TRANSRECTAL BIOPSY OF THE PROSTATE GUIDED BY TRANSRECTAL ULTRASOUND IN AN ASEAN POPULATION:CORRELATION OF DIGITAL RECTAL EXAMINATION, PROSTATE SPECIFIC ANTIGEN LEVELS AND IMAGING WITH HISTOLOGY.

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ABSTRACT

Transrectal ultrasound (TRUS) followed, in the same sitting, by TRUS guided biopsy of the prostate was performed on 131 cases. Histological findings were prostatic carcinoma in 26 cases (19.8%), prostatitis in 11 cases (8.4%) and glandular atypia in 9 cases (6.9%).

The typical findings on digital rectal examination (DRE) were a hard, multinodular prostate for prostatic carcinoma and a hard, uninodular prostate for both prostatitis and glandular atypia. However its high false positive and false negative rates, 37.6% and 50% respectively, limits its role in predicting prostate pathology.

In terms of the Prostatic Specific Antigen (PSA), the mean levels for prostatic carcinoma, prostatitis and glandular atypia were 366, 17.5 and 7.2 ng/dl respectively.

On TRUS imaging, extracapsular and inhomogenicities in the peripheral zone (PZ) breach posted positive predictive values (PPV) of 100% and 71.4% for carcinoma respectively. Well defined solitary nodules were non specific and pointed move towards benign conditions such as prostatitis and atypia rather than carcinoma.

Patient acceptance of the procedure was high. Complications of the procedure were mild pain (23 cases), haematuria (12 cases), passing blood per rectum (4 cases) and fever (2 cases).

Key words: Transrectal ultrasound (TRUS) ; digital rectal examination (DRE); Prostatic Specific Antigen (PSA); prostatitis; glandular atypia.

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INTRODUCTION

The role of transrectal ultrasound (TRUS) in the evaluation of prostate pathology has been gaining considerable ground since its inception in 1971. In the early eighties, the introduction of spring driven biopsy mechanisms as well as sophisticated probes with needle guide capability made TRUS guided biopsy an accurate and relatively simple procedure (1). TRUS guided biopsy soon overtook trans-perineal biopsy as the method of choice in prostatic tissue sampling. As a consequence of this, there has been a flurry of reports co-relating endosonographic and histologic findings (2-5).

TRUS has played a critical role in establishing the commonest site of prostatic carcinoma as the peripheral zone (PZ). However, the debate concerning the acoustic properties of prostatic lesions is still on going (6).While investigators first thought of malignant lesions as echogenic (7), the currently accepted view is that a hypoechoic lesion in the peripheral zone is highly suggestive of malignancy (8). The utility of digital rectal examination (DRE) and serum Prostatic Specific Antigen (PSA) as predictors of prostatic carcinoma has yet to be ascertained, in spite of considerable study. Furthermore, although the use of TRUS guided transrectal biopsy is well reported in the West, the experience in South-East Asia is relatively limited. As such our prospective study was conducted to shed light on the current controversy and to recommend guidelines for TRUS guided biopsy. The role of both directed as well as random biopsies will also be discussed.

MATERIALS AND METHODS

Between January 1993 and August 1994, the Department of Diagnostic Imaging, Tan Tock Seng Hospital, Singapore, performed TRUS and TRUS guided biopsy on 131 consecutive cases. These were male patients, of age between 46 and 91 (mean=71) years. All had either symptoms suggestive of prostatomegaly, an abnormal DRE or a raised PSA level.

115 patients had PSA levels taken prior to TRUS. PSA measurement was made using a monoclonal antibody assay (Abbott Laboratories, Abbott Park, Illinois, USA).

All patients also received prophylactic antibiotics. The departmental regime comprised two tablets of Bactrim (Sulphamethoxazole 400 mg and Trimethoprim 80mg) twice daily for three days, commencing 24 hours before the examination. For cases of sulphur drug allergy, one capsule of Augmentin 375 mg thrice daily for three days was given. On the eve before the examination a laxative, to be taken orally, was given.

Informed consent was taken before the appointment for the procedure was given. On the appointed date, the radiologist would run through the procedure with the patient. A conscientious attempt was made to talk to the patient throughout the examination to reassure him.

The patient was placed in the left lateral decubitus, knee-chest position throughout the entire procedure. A pre-scan DRE was performed and all findings were documented, with a special emphasis on gland size, consistency and the presence of nodules (solitary or multiple).

TRUS was performed by three ultrasonologists (SN, DW and ST) familiar with the protocol using the Acuson 128 x P/10 console and 7.0 MHz transducers V714T and V714S. PSA levels were known to the ultrasonologists in some cases. Scanning was performed systematically, first in the transverse, and then in the sagittal plane. The TRUS examination was considered positive if a focal lesion, i.e.a nodule, was detected.

All patients were then subjected to a 4 quadrant transrectal biopsy under TRUS guidance. This biopsy was initiated by locating 4 anatomical sites from the upper and lower quadrant of each lobe of the prostate gland. A computer generated trajectory was then projected onto the monitor. If a focal lesion was demonstrated on TRUS, this lesion was brought into the trajectory by manipulating the transducer.

All biopsies were performed using an 18-gauge needle (Biopty-Cut; Bard Urological, Covington, Ga) with a spring-driven automatic firing device to obtain core biopsy samples, each of 1.7 cm in length, starting with the quadrants where a focal lesion is localized to. Random biopsies were then performed on each of the "uninvolved" quadrants.

Each specimen was placed separately in buffered formaldehyde (4%) solution.

No analgesics or anesthetics were used before, during, or after the biopsy. Patients were allowed to leave the department immediately after the biopsy. They were warned of possible complications and follow-up was carried out for a week post-biopsy.

RESULTS

TRUS guided biopsy performed on all 131 cases provided adequate tissue for histological analysis. Biopsy results were positive for malignancy in 26 cases (19.8%), prostatitis in 11 cases (8.4%) and glandular atypia in 9 cases (6.92%) (Table 1). Of the 26 cases of prostatic carcinoma, 24 were primary adenocarcinoma of the prostate, 1 was invasive transitional cell carcinoma of the bladder involving the prostate, and 1 was a case of disseminated gastric carcinoma with a peritoneal drop metastasis involving the prostate. Ages of these patients ranged from 53 to 83 (mean = 71) years of age.

DRE was considered abnormal if the prostate consistency was hard or if a nodule (or nodules) were felt. The incidence of abnormal DRE was 16 (62%), 3 (27.3%) and 4 (44.4%) for carcinoma, prostatitis and glandular atypia respectively. However, abnormal DRE was also recorded in 37.6% (32 of 85) of cases who were histologicaly normal.

The mean PSA levels for prostatic carcinoma, prostatitis and glandular atypia were 339.4, 17.7 and 10.1 ng/dl respectively (Table 1). All 18 cases with a PSA of more than 35ng/ml were positive for carcinoma irrespective of DRE or TRUS findings. (i.e. there were no cases of prostatitis or glandular atypia with PSA>35) (Table 2). 5 of 41 patients with a PSA range of 4 - 35 ng/ml had carcinoma. There were two cases of carcinoma with a normal PSA.

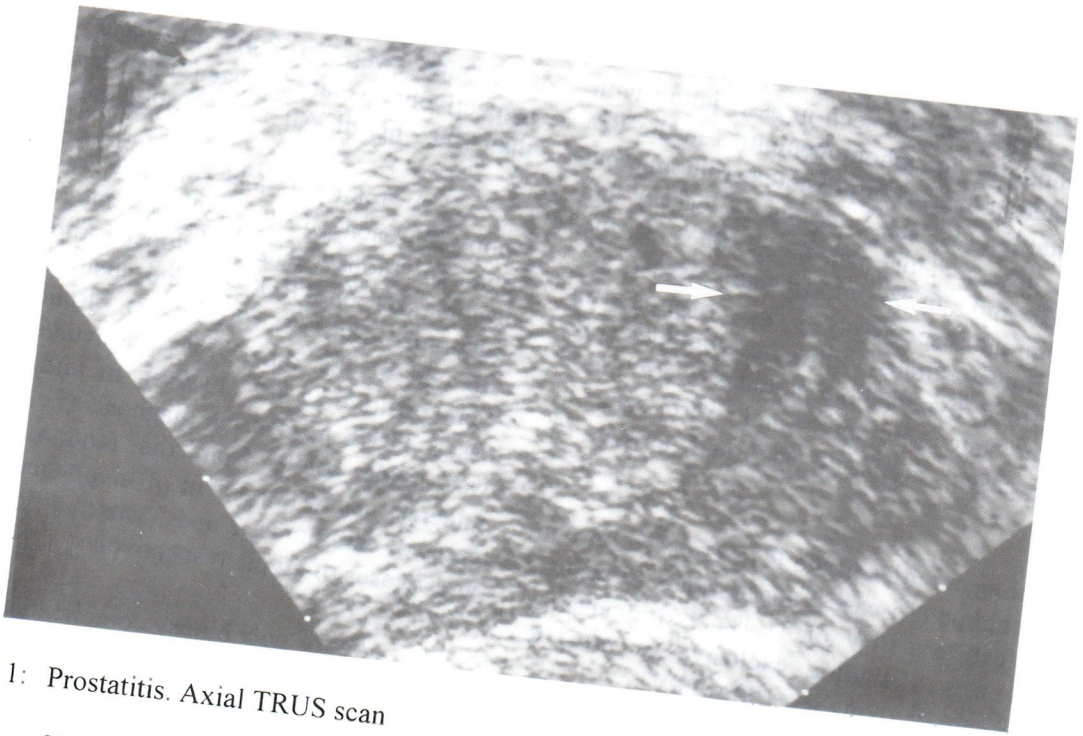

Fig. 1: Prostatitis. Axial TRUS scan

Shows well defined hypoechoic nodule (arrows) at junction of (L) PZ and transitional zone (TZ). Note curvilinear echoes within. This feature was only seen in cases of Prostatitis

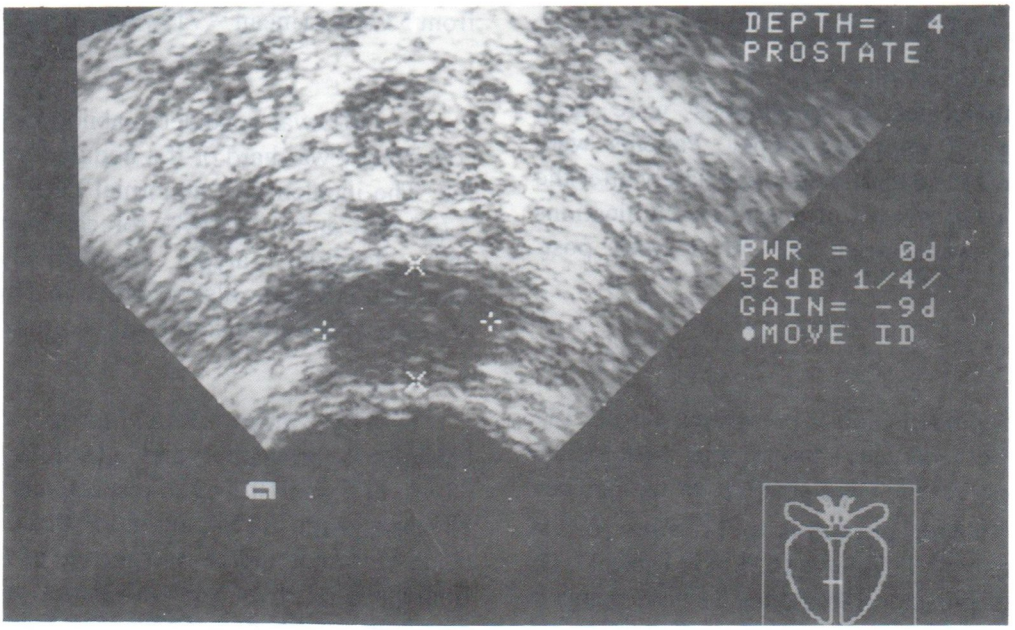

Fig. 2: Early Prostatic Carcinoma

Axial TRUS scan shows well defined hypoechoic nodule (cursors) in PZ.

The TRUS findings are summarized in Table 3. Hypoechoic nodules were generally discrete and well defined. They were not seen in association with hyperechoic nodules nor inhomogenicities in the PZ. They were noted in 8 cases of prostate carcinoma, but also in prostatitis (3 cases), atypia (2 cases) and normals (17 cases). This makes the PPV of this finding 43.3% and 26.7% for prostate disease and prostate carcinoma respectively. 2 cases of prostatitis showed curvilinear echoes within these nodules (Fig. 1). Well defined hyperechoic nodules were not a feature of prostate carcinoma, but were seen in prostatitis (3 cases), atypia (1 case) and normals (3 cases).

Inhomogenicities in the PZ were seen only in prostate carcinoma (15 cases) and normals (6 cases), giving this feature a PPV of 71.4%. Extra-capsular involvement was a finding exclusive to prostate carcinoma (9 cases), giving it a 100% PPV.

To correlate TRUS findings with extent of involvement and PSA levels the carcinoma group was further divided into 3 subgroups based on TRUS findings, i.e. Groups I (normal TRUS), II (well defined hypoechoic nodules) (Fig. 2) and III (poorly defined areas of mixed echogenicity) (Table 4). All 9 cases with extra-capsular involvement were in Group III (Fig. 3 and 4). The mean PSA levels in these subgroups were 168.4, 408 and 736 ng/ dl respectively. 5 cases posted PSA levels of greater than 999.9 ng/ dl. All 5 were found in Group III.

A total of 524 prostate quadrants were biopsied, each of the 131 patients receiving a 4 quadrant biopsy. The 69 biopsies directed at focal lesions seen on TRUS yielded positive results in 58 quadrants (84.1%) (Table 5). Random biopsies directed at the other 455 "uninvolved" quadrants were positive in 61 (13.4%). In terms of absolute cases, TRUS missed the diagnosis (i.e. the diagnosis was made solely from the random biopsy) and underestimated the extent of involvement in 4 and 7 cases of carcinoma, 2 and 5 cases of prostatitis and 6 and 7 cases of atypia respectively.

As for post biopsy complications, 23 patients (17.6%) felt mild pain during the procedure. 4(3%) experienced pain following the procedure. 2 patients (1.5%) developed a urinary tract infection after the biopsy. Both resolved with antibiotic treatment alone. 12 (9.1%) developed gross haematuria not requiring transfusion, of which 1 required catheterisation due to clot retention. All cases resolved spontaneously.

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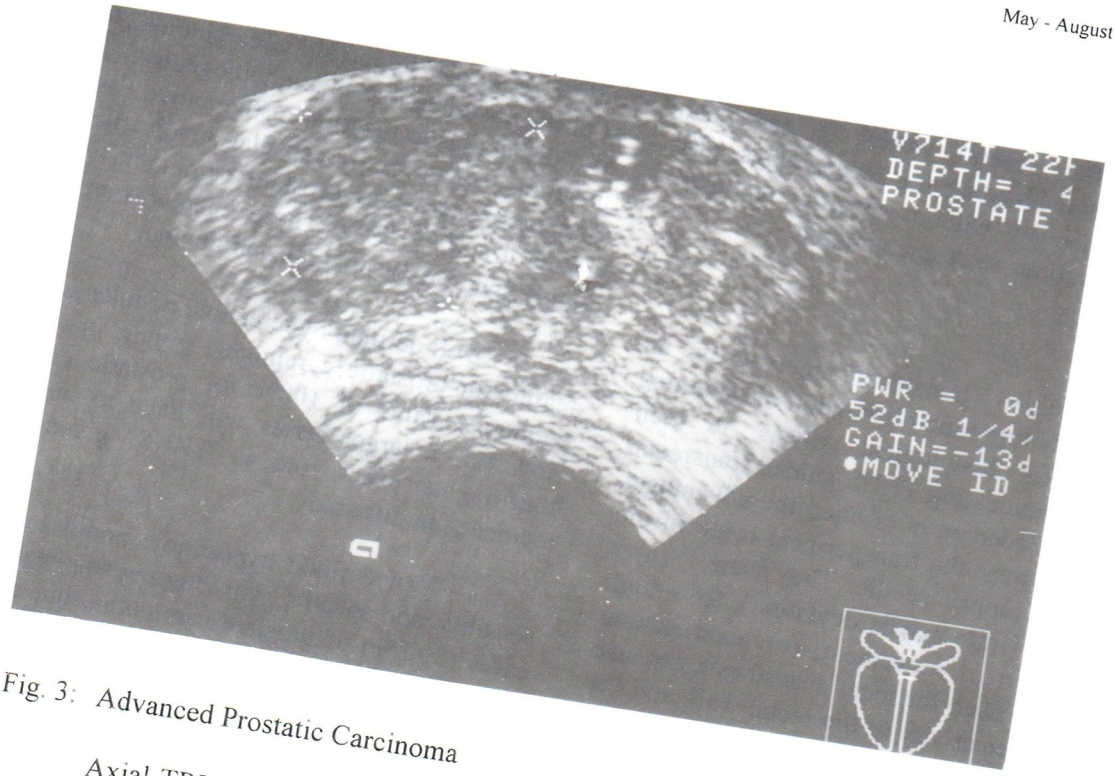

Fig. 3: Advanced Prostatic Carcinoma

Axial TRUS scan shows a poorly defined heterogeneous area (cursors) the (R) PZ, invading into the TZ anteromedially and distorting the prostatic capsule.

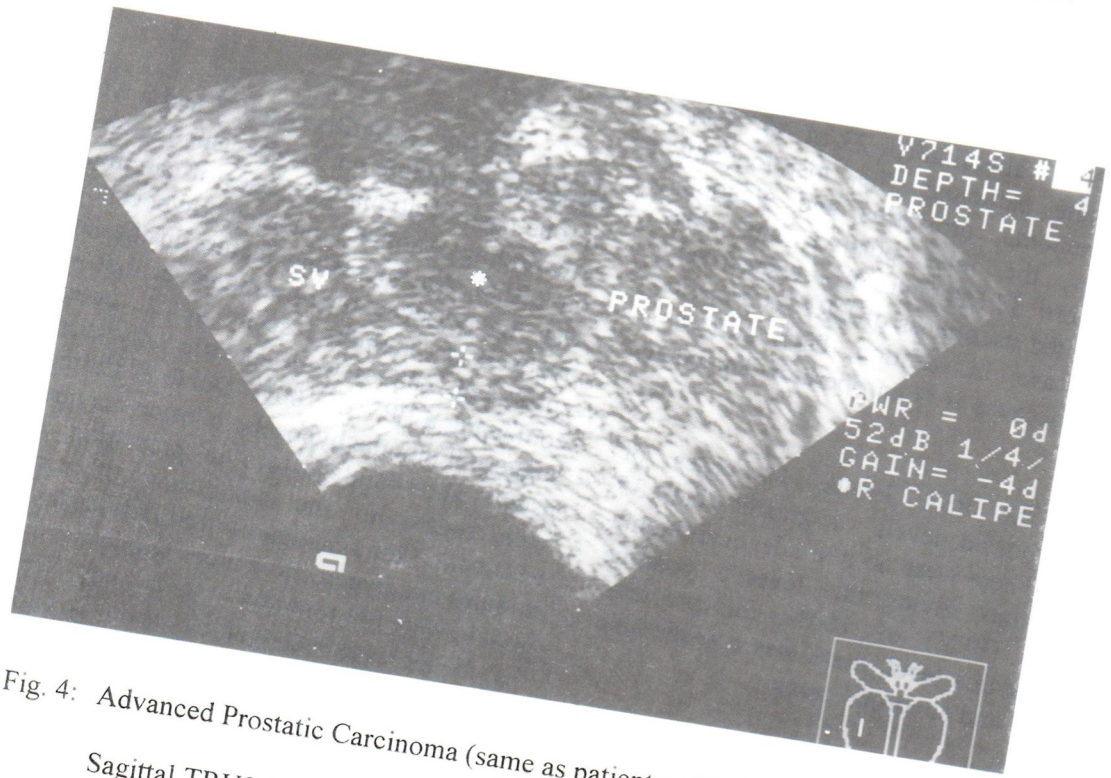

Fig. 4: Advanced Prostatic Carcinoma (same as patient as Fig 3).

Sagittal TRUS scan same area along the superior aspect of the PZ (asterisk), causing obliteration of the distal end of the seminal vesicles (cursors).

There was 1 case of haemospermia, also resolving spontaneously after several weeks. 1 case had continued per rectal bleeding for several days, also resolving spontaneously without specific treatment. No major complications were encountered.

DISCUSSION

TRUS guided transrectal biopsy is an accurate and highly reproducible method of obtaining prostatic tissue for histological anlysis. In their landmark article advocating TRUS guided transrectal biopsy (2), Torp-Pederson et al cited the advantages of the transrectal over the transperineal route in the placement of the biopsy needle. They were " (a) a short needle path (little needle deviation), (b) a high degree of freedom of movement, (c) good patient tolerance and no need for local anaesthesia because of the relative insensitivity of the rectal wall, and (d) a quick procedure (no skin preparation, no local anaesthetics)."

Our high success rate in obtaining adequate tissue sample reflects the efficacy of the procedure.

This increased availability of histological data in turn provided a gold standard by which we could correlate the DRE, PSA and TRUS findings.

The DRE was abnormal in 23 of 46 (50%) cases with prostate pathology (i.e. histologically proven adenocarcinoma, prostatitis and glandular atypia). However, the false positive and false negative rates were 37.6% and 50% respectively, reflecting the limited usefulness of DRE as a marker for prostatic disease. In addition, DRE suffers a major drawback because it is an operator dependent assessment.

As for the PSA levels, 18 cases of adenocarcinoma posted levels of greater than 35 ng/ml (Table 2). There were no non adenocarcinoma cases in this group, giving this level a positive predictive value (PPV) of 100% for prostatic carcinoma. Below this level, there was considerable overlap of normal and abnormal cases.

In terms of the TRUS findings of prostatic carcinoma, the PZ was the commonest site of involvement, all cases with positive TRUS findings having their lesions sited here (Table 3). Poorly defined inhomogenicities in the PZ was seen in 15 cases of prostatic carcinoma and 6 normals, yielding a PPV of 71.4% for prostatic carcinoma. Greenberg et al (9) postulate that this inhomogenicity is a result of a desmoplastic reaction of the native tissue to the invading cancer. Extra-capsular involvement was a finding exclusive to prostate carcinoma (9 cases), giving it a 100% PPV. These 3 features as such, are highly specific for prostatic carcinoma.

Well defined hyperechoic nodules were not a feature in prostatic carcinoma, giving it a negative predictive value of 100% for prostatic carcinoma. However, a larger series will have to be done to confirm its exact role in TRUS, given its low incidence in this study.

Well defined hypoechoic nodules were less sensitive and specific. This finding was featured in 8 cases (30.8%) of prostate carcinoma, but also in 20 normals (23.5%). However in the presence of a positive DRE and/ or a raised PSA, this finding is more indicative of early, rather than late, disease. This was confirmed when we compared all cases with this finding against those with poorly defined inhomogenicities in the PZ (Table 4), the former group (i.e. Group 2) having a lower mean PSA and quadrant involvement than Group 3. In addition, Group 2 cases did not post evidence of extra-capsular spread.

Of the prostatitis cases, 3 had a well defined hyperechoic nodule on TRUS. This feature was seen in one case of atypia. No cases of carcinoma posted this finding. Another 3 cases had hypoechoic nodules on TRUS. An interesting feature in the latter group was the presence of culvillinear echoes within the hypoechoic nodules, seen in 2 cases. These curvilinear echoes were specific only to prostatitis, conferring a PPV of 100%. Doble & Carter (10) had suggested that the hypoechoic lesion may be the most useful ultrasound feature in prostatitis, especially with regard to the monitoring of response to treatment. Our findings of well defined hyperechoic nodules and hyperechoic areas within the hypoechoic nodule were not reported in their study. We postulate that the increased echogenicity is due to early abscess formation in the former group, and to debris within a liquified abscess in the latter. While the number of such cases is small, we suspect that these findings will be a useful marker for prostatitis and will be reporting on this in a future article.

Our analysis of directed versus random biopsies show that directed biopsies provided the diagnosis in 34 cases (Table 5). Random biopsies provided the diagnosis in 12 cases. As such, these 12 cases would have been dismissed as negative had only directed biopsies been performed. Shinohara et al (11) postulate that any disease process that insinuates between normal prostate tissue can contain many echo-reflective interfaces and thus appear isoechoic on TRUS. These findings justify the need for random biopsies of benign looking quadrants (12).

No major complications were encountered. The 2 commonest were intraprocedural pain (17.6%) and mild haematuria (9.1%), findings which to those from other studies (4).

CONCLUSION

TRUS guided transrectal biopsy of the prostate is a safe procedure with a low complication rate, and high patient acceptance. It's utility in management is based on the patient's symptoms.

1. For those presenting with fever and/ or pain referable to the prostate, where prostatitis is the issue in question, the following is recommended:

(A) There is no need for transrectal biopsy in the first visit. If a focal lesion is detected, repeat TRUS should be performed after a course of antibiotics.

(B) Biopsy is recommended only if a focal lesion persists on follow up TRUS.

2. For those presenting with prostatism and/ or haematuria, where prostatic carcinoma is the issue in question, the following flow chart is recommended:

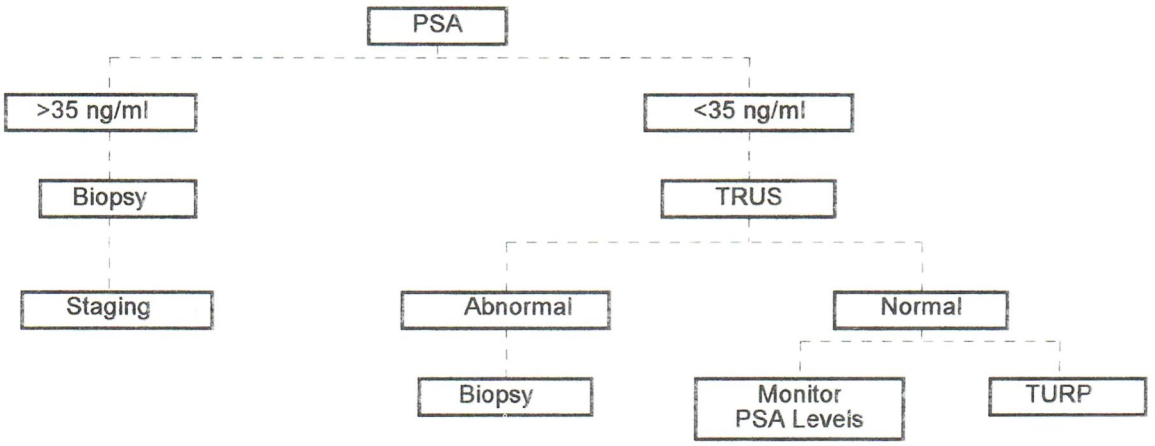

TABLE 1: DRE, PSA and TRUS Findings of the Different Histological Groups

Histology	No. of Cases (%)	AbN DRE (%)	PSA (ng/dl)	AbN TRUS (%)
Carcinoma	26 (19.8)	16 (62)	339.4	21 (80.8)
Prostatitis	11 (8.4)	3 (27)	17.7	6 (54.5)
Atypia	9 (6.9)	4 (44.4)	10.1	3 (33.3)

TABLE 2: Incidence of Cases Classified under PSA Range for Different Histological Groups

PSA Range	No. of Patients (n=115)	No. with Carcinoma (n=26)	No. with Prostatitis (n=8)	No. with Atypia (n=8)	Normals (n=73)
>35 ng/ml	18 (16%)	18 (69%)	0	0	0
4-35 ng/ml	53 (46%)	6 (23%)	7 (88%)	5 (63%)	35 (48%)
0-4 ng/ml (normal)	44 (38%)	2 (8%)	1 (12%)	3 (37%)	38 (52%)

TABLE 3: TRUS Findings and their incidence in the Different Histological Groups

TRUS FINDING	No. of Carcinoma Patients	No. of Prostatitis Patients	No. of Atypia Patients	No. of Normal Patients
Hypoechoic Nodule	8	3	2	17
Hyperechoic Nodule	0	3	1	3
Inhomogenicity in PZ	15	0	0	6
Extracapsular Breach	9	0	0	0

TABLE 4: TRUS and PSA Findings of Prostate Carcinoma Subgroups

Prostatic Carcinoma Subgroup	No. of Cases	TRUS Findings	Extracapsular Breach	Mean PSA (ng/ dl)
1	5	Normal	-	168.4
2	8	Well defined hypoechoic nodule	-	408
3	13	Poorly defined heterogenous areas	9	736

TABLE 5: Histological Diagnosis of Directed vs Random TRUS Guided Transrectal Biopsies Performed on 524 Quandrants

Biopsy	Nodule on TRUS	Histology				
		Carcinoma	Prostatitis	Atypia	Normal	Total No. of Quandrants
Directed	+	48	6	4	11	69
Random	-	33	21	7	394	455
Total		81	27	11	405	524

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