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Research Article

Prostate tumours

Prostate tumours-TR-colour Doppler evaluation & correlation with PSA & Histo-Pathology

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Introduction: Prostate gland is site of two common diseases in ageing man, benign prostatic hyperplasia and prostate cancer. Advanced TRUS techniques may help in better tissue characterization, hence in armamentarium of non- invasive techniques. TRUS provides direct visualisation of echopattern, site and size of lesion and also helps in proper interpretation of focal prostatic lesions. M**aterial and methods:** A Prospective study was conducted in Dept. of Radio-Diagnosis in 50 patients who were suspected to have prostatic tumours by clinical & TAS examination were subjected TRUS and colour Doppler followed by their histopathological correlation to study sensitivity and specificity of TRUS and colour Doppler for diagnosis of prostatic tumours. **Results:** Majority of patients 03 out of 07 pts with cancer belonged to age group of 61- 70 years. Majority of patients 30 out of 43 (70%) of BPH cases belonged to age group of 61-80 yrs. At age of 80 yrs, of BPH patients are found to be 35 0f 43 (81.4%). This study comprised of 50 patients. Among 50 patients diagnosed as prostatic tumours by clinical examination and imaging out of which 07 cases diagnosed as cancer & rest 43 cases to be benign by histopathological examination. TRUS correctly diagnosed 45 patients wrongly diagnosed 05. So TRUS is accurate in diagnosing 90% of prostatic tumours. TRUS with colour Doppler correctly diagnosed 47 patients wrongly diagnosed 05. So it is accurate in diagnosing 94% of prostatic tumours. **Conclusion:** TRUS with colour Doppler proves to be a valuable, cost effective and non invasive initial modality of imaging in accurately evaluating morphologic distribution of prostatic tumours. Technological advances in imaging have created a new role for various tests in management of prostate cancers. Advances in imaging exploit biology of disease, and in doing so, allow more accurate detection of location, extent, and aggressiveness of malignancy. In this article, we review current status of imaging in prostate cancer diagnosis, staging, and monitoring of recurrence.

Keywords: BPH, prostate carcinoma, TRUS, colour Doppler, PSA

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Introduction

Prostate cancer is a major public health problem worldwide. It is the commonest visceral malignancy in men and the second leading cause of cancer death in the Western world after lung cancer. In India, its incidence is stated to be lower than in the Western countries [1]. With the significant increase of the average lifespan in the industrial world, the number of elderly people, as a proportion of the total population, has risen dramatically. It has been estimated that this trend will accelerate and that, by the year 2020, the number of people aged >80 years will soar by 135%. With age being the greatest risk factor for prostate cancer, this disease has understandably become one of the greatest public health concerns [2]. Screening by digital rectal examination (DRE) and serum prostate-specific antigen (PSA) is used despite its limitations. Gray-scale transrectal ultrasound (TRUS), used to guide multiple random prostatic biopsies, misses up to 20% cancers and frequently underestimates the grade of malignancy. Increasing the number of biopsy cores marginally increases the yield. Evolving techniques of real-time ultrasound elastography (RTE) and contrast-enhanced ultrasound (CEUS) are being investigated to better detect and improve the yield by allowing "targeted" biopsies [3]. The manifestation of PCa ranges from indolent to highly aggressive disease and due to this high variation in PCa progression, the diagnosis and subsequent treatment planning can be challenging [4].

Ultrasonography is the most common method used for direct visualization of the prostate, primarily because it is indispensable to imaging-guided prostate biopsies. Ultrasonography has the advantages of real-time imaging, portability, ease of use, and low cost. It can visualize intraprostatic zonal anatomy, with the peripheral zone showing slightly increased echogenicity compared with the central gland. Prostate carcinoma typically presents as a hypoechoic area within the peripheral zone [5]. TRUS targeted a visual lesion increased the detection rate about two times compared with systematic biopsy, but also missed about 30% cancer [6,7].

The currently used ultrasound contrast agents consist of microbubbles with a diameter smaller than red blood cells. So CE-TRUS Can observe these new microvessels [8]. Some reports demonstrate that CE-TRUS targeted biopsy increased the detection of prostate cancer with fewer biopsy cores [9-19].

The discovery of prostate-specific antigen (PSA) has revolutionized the management of prostate cancer. Catalona *et al.* has made substantial contributions in prostate cancer diagnosis [20]. The presence of an abnormal digital rectal examination (DRE) or an elevated PSA level were associated with increased risk of prostate cancer, and they are common indications of transrectal ultrasound (TRUS)-guided prostate biopsy[20].

Material and Methods

This prospective study of evaluating prostatic tumours by Transrectal ultrasound & colour Doppler with PSA & histopathological correlation was performed on 50 patients. The study was conducted in the Department of Radio-Diagnosis from referred patients from department of Urology SCB Medical College, Cuttack.

Thorough clinical history taken & clinical examination & TAS (transabdominal ultrasound) were done prior to TRUS examination and those patients with prostatic enlargement on TAS & clinical diagnosis were subjected to TRUS and followed up for pre-operative biopsy and till surgery for confirmatory histopathological diagnosis.

Study design: Prospective study

Study Period: April'2013 to May'2015.

Inclusion Criteria: Age groups more than forty years male with prostatic enlargement on transabdominal ultrasound, who needed transrectal biopsy for suspected carcinoma of prostate either by digital rectal examination or elevated serum PSA level and clinical diagnosis of prostate hypertrophy made in department of Urology, SCB Medical College were included.

Exclusion Criteria: All cases with prostatic cysts, abscess and symptomatology due to infections, anal fissures, haemorrhoids, perianal infections, and patients outside medical college were excluded.

Collection of data: Male patients attending our outpatient department with history of lower urinary tract symptoms were evaluated. A detailed clinical examination including digital rectal examination

(DRE) was performed. Patient with suspected DRE findings or elevated PSA or both were advised to undergo TRUS guided prostate biopsy after routine investigations.

Methods: Ultrasound machine & TRUS technique: All scans in this study were performed using PHILIPS HD7 ULTRASOUND Machine equipped with a 4-8 MHz broadband curved array endocavitary transducer. Patient is advised to lie in left lateral decubitus position with knees flexed and applied closely to chest. TRUS was done by transrectal probe wrapped in a rubber sheath (condom). To ensure acoustic contact the sheath contained ultrasound gel. The sheath was coated with gel, then it was inserted into rectum. After imaging the midline, the probe was rotated clockwise and counterclockwise to see all portions of the gland.

TRUS included imaging in the transverse and sagittal planes using both gray-scale and colour Doppler US. Gray-scale imaging was performed first, followed by colour Doppler US imaging. The colour window sector width was increased to include the entire transverse width of the gland. To optimize low-velocity flow detection, the pulse repetition frequency was set to 800 Hz with a wall filter of 50 Hz. Doppler amplification was controlled so that normal prostatic tissue did not display any noise. Positive contour-bulging was defined as asymmetric bulging of the contour of the prostate.

The following US characteristics of focal suspicious lesions were evaluated. The prostate gland was evaluated for assessment of the presence of any focal lesion and their echo pattern, as homogeneous or heterogeneous, capsular integrity, extension of the disease process outside the limits of the gland margin. Enlarged prostate gland with or without median lobe enlargement with symmetric benign prostatic hyperplasia (BPH).

Normal or enlarged gland with focal lesion in peripheral zone with or without increased vascularity, with or without capsular breach is suggestive carcinoma. The transrectal ultrasonographic diagnosis was correlated with the histopathological examination of biopsied /post-operative specimen.

Statistical Analysis: Numerical variables are reported as mean ± 1 SD and ordinal variables in percent. Chi-square test was used to find association while analysis of variance and P value less than 0.05 was considered significant.

Statistical software: The statistical software SPSS 10.0 was used for the analysis of the data and Microsoft word and excel have been used to generate graphs, tables etc.

Observation and Results

This study comprised of 50 patients. Among 50 patients diagnosed as prostatic tumours by clinical examination and imaging out of which 07 cases diagnosed as cancer & rest 43 cases to be benign by histopathological examination.

05 cases diagnosed as BPH found to be cancer in 02, BPH with prostatitis in 02, BPH with Abscess in 01 &, 03 cases diagnosed as cancer found to be BPH in 02 and BPH with prostatitis in 01 by histopathological examination.

Table No.-1: Age distribution prostatic tumours.

Age gp. In yrs	No. of patients	%
41-50	0	0
51-60	01	14
61-70	03	43
71-80	02	29
>80	01	14
Total	07	100

The study included 50 patients ranging in age between 45 and 82 years.

Majority of the patients 03 out of 07 pts with cancer belonged to the age group of 61- 70 years.

So the the median age group for prostate cancer in my study is 61-70 yr & the median age is 66 yrs.

Table-2: Age distribution of benign prostatic tumours (BPH) in the study population

Age gp. In yrs	No. of patients	%
41-50	02	04
51-60	03	07
61-70	12	28
71-80	18	42
>80	08	19
Total	43	100

Majority of the patients 30 out of 43 (70%) of BPH cases belonged to the age group of 61-80 yrs.

So median age group for BHP in my study is 61-80 yrs & mean age is 68.9 yrs. At the age of 80 yrs, of BPH patients are found to be 35 0f 43 (81.4%).

Table-3: TRUS & colour Doppler with PSA & HPE correlation

HPE Diagnosis		TRUS Diagnosis	TRUS with Color Doppler diagnosis	PSA (I/N)
Prostate cancer	07	05	06	04 (I)
BPH	39 40	40	41	28 (N)
BPH withprostatis	03	-	-	-
BPH with abscess	01	-	-	-

This study comprised of 50 patients. Among 50 patients diagnosed as prostatic tumours by clinical examination and imaging out of which 07 cases diagnosed as cancer & rest 43 cases to be benign by histopathological examination.

TRUS correctly diagnosed 45 patients wrongly diagnosed 05. So TRUS is accurate in diagnosing 90% of prostatic tumours. TRUS with colour Doppler correctly diagnosed 47 patients wrongly diagnosed 05. So it is accurate in diagnosing 94% of prostatic tumours.

Prostatitis and abscess are excluded from my study & so their values not used calculating the percentages. PSA increased in 4 cancer patients and normal in 28 BPH patients. So it correctly diagnosed 32 patients & wrongly diagnosed 18 patients with prostatic tumours with an accuracy of 64%.

So according to my study TRUS with colour Doppler is more accurate than PSA.

Table-4: TRUS with HPE correlation.

TRUS	HPE		Total
	Cancer	BPH	
CANCER(08)	05	03	08
BPH(42)	02	40	42
50	07	43	50

TRUS showed 08 cases as prostate cancer and 42 as BPH. However HPE diagnosed 07 as cancer & 43 as BPH. Of the 08 cancers diagnosed by TRUS 05 are confirmed by HPE & and 03 were found to have BPH (false Positive). Of the 42 cases diagnosed as BPH by TRUS, 40 were confirmed by HPE and 02 were found to have cancers (false negative).

Sensitivity (Sn): a / a + c = 5/7 = 71.5%
Specificity (Sp): d / b + d = 40/43 = 93%
Positive Predictive Value (PPV): a / a + b = 5/8 = 62.5%
Negative Predictive Value 9 (NPV): d / c + d = 40/42=95.2 %
cy: a + d / a + b + c + d = 45/50 = 90%

Table-5: TRUS & colour Doppler with HPE correlation.

TRUS & COLORDOPPLER	HPE		Total
	Cancer(07)	BPH(43)	
CANCER(08)	06	02	08
BPH(42)	01	41	42
50	07	43	50

TRUS with colour Doppler showed 08 cases as prostate cancer and 42 as BPH. However HPE diagnosed 07 as cancer & 43 as BPH. Of the 08 cancers diagnosed by TRUS with Doppler 06 are confirmed by HPE & and 02 were found to have BPH (false Positive). Of the 42 cases considered as BPH by TRUS, 41 were confirmed by HPE and 01 was found to have cancers (false negative).

Sensitivity (Sn): a / a + c = 6/7 = 85.7%
Specificity (Sp): d / b + d = 40/43 = 95.3%
Positive Predictive Value (PPV): a / a + b = 6/8 = 75%
Negative Predictive Value 9 (NPV): d / c + d = 41/42 =95.2%
Accuracy: a + d / a + b + c + d = 47/50 = 94%

Discussion

This study included 50 patients who were found to have prostatic enlargement on clinical diagnosis & TAS were subjected to TRUS & colour Doppler and followed up for pre-operative biopsy and till surgery for confirmatory histopathological diagnosis.

Table 1 Shows that majority of the cancer patients 03 out of 07 (42%) belonged to the age group of 61- 70 years. So the the median age group for prostate cancer in my study is 61-70 yr & the mean age is 65.7 yrs.

Table 2 Shows Majority of the patients 30 out of 43 (70%) of BPH cases belonged to the age group of 61-80 yrs. So median age group for BHP in my study is 61-80 yrs. & mean age is 68.9 yrs.

This correlates with study done by Ho Yun Lee,et al[21]in 2009 in 350 patients. Of these patients, 147 patients had prostatic cancer (mean age, 69.7 ± 8.0 years; age range, 49-94 years) and 203 patients had no malignancy (mean age, 64.1 ± 8.6 years; age range, 33- 85 years). Kuligowska E, Barish MA et al [22]. In 2001 stated the mean age for prostate cancer was 63 yrs in a study of 544 patients.

At the age of 80 yrs, BPH patients are found to be 35 of 43 (81.4%). This correlates with the study on 210 patients done by Verhamme, K et al [23]. (2002). "Incidence and Prevalence of Lower Urinary Tract Symptoms Suggestive of Benign Prostatic Hyperplasia in Primary Care. Mild variation may be due to small sample size in my study.

Out of 50 patients in my study TRUS diagnosed 08 cases as prostate cancer and 42 as BPH. However HPE diagnosed 07 as cancer & 43 as BPH. Of the 08 cancers diagnosed by TRUS 05 are confirmed by HPE & and 03 were found to have BPH (false Positive). Of the 42 cases diagnosed as BPH by TRUS, 40 were confirmed by HPE and 02 were found to have cancers (false negative). The sensitivity, specificity, positive & negative predictive values and accuracy of Gray scale TRUS for detecting prostatic tumours were 71.5%, 93%, 62.5%, 95.2% & 90% respectively.

A study done by K. Shigeno , M.Igawa et al[24]. In Izumo, japan on 278 patients which showed the sensitivity, specificity, positive & negative predictive values of gray scale TRUS for detecting prostatic cancers were 74.9%, 92, 5%, 60.1%, & 96.1% respectively. A study done by Ewa Kuligowska et al [22]. in Boston on 544 patients which showed the sensitivity, specificity, positive & negative predictive values of gray scale TRUS for detecting prostatic cancers were 41%, 85%, 52.7%, 72% & 67% respectively.

TRUS with colour Doppler showed 08 cases as prostate cancer and 42 as BPH. However HPE diagnosed 07 as cancer & 43 as BPH. Of the 08 cancers diagnosed by TRUS with Doppler 06 are confirmed by HPE & and 02 were found to have BPH (false Positive). Of the 42 cases considered as BPH by TRUS, 41 were confirmed by HPE and 01 was found to have cancers (false negative). The sensitivity, specificity, positive & negative predictive values and accuracy of Gray scale TRUS with colour Doppler for detecting prostatic tumours were 85.7%, 95.3%, 75%, 97.6% & 94% respectively.

It shows that with colour Doppler, Sn, Sp, & accuracy increased. So TRUS with colour Doppler is a better modality than Gray scale TRUS alone which can diagnose isoechoic tumours showing asymmetrical increased vascularity. In my study 1 extra case (14%) diagnosed as cancer with TRUS with Doppler as compared to TRUS alone. A study done by K.Shigeno, M. et al [24]. in Izumo ,japan on 278 patients which showed the sensitivity, specificity, positive & negative predictive values of Gray scale TRUS with colour Doppler for detecting prostatic cancers were 81.2%, 93%, 63.7% & 97% respectively.

Jyotsna Sen, et al [25]. In 2008 in a study of 43 patients, the sensitivity and specificity of G ray scale TRUS with colour Doppler for detecting prostatic cancers were 83.33% and 66.66%, respectively. A study done by Ewa Kuligowska et al [22]. in Boston on 544 patients which showed the sensitivity, specificity, positive & negative predictive values of Gray scale TRUS with colour Doppler for detecting prostatic cancers were 56, 8%, 61%, 44%, 73% & 60% respectively. Srikanth Iyengar et al[26], in a study the sensitivity, specificity, positive & negative predictive values of Gray scale TRUS with colour Doppler for detecting prostatic cancers were 81%, 43%, & 56% respectively.

In our study TRUS with colour Doppler correctly diagnosed 47 patients, wrongly diagnosed 05. So it is accurate in diagnosing 94% of prostatic tumours. The sensitivity, specificity, positive & negative predictive values and accuracy of Gray scale TRUS with colour Doppler for detecting prostatic tumours were 85.7%, 95.3%, 75%, 97.6% & 94% respectively. Ewa Kuligowska et al [22]. in Boston studied on 544 patients which showed the sensitivity, specificity, positive & negative predictive values & accuracy of Gray scale TRUS with colour Doppler & raised PSA for detecting prostatic cancers were 81.6%, 43.5%, 43.7%, 81.5% &56.8% respectively.

So the discrepancy /variation in my study may be due to all cases where PSA raised where TRUS with Doppler is positive which may be due to PSA was >20 ng/ml in 3 of 4 cases & in no case it is raised where TRUS with Doppler is negative, small sample size, all cases not referred from department of Urology & Geographical variation.

Conclusion

TRUS with colour Doppler proves to be a valuable initial modality of imaging in accurately evaluating the morphologic distribution of prostatic tumours. It is noninvasive, cost effective. Future prospective would be Advanced TRUS techniques like contrast enhanced TRUS using microbubble

Contrast enhanced technique, Elastography, MR-TRUS fusion biopsy, diffusion weighted imaging techniques may help in better tissue characterization. Experience is limited, but this is a very promising development that would overcome the limitation of TRUS in detecting cancer while retaining the flexibility and convenience of TRUS-directed needle biopsy.

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