

Original article

Power Doppler imaging guided biopsy in the detection of prostate cancer – An Indian perspective

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Abstract:

Introduction: Prostate cancer is the commonest malignancy of the genitor urinary tract. Confirmation of prostate cancer is done by Trans rectal ultrasound guided biopsy. Due to the high incidence of false positives and false negatives in the standard TRUS imaging, we evaluated the utility of power doppler imaging guided biopsy in the detection of prostate cancer among the Indian patients.

Materials and methods: Between 2006 and 2009, a prospective trial was conducted in a tertiary care center, by including all the patients with prostate specific antigen(PSA) more than 4 mg% and / or positive rectal examination. All patients underwent TRUS with standard 7.5MHz probe with power doppler imaging. Targeted biopsies were taken from both the hypoechoic areas and hypervascular areas along with standard 12 core biopsies. The results were analysed.

Results: 38% among 175 patients were positive for carcinoma prostate. DRE had a low sensitivity and specificity. Targeted biopsy against the hyper vascular area had a sensitivity, specificity, positive predictive value and negative predictive value of 88.%, 87.4%, 81.5%, 92.0% respectively. This was significantly higher than that of hypoechoic are directed biopsy. Targeted biopsy on the hypoechoic area showing hypervascularity had positive predictive value of 94.4% and specificity of 98%. 3 patients with prostates more than 50ml volume had positive targeted biopsy (hyper vascular area), but negative 12 core biopsy.

Conclusion: Power doppler imaging guided biopsy is feasible and effective in Indian population, and targeted biopsy with standard core biopsies increase the yield of prostate biopsy.

Introduction

Prostate cancer is the most common noncutaneous cancer among males and accounts for 10% of cancer related deaths¹. With the development of prostate-specific antigen (PSA) screening and TRUS, prostate cancer is being diagnosed earlier in the disease course. In the present era, most patients are incidentally detected by abnormalities in Prostate Specific Antigen (PSA) level or positive digital rectal examination (DRE) findings while evaluating for BPH, rather than metastatic symptoms². The

combination of DRE and serum PSA is the most useful first-line test for assessing the presence of prostate cancer in an individual.² The presence of prostate disease (prostate cancer, BPH, and prostatitis) is the most important factor affecting serum levels of PSA.^{3,4,5} PSA elevations may indicate the presence of prostate disease, but are not specific for cancer. A number of studies have confirmed the inability of TRUS to localise early prostate cancer.^{6,7,8} Any patient with a DRE suspicious for cancer or a PSA elevation should

undergo prostate biopsy regardless of TRUS findings if an early diagnosis of cancer would result in a recommendation for treatment. To improve the detection rate with TRUS biopsy various additional modalities have been tried. This includes power Doppler ultrasonography to evaluate the neovascularity in patients with prostate cancer, elastography and contrast ultrasonography.. Various studies have shown increased cancer detection rates using Doppler-targeted biopsy strategies.^{9,10,11} Though Magnetic Resonance Imaging (MRI) guided and MRI – TRUS fusion biopsies are being performed in a handful of Indian centres nowadays, TRUS guided prostate biopsy is the most commonly available investigation for detecting prostate cancer. Hence, To improve the TRUS guided biopsy outcomes, we conducted a study to evaluate the utility of power Doppler ultrasonography guided biopsy in the detection of prostate cancer.

Aims and Objectives:

To evaluate the utility of Trans Rectal Ultrasound with power Doppler imaging guided biopsy in comparison with grey scale imaging in the detection of prostate cancer.

Materials and methods

A prospective study was conducted in the time period between July 2006 and May 2009 in a tertiary care hospital to evaluate the efficacy of power doppler imaging guided biopsy in the detection of prostate cancer. All the patients aged more than 50 years who presented to the outpatient department were screened for inclusion in the study. Patients who had lower urinary tract symptoms with abnormal digital rectal examination and/or PSA \geq 4 ng/ml were evaluated for inclusion in the study. Subjects who did not consent for the procedure and those who had persistent urinary tract infection or untreated

coagulopathy were excluded from the study. After obtaining informed consent all the patients were enrolled into the study. Routine clinical evaluation was done. Basic biochemical and clinical pathology work up was done. All the patients underwent trans rectal ultrasound. On the day prior to the procedure, ciprofloxacin 500mg twice daily and metronidazole 400 mg thrice daily were prescribed, which was continued for 2 days post procedure. Proctoclysis enema was given on the day of the procedure. Intravenous pethidine was given as analgesic if the patient did not tolerate pain.

Patients were examined using the standard ultrasonogram machine. Power Doppler ultrasound was carried out with a Power Flow Unit and 7.5 MHz broadband endoluminal probe. The patients were examined in the left lateral decubitus position. All patients underwent greyscale TRUS of the entire prostate gland in the sagittal plane, from the right to left lateral aspects of the gland, and in the axial plane from the seminal vesicles to the apex. The size and weight of the gland were calculated from the anteroposterior, transverse and cephalo caudal measurements. $(0.52 \times D1 \times D2 \times D3)$. Power Doppler Imaging(PDI) was performed using the same ultrasound system as for conventional TRUS. The power Doppler gain was set to a point below the range at which blood flow in the neurovascular bundles was identified with no background artefact. Scanning to detect flow was continued for 10 min in each patient. The vascularization of a hypoechoic lesion in the PZ was evaluated by comparison with that of the area surrounding it. Equivocal and isoechoic lesions were also assessed for hypervascularity. All patients underwent systematic core biopsies initially at the hypervascular areas and hypoechoic areas if seen and then standard 12 core

biopsy was taken from the prostate. 18 G automatic core biopsy needles were used. Biopsy samples from each site were placed in separate containers of formalin and labelled as to the site of origin. The biopsy results were analysed statistically to evaluate the differential efficacy of the hypoechoic nodule and hypervascular areas.

Results

A total of 194 patients were included in the study period. 75 patients (38%) had cancer detected in the biopsy. The mean age group of the patients was 65.63 years in the age range between 55 and 80 years. The most common age group involved was between 56 and 70 years involving 80% of the patients. 73 of the 194 (37%) patients had a normal DRE. The PSA value of the patients ranged from 2 ng / ml to 632 ng / ml with a mean value of 31.23 ng / ml. The mean prostate volume was 32.7g in the range between 12 and 155g.

The proportions of patients who are negative for cancer were more in the age group 56-60 years. The highest incidence of cancer was in the age group 66-

70 years. 89 % of patients with PSA between 4 and 10 ng/ml were negative for malignancy. Even with a PSA of > 20 ng/ml, 30% had negative result for malignancy. Most of the patients with cancer were in the PSA range of 21-50ng/ml.

Table - 1 summarises the comparison of the various diagnostic modalities in comparison with standard 12 core biopsy as gold standard.

Table 2 summarises the statistical parameters evaluated for the study. Overall the sensitivity was highest for the hypervascular area directed biopsy and it also had the highest negative predictive value. Hypoechoic area directed biopsy alone had a poor positive predictive value and negative predictive value. Presence of hypervascularity in a hypoechoic area is highly specific for the presence of tumour.

A total of 8 patients had complications. They were grade I / II according to the Clavien Classification of Surgical Complications. Febrile UTI was the most common complication involving 5 patients. 2 patient had post procedure retention and one patient developed hematuria

Table-1: Comparison of the various diagnostic modalities in the detection of prostate cancer.

	Prostate Ca +	No Ca
DRE + ve	56	65
DRE - ve	19	54
Hypoechoic Area present	47	51
Hypoechoic area absent / Negative biopsy	28	68
Hyper vascular Area present	66	15
Hyper vascular area absent / negative biopsy	9	104
Hypervascularity in Hypoechoic area	34	2
No hypervascularity in hyperechoic area	41	117

Table- 2: Statistical comparison of hypervascular area with hypoechoic area directed biopsy

	Hypervascular area	Hypoechoic area	Hypervascularity in hypoechoic area
Sensitivity	88.%	62.6%*	45.3%*
Specificity	87.4%	57.1% *	98.3%*
PPV	81.5%	47.9% *	94.4%¶
NPV	92.0%	70.8 %.*	74.1%¶

¶-p-Not significant, *-p<0.01, β-p<0.05 (compared with PDI)

Table-3: Previous studies on the effectiveness of hypervascular area targeted biopsy in the detection of prostate cancer.

Ca %	No.(Pts)	Sen	Spe	PPV	NPV	Study
36	136	82.8%,	78.8%,	87.9%	89.7%,	Remzi et al ²⁵
40	108	90%,	90%	84%,	94%	Satoru et al ²⁶
55	323	92.4%	72%	83%	80.6%	Sauvain et al ²⁷
36	36	90%,	75%	82%	88%	Sakarya et al ²⁸
42	28	74%,	96%	74%	78%	Franco et al ²⁹
40	108	90%	90%	84%	94%	Takahashi et al ¹⁶
38	218	88%	87.4%	81.5%	92%	Anandan et al*

* - present study

Discussion

Nowadays, most of the prostate cancers are diagnosed incidentally in the developed countries. But even now, in a developing country like India, patients present with lower urinary tract symptoms or other metastatic symptoms¹².As the diagnostic modalities such as serum PSA and DRE have significant false positive and false negative rates¹³, histological diagnosis by TRUS guided biopsy is considered the gold standard to diagnose prostate cancer. Though it is considered the primary investigation, it has only 85% sensitivity and 75% specificity, even with extended core biopsy.^{14,15} To increase the yield various associated modalities are used, such as the power Doppler imaging¹⁶. The mean age of the patients was 65.6 years ranging from 55 to 80 years, majority were in the age group between 56 and 70 years, around 80%. On stratifying the patients according to the age group, patients in

the age group between 56 and 70 years had proportionately higher incidence of negative biopsies and the age group of 66 to 70 years had higher incidence of positive biopsies. This shows the increasing incidence of prostate cancer with age.

10% of the patients had prostate size of more than 50ml. The mean prostate size was 32.7 grams. Prostate size did not correlate with the presence of ca prostate. (correlation coefficient - 0.06). The mean serum PSA in positive patients was 31.23 ng/ml and mean PSA among negative patients was 18.2 ng/ml. Although PSA more than 4 ng/ml is considered to be the cut off for ca prostate, many patients (28%) with PSA more than 20 had prostatitis in the biopsy without malignancy. The higher incidence of infections and prostatitis in Indian patients may be the reason for elevation in serum PSA.Targeted biopsy against the hypoechoic area was the modality of diagnosis practiced in the late

1980s^{17,18}. The hypoechoic nodule directed biopsies were found to have a sensitivity of around 70% and specificity on the range of 60%. In our study, the sensitivity was 62.7%, Specificity was 57.14%, Positive Predictive value 47.96% and Negative predictive value was 70.83%. This confirms the poor efficacy of hypoechoic nodule directed biopsy in the detection of prostate cancer.

Tumours are found to be hypervascular due to the neovascularity¹⁹. Power Doppler imaging, which deciphers the tissue vascularity, may be used in the evaluation of vascularity of lesions. Biopsies directed towards the hypervascular areas were found to have a higher sensitivity of around 90% and specificity of 85% in various studies^{16, 20-24}. In our study, the sensitivity was 88.5% for detection of cancer in comparison with 12 core biopsy. This shows that hypervascular area directed biopsy definitely scores over hypoechoic area targeted biopsy in the detection of prostate cancer. The majority of false positives had prostatitis as pathological diagnosis. 55% of false negatives had Gleason's score of 6. Prostatitis and low grade tumours constitute false positives and false negatives respectively.

Overall 38% patients were detected to have cancer. The specificity of power Doppler in the detection of prostate cancer in our study was 87.39%. Positive predictive value (81.48%) and negative predictive value(92.04%) were significantly better than the hypoechoic area targeted biopsy. The comparison of the other studies with power Doppler image guided prostate biopsy is given in Table 3. In our study, in 3 patients with carcinoma, the tumour was picked up by hypervascular area directed biopsy, but it was not diagnosed by 12 core biopsy. In all these patients the prostate volume was more than

50ml. Though the values are not statistically significant, we can advise hypervascular area directed biopsy combined with standard 12 core biopsy in patients with large prostates. Similar findings were reported in a study by Saturo et al, where 3 patients with a negative sextant biopsy had a positive targeted biopsy.²⁶

The presence of hypervascularity in hypoechoic nodules is associated with a positive predictive value of 98% and specificity of 98.3%. So, if TRUS demonstrates such findings, along with standard core biopsies, additional targeted biopsies may increase the yield. On evaluating the statistical parameters using the test of proportions, hypervascular area directed scores over the hypoechoic area targeted biopsy in all statistical parameters.

The complication rate in our study was 5%. They were grade I / II according to the Clavien Classification of Surgical Complications. The most common complication was UTI, which was managed conservatively with antibiotics. These infections do occur even after antibiotic prophylaxis, so patients need to be counselled prior to procedure regarding possible complications. 1 patient had minimal hematuria which was managed conservatively.

Though MR imaging is used more frequently now, to assess the prostate and guide biopsies²⁹, it may not be cost effective in a developing country. Power Doppler imaging guided biopsy is useful in increasing the yield of biopsies. If standard core biopsies are negative with persistently elevated PSA, repeat biopsies targeted against hypervascular areas may increase the yield³⁰.

Conclusion:

Power Doppler imaging guided Hypervascular area directed biopsy is efficient in the detection of prostate

cancer in comparison with hypoechoic nodule directed biopsy. Additional targeted biopsy cores from the hypervascular areas in large prostates and in those hypoechoic areas depicting hypervascularity increase the yield of biopsy. This method is better

than Grey scale TRUS guided biopsy alone, till there is wide spread use of MRI – TRUS fusion biopsies.

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