CI, if a patient had serum PSA level > 30.61 ng/ml there is significant chance that TRE findings will be positive and if the serum PSA level is < 7.73 ng/ml then there is significant chance that TRE findings will be negative. In case of positive biopsy findings, serum PSA levels were higher as compared to TRE. At 95% CI, if a patient had serum PSA level > 40.85 ng/ml there is significant chance that biopsy will be positive and if the serum PSA level is < 8.72 ng/ml then there is significant chance that biopsy will be negative.

Among 23 patients with biopsy proven prostatic malignancy TRUS was positive in 19 patients (82.6%) and TRE showed positivity in 20 patients (86.9%). Overall sensitivity, cancer detection rate and cancerous focus detection rate of TRE were higher as compared to TRUS (Table 3).

Table 3. Comparison of TRUS and TRE in cancer detection (n=66)

| Imaging modality | Overall positive cases | False positive cases | True positive cases | Cancer detection rate (%) | Total positive sites (out of 90) | Cancer site detection rate (%) |
|------------------|------------------------|----------------------|---------------------|---------------------------|----------------------------------|--------------------------------|
| TRUS | 19 | 5 | 14 | 60.8 | 42 | 46.6 |
| TRE | 20 | 1 | 19 | 82.6 | 70 | 77.8 |

DISCUSSION

Systematic six-core prostate biopsy was widely used for diagnosis of prostate cancer long ago. Multiple core (10-12 core) prostate biopsy has been proven safe and effective procedure with significantly increased diagnostic rate compared to six-core biopsy.⁵ However, Tobium et al. and Hu et al. found no significant difference between 12-core and 6-core biopsy in patients with PSA 10-20 ng/ml and ≥ 20 ng/ml and respectively.^{5,6} Hu et al. even recommended

six-core biopsy in patients with PSA ≥ 20 ng/ml due to no significant difference in diagnostic yield of six-core and 12-core prostate biopsy.⁵ Our study was done with initial experience of TRUS guided prostate biopsy in our institution, thus six-core biopsy was chosen.

Prostate cancer detection rate of TRE was 82.6% in our study. Zhang et al. and Aboumarzouk et al. compared TRE findings with histopathology of radical prostatectomy and radical prostatectomy/TRUS biopsies respectively.^{7,8} They found high accuracy of TRE with sensitivity of 72% and 71-82%, but slightly lower as compared to our study. Sensitivity of TRE in prostate cancer detection was also lower in study done by Tomoaki Miyagawa et al. (72.6%) and Kamoi et al. (68%).^{9,10} Sensitivity of TRE in the study done by Pallwein et al. (84%) was similar to our study.¹¹ However sensitivity of TRE in our study was lower as compared to the study of Yan et al. (91.7%) and Naoto et al. (93%).^{12,13}

Sensitivity of DRE (34.3%) in our study was much lower as compared to TRE (82.6%). Concordant findings were seen in study done by Yang et al. and Naoto et al.^{12,13}

TRE had higher cancer detection rate (82.6%) as compared to TRUS (60.8%) for the detection of prostate cancer. Similar results of higher cancer detection rate of TRE was observed in the studies done by Tomoaki Miyagawa et al., Naoto et al., Pallwein et al., Kamoi et al., Yan et al. and Aboumarzouk et al.⁸⁻¹³

Detection rate of cancerous foci for TRE in this study was 77.8% which was slightly low as compared to study done by Pallwein et al. (80%) and slightly high as compared to study done by Sumura et al. (74.1%) and Salomon et al. (75.4%).^{11,14,15}

Cancer detection rate of TRE may also depend on Gleason scores as higher scores represent increased cell density and stiffness, thus the higher sensitivity of TRE.¹⁶ Addition of TRE targeted biopsy to standard biopsy can increase prostate cancer detection rate. Schiffman et al. also found high specificity (90.9%) of elastography targeted prostate biopsy.¹⁷ Wang et al. found 13.9% increase in cancer detection with TRE guided biopsy as compared to TRUS guided systemic biopsy.² Metanalysis conducted by Tu et al. showed no significant difference in terms of prostate cancer detection with TRE targeted biopsy and systematic biopsy.¹⁸ However, they found relative sensitivity of TRE targeted biopsy was high as compared to systematic biopsy in core-by-core analysis. This may reduce number of sampled cores in prostate biopsy, which will reduce morbidity and patient discomfort as well as decrease cost for sample analysis.

Limitations of this study include smaller sample size and initial preliminary experience with TRE in our institution. Another limitation includes inhomogeneous sample as most of the patients were in advanced stage of cancer in our study. MRI has become more popular for evaluation of prostate cancer these days, and we didn't correlate TRE findings with MRI in our study.

CONCLUSION

We found high sensitivity of transrectal real time elastography over digital rectal examination and transrectal ultrasound for detection of prostate cancer. Larger sample

size, biopsy core samples and correlation with MRI would have provided more accurate results. Still, this more accurate, non-invasive and low cost clinical tool has a great potential in diagnosing prostate cancer.

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