Transrectal Ultrasonography Guided Prostate Biopsy in Evaluating Prostate Cancer with Histopathological Evaluation and Prostate Specific Antigen Correlation

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ABSTRACT

BACKGROUND

Prostate cancer is the second most common cause of cancer related deaths among men in the United States. In India, prostate cancer affects 4-5 men per 100,000 population¹. Although it is a common disease, it is slow to manifest clinical signs. It is estimated that 30% of men over 45 yrs, harbor latent prostate cancer and will remain latent until death. The objective of the study was to evaluate the role of Transrectal Ultrasound (TRUS) guided biopsy with histopathological evaluation (HPE) in the detection of prostate cancer on the basis of elevated prostate-specific antigen levels (PSA).

METHODS

This prospective study was done on 36 patients who were referred to department of Radio-Diagnosis at Yenepoya Medical College Hospital, Mangalore for TRUS guided biopsy. TRUS guided biopsy was performed using the sextant core biopsy technique & samples were sent to the department of pathology for histopathological evaluation and results were documented. Results were analysed based on frequency and percentage.

RESULTS

Prostatic diseases were more common in the older age group and incidence increases with age. Most of the patients in our study had grade II prostatic enlargement. Our study showed diagnostic rate of 6 core biopsy with serum PSA levels 4-10 ng/ml was in 11.1% cases, while the diagnostic rate was 0% with serum PSA levels 11-20 ng/ml, 16.75% levels of 21-30 ng/ml, 25% with levels of 41-50 ng/ml and diagnostic rate was 100 % with serum PSA levels of >51 ng/ml, indicating strong correlation of PSA level with tumour diagnosis by TRUS guided biopsy.

CONCLUSIONS

TRUS guided sextant core biopsy is a safe and effective procedure in diagnosing prostate cancer and has high diagnostic rates for patients with PSA levels of >50 ng/ml and gland volume between 30-50 cc.

KEY WORDS

TRUS, Guided Biopsy, Prostate Carcinoma

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BACKGROUND

Prostate cancer is the second most common cause of cancer related deaths among men in the United States. In India, prostate cancer affects 4-5 men per 100,000 population.¹ Although it is a common disease, it is slow to manifest clinical signs. It is estimated that 30% of men over 45 yrs, harbor latent prostate cancer and will remain latent until death. Unfortunately, anatomic location of prostate does not lend itself to straight forward examination. Historically, digital rectal examination has been the principal method of examination of prostate. However, this technique has its own limitation. The advent and refinement of ultrasound technology have provided a new method. Transrectal ultrasound with prostate biopsy, which is correlated with histopathological examination in conjunction with development of serum assays for PSA, has resulted in an impressive change in manner of diagnosis of prostate cancer. Transrectal ultrasonography (TRUS) is the most commonly used modality for imaging the prostate gland. It enables accurate determination of prostate size. When a cancer is visualized by ultrasonography, it is usually hypoechoic relative to normal tissue. However, the majority of hypoechoic foci detected by TRUS are not malignant; therefore, both its sensitivity and specificity are low. TRUS is mainly used to guide prostate biopsies. TRUS-guided biopsy is the most reliable method, at present, for accurate sampling of prostatic tissue in men considered at high risk for prostatic cancer. On the basis of digital rectal examination (DRE) and prostate specific antigen (PSA) findings, the TRUS-guided biopsy technique has become the accepted standard for prostate cancer diagnosis worldwide.

Transrectal ultrasound (TRUS) was initially described as a technique to evaluate rectal pathology.² In 1963, Takahashi and Ouchi³ were the first to describe the use of TRUS to evaluate the prostate. However, medical ultrasound was rather primitive at this time, so the images created with this array were of such poor quality that they carried little medical utility. The first clinically applicable images of the prostate obtained with TRUS were described in 1967 by Watanabe⁴. They used a 3.5 MHz transducer, which at that time was considered to be state of the art, to obtain images that were clinically meaningful. As ultrasound technology has become more refined, the use of TRUS in the evaluation of prostatic disease has increased. By the mid 1980s, the 7 MHz ultrasound probe, which more clearly delineated the architecture of the prostate, had become a standard diagnostic instrument. Astraldi⁵ performed the first transrectal biopsy in 1937. In the mid 1980s,² a transperineal ultrasound array was fitted with biopsy apparatus to allow direct correlation of the sonographic appearance of focal prostatic lesions with the histology of these lesions. Several years later, a spring-loaded core biopsy device was developed that operated via a TRUS probe. In 1987,² the first literature appeared describing the use of TRUS with transrectal biopsy. Since then, as ultrasound technology has become more refined, this technique has been described as a superior method of performing a core biopsy of the prostate. Since the initial reports of TRUS of the prostate by Wild and Reid,⁶ substantial technologic advances have improved the diagnostic capabilities of this modality. The current state of the art TRUS probe is a 5-8 MHz hand-held, high-resolution probe

with multi-axial planar imaging capabilities, which has the capacity for both transverse and sagittal imaging of the prostate in real time. This probe can be fitted with an adapter that accepts the needle of a spring-loaded biopsy gun, thus allowing multiple cores of tissue to be easily obtained. The visualization provided by the new higher resolution transducers, coupled with the ability to direct the biopsy needle into various regions of interest and to provide uniform spatial separation of the areas to be sampled, has helped to make TRUS-guided prostate biopsy a standard technique in the diagnosis of prostate cancer.

Hodge et al⁷ published the landmark paper demonstrating the efficacy of systemic sampling of prostate during TRUS-guided biopsy. They were the first to report that systemic sampling of the prostate guided by TRUS improved the detection rate of prostate cancer over merely sampling hypoechoic or other lesions. By taking sextant(six-core) biopsies from the mid-lobe (Parasagittal) of each side of prostate at the apex, middle and base, the cancer detection rate was superior to lesion directed biopsies.

We wanted to evaluate the role of Transrectal Ultrasound (TRUS) guided biopsy with histopathological evaluation (HPE) in the detection of prostate cancer on the basis of elevated prostate-specific antigen levels (PSA).

METHODS

This Prospective study was carried out on 36 patients over a period of 2 years from November 2014 to July 2016 in the Radiology Department. The patients who were referred with urinary symptoms suggestive of prostatic disease, were diagnosed using GE VOLUSON E8 ultrasound machine. This study includes patients with elevated PSA levels (>4 ng/ml) and prostatic lesions noted on TRUS. Informed consent was obtained from all participants, and a full explanation about the procedure risks involved and post procedure complications were explained to the patients.

All patients were subjected to DRE to ensure no rectal abnormalities, serum PSA testing, trans-abdominal ultrasound examination and TRUS, as well as biopsy. Before the procedure, the patients were given broad spectrum antibiotics to protect them against infection, they also underwent rectal enema to empty the rectal canal before the procedure to obtain clear images, and intra-rectal instillation of 20 ml of local anaesthetic gel (Lidocaine 2%) was used to alleviate pain and discomfort during the procedure.

A transrectal ultrasound probe (6-12 MHz range) with a combination of end-viewing and side-viewing transducer attached to GE VOLUSON E8 ultrasound machine was used. Local anaesthetic gel (Lidocaine 2%) was applied over a latex condom applied onto the probe. All patients were examined in the left lateral decubitus position and it was well tolerated. A full urinary bladder was ensured to help in better visualization of the gland prior to the procedure.

The prostate was imaged in both axial and sagittal planes with assessment of volume, echogenicity, surface, calcification, and the presence of nodules. Each nodule was assessed for size, location in the gland, morphology, echogenicity, margin, and extent. Colour Doppler ultrasonography was then performed to assess colour mapping of the nodules and

the surrounding prostate tissue. Sampling of the prostate was performed in the sagittal plane. Biopsies were obtained using automatic BARD MAX-CORE biopsy gun needle (18G × 25 cm). The most commonly used protocol was the “targeted plus systematic” sextant (Six-core) biopsy protocol and an additional sample from the suspicious lesion if noted were taken. After biopsy samples were obtained, they were persevered in formaldehyde solution and were sent to the Pathology section for histopathological analysis. The patient’s rectum was then packed with lidocaine gel coated gauze packs to achieve haemostasis. After the procedure the patient was assessed for any complications and appropriate action was taken if necessary. Post procedure the patient was transferred to the urology/surgery ward for further observation and management.

Inclusion Criteria

1. Palpable mass on DRE (Digital Rectal Examination).
2. PSA (Prostate Specific Antigen) >4 ng/ml.
3. Nodule visible on TRUS.
4. Excessive PSA Velocity.

Exclusion Criteria

1. Prostatitis.
2. Uncorrectable bleeding diathesis (abnormal coagulation indices).
3. Uncooperative patient.

Statistical Analysis

The data were entered and analysed in SPSS. Frequency and Percentages of all the variables were computed. The chi-square test was used to compare the association presenting symptoms, prostate size and volume, echotexture, calcification, radiological findings, serum PSA levels. The results were considered statistically significant if the p-value was <0.05.

RESULTS

1. Age Distribution

Out of 36 patients studied 17 (47%) subjects were between the age of 61-70 yrs. and least affected group was in the range of 40-50 yrs (8.5%). Incidence of cancer in our study was found in subjects belonging to elderly group ranging between 60-80yrs. In our study we found that the prostatic cancer was seen in elderly. The mean age was 65.86 yrs. These findings correlate with studies by Berry et al.¹¹ In our study we found that the prostatic disease affected people above 40 yrs. with peak incidence being in the group 61-80yrs. Similar findings were noted in a study by Chukwudi and co-workers¹² in which the patients’ ages ranged from 30 to 86.

2. Correlation of Presenting Symptoms

Our clinical data revealed that prevalence of symptoms of voiding difficulties was 78% and dysuria was 22%, 18(69%) out of 26 subjects with voiding difficulties were benign and 8 subjects (31%) were malignant on HPE. Among patients with dysuria symptoms were 9(90%) out of 10 were benign and 1 (10%) was malignant on HPE. In a study by Kazuhiro¹³ the

prevalence rates of urinary symptoms of voiding were 37.0%, in our study it was 78%. The p value for this correlation is not significant in our study.

Complaints		Histopathology		Total
		Benign	Malignant	
Voiding	Count (%)	18(69.2%)	8(30.8%)	26(100.0%)
Dysuria	Count (%)	9(90.0%)	1(10.0%)	10(100.0%)
Total	Count (%)	27(75.0%)	9(25.0%)	36(100.0%)

Table 1. Correlation of Presenting Symptoms with HPE

X² test, p value = 0.197.

3. Correlation of Prostate Size and Volume

In our study out of 36 subjects 47%, 25%, 22% and 5% of subjects had prostate gland with volumes of 31-50 cc, 51-80 cc, 21-30 cc and >81 cc and 77% of the malignancies were found in subjects having prostate volume of 31-50 cc on HPE correlation, which was statistically not significant. Study by Levine et al¹⁴ demonstrated increased cancer rate detection was 43%, 27% and 24% of men with prostate volumes of <30 cc, 30-50 cc and >50 cc respectively. Karakiewicz et al¹⁵ also evaluated the positive of sextant biopsy according to gland size. The positive rate of biopsy for glands of 20 cc was 40% vs 10 % for gland of 80-90 cc.

Prostate Size		Histopathology		Total
		Benign	Malignant	
21-30 cc	Count (%)	8(100.0%)	0(0.0%)	8(100.0%)
31-50 cc	Count (%)	10(58.8%)	7(41.2%)	17(100.0%)
51-80 cc	Count (%)	8(88.9%)	1(11.1%)	9(100.0%)
>81 cc	Count (%)	1(50.0%)	1(50.0%)	2(100.0%)
Total	Count (%)	27(75.0%)	9(25.0%)	36(100.0%)

Table 2. Correlation of Prostate Size and Volume with HPE

X² test, p value = 0.085

4. Echotexture of the Prostate Gland

In our study 27 (75%) out of 36 subjects prostate had heterogeneous texture on TRUS and 9 subjects (25%) prostate had homogenous echotexture. Most of patients in our study had heterogeneous echotexture. All the patients who had malignancy on HPE correlation had heterogeneous echotexture was statistically significant.

5. Association between Calcification and Prostatic Malignancy

Calcification was seen in both benign and malignant disease in the prostate in a study by Deland and his colleagues.¹⁶ In a study by Chan Gyu et al¹⁷ they concluded that prostatic calcifications can aggravate lower urinary tract symptoms. In our study 8 subjects showed the presence of calcific foci in the transition and central zone which were benign on HPE correlation, statistically was not significant.

6. Correlation between Radiological and Histological Diagnosis

All the 36 subjects who were referred to us for TRUS guided biopsy were clinically diagnosed as carcinoma prostate. On radiological examination 33(92%) out of 36 subjects showed benign prostatic hyperplasia features, 3 subjects (8%) were considered malignant based on solid hypoechoic lesion in the peripheral zone. On histopathological correlation 9 subjects (25%) were found to have malignant features and 27 subjects (75%) were found to have benign features. Out of 9 subjects who were found malignant, 8 had adenocarcinomas and 1 had PIN, out of 27 subjects who were found benign 20 (74%) had benign prostatic hyperplasia and 7 patients (26%) had

benign prostatic hyperplasia with prostatitis. Statistically there was no significant correlation.

Radiological Findings		HPE Findings		Total
		Benign	Malignant	
Benign	Count (%)	25(75.8%)	8(24.2%)	33(100.0%)
Malignant	Count (%)	2(66.7%)	1(33.3%)	3(100.0%)
Total	Count (%)	27(75.0%)	9(25.0%)	36(100.0%)

Table 3. Correlation between Radiological and HPE Findings

χ^2 test, p value = 0.728

7. Correlation of PSA with HPE Findings

Out of 36 patients 9 patients who were found to be malignant 6 patients (83.33%) had PSA levels of >51 ng/ml, 27 patients who were benign on HPE correlation patients had PSA levels between 4-50 ng/ml. In our study (Table 1) with serum PSA levels 4-10 ng/ml, TRUS guided biopsy detected cancer in 11.1% cases, while the detection rate was 0% with serum PSA levels 11-20 ng/ml, 16.75% levels of 21-30 ng/ml, 25% with levels of 41-50 ng/ml and detection rate was 100 % with serum PSA levels of >51 ng/ml. This data showed a strong correlation of PSA level with tumour diagnosis, statistically significant was very much significant with p value of 0.000. A study by Lojanapiwat, et al¹⁸ also demonstrated specificity of PSA levels of 4-10, 10.1-20, 21-50, 50-100 and >100 ng/ml in the diagnosis of prostate cancer was 9.3, 55.5, 87.5, 98.2 and 99.7 respectively. Other studies by Ahmed Alghazo et al¹⁹ showed PSA levels between 4-10 ng/ml, between 10-20 ng/ml and above 20 ng/ml, the cancer detection rate by TRUS guided biopsy was 20.6%, 32.4 % and 47 % respectively. In study by Hyeon Jeong et al²⁰ cancer detection rate was 34 % with serum PSA level of 10-20 ng/ml.

Serum PSA Levels		Histopathology		Total
		Benign	Malignant	
4-10 ng/ml	Count (%)	8(88.9 %)	1(11.1%)	9(100.0%)
11-20 ng/ml	Count (%)	8(100.0%)	0(0.0%)	8(100.0%)
21-30 ng/ml	Count (%)	5(83.3%)	1(16.7%)	6(100.0%)
31-40 ng/ml	Count (%)	3(100.0%)	0(0.0%)	3(100.0%)
41-50 ng/ml	Count (%)	3(75.0%)	1(25.0%)	4(100.0%)
>51 ng/ml	Count (%)	0(0.0%)	6(100.0%)	6(100.0%)
Total	Count (%)	27(75.0%)	9(25.0%)	36(100.0%)

Table 4. Correlation between PSA Levels and HPE

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)	Point Probability
Pearson Chi-Square	22.815 ^a	5	.000	.000	-	-
Likelihood Ratio	24.304	5	.000	.000	-	-
Fisher's Exact Test	18.389			.000	-	-

Table 4a. Correlation between PSA Levels and HPE

8. Correlation of Complications Post TRUS Biopsy

Out of 36 patients who had the procedure under local anaesthetic none of the patients had post procedure complications like rectal bleeding, need for anaesthesia or prolongation of hospitalization. Similar studies by Tobium et al²¹ none of the patients showed rectal bleeding or need for anaesthesia, only few patients had minor complications.

9. Gleason Score

In our study a Gleason score of 7 was noted in 61% of malignant cases. Similar studies like Kumari K, Baru R²³ and Song et al²⁴ revealed a Gleason score of 7 in 51.61% cases and 6 in 60 % of patients respectively.

Figure 1. TRUS Image of 65-Year-Old Showed Enlarged Prostate with Heterogenous Echotexture with Focal Hypoechoic Lesion in the Left Lobe, Biopsy was Suggestive of Adenocarcinoma of Prostate

Figure 2. TRUS Image of 48-Year-Old Shows the Path of the Biopsy Needle

DISCUSSION

Analysis of collected data and interpretation data in comparison to other studies. In our study trans rectal ultrasound guided needle core sextant biopsy with histopathological evaluation was done. We evaluated 36 subjects between age groups of 40-90 yrs. from November 2014 to July 2016 at Yenepoya Medical Hospital, Deralakatte, Mangalore.

The incidence of prostate cancer differs internationally with the lowest incidence being in Southeast Asia.⁸ Over the past two decades the incidence of prostate cancer has increased significantly⁹ and is the most commonly diagnosed cancer in males.¹⁰ In today's competitive world the need for improving current standards of medical care is one of the top most priorities and in order to fulfil this essential goal various modalities of investigations being developed and their efficacies studied. The diagnosis of a clinically enlarged prostate is confirmed by the radiologist on the basis of an enlarged prostate either with ultrasound or three-dimensional diagnostic imaging studies of the male pelvis. Prostatic biopsy is one of the most important investigations for diagnosing and excluding prostate cancer by histological analysis and was first described in 1937 by Astraldi. In view of this we decided to study the co-relation of TRUS and histopathological findings in diagnosing prostatic diseases.

CONCLUSIONS

TRUS guided sextant core biopsy is a safe and effective procedure in diagnosing prostate cancer and has high diagnostic rates for patients with PSA levels of >50 ng/ml and gland volume between 30-50 cc.

Limitations

It's a short-term study hence long-term changes in the prostate are not studied in the younger population. The size of the study population was very small and sample size was very low. Long term follow-up of those patients with elevated serum PSA and normal HPE is necessary.

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