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THE SIGNIFICANCE OF HYPOECHOIC LESION DIRECTED AND TRANSITION ZONE BIOPSIES IN IMPROVING THE DIAGNOSTIC ABILITY IN PROSTATE CANCER

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ABSTRACT

Contemporarily, systematic peripheral zone (PZ) biopsies under transrectal ultrasonography (TRUS) guidance are the standard procedure in the diagnosis of prostate cancer. Although, it is widely accepted that the most common appearance of cancer tissue is hypoechoic nodule in the PZ, the diagnostic yield of additional lesion directed biopsies is the subject of debate. Similarly, the place of routine application of transitional zone (TZ) biopsies is not clear. In this study, the diagnostic contribution of lesion directed and TZ biopsies into systematic PZ biopsies were assessed.

A total of 271 patients were admitted to the outpatient department with lower urinary tract symptoms underwent TRUS guided prostate biopsies owing to elevated prostate specific antigen (PSA > 4 ng/ml) and/or abnormal digital rectal examination findings.

All biopsies were performed with a systematic approach (3 specimens taken from the base, midgland, apex of the right and left sides of PZ) and hypoechoic lesion directed biopsies plus systematic random TZ biopsies (one core taken from each side). Prostate cancer was detected in 89 patients (32.8%) undergoing biopsy. The sonographic appearance of hypoechoic PZ lesions was observed in 120 patients.

Of the patients with carcinoma, 66.3% (59/89) had hypoechoic PZ lesions. Among the patients hypoechoic PZ lesions on TRUS 49.2% (59/120) revealed carcinoma on biopsy, whereas 33.7% of patients (30/89) harboring cancer demonstrated no sonographic abnormalities. In contrast, among the 55.7% of men (151/271), who had no hypoechoic PZ lesions on TRUS, 20% had cancer. Only 3 patients had their cancer found uniquely in the biopsy sample taken from the hypoechoic PZ lesion with negative systematic PZ biopsies. Consequently, 3.4% of cancer cases would have been missed in the absence of the lesion directed biopsies. On the other hand, the cancer detection rate on systematic biopsy within the TZ was 1.5%; in all of these cases systematic biopsies from PZ also positive.

As a conclusion, although the detection rate of lesion directed biopsies was low, since insertion of an additional needle bears very little infliction for the patient, it is justified to perform lesion directed biopsies. On the other hand, TZ biopsies had no significant yield in cancer detection in patients undergoing initial systematic TRUS guided biopsy.

Key words: prostatic neoplasms; biopsy; diagnosis; ultrasonography
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INTRODUCTION

Transrectal ultrasonography (TRUS) provides significant information regarding the internal architecture and detailed anatomy of the prostate gland while it enables precise insertion of biopsy needle into relevant regions of the gland for the performance of strategic biopsies. Currently, systematic sextant biopsies consisting of three biopsies (base, midgland and apex) from each half of the gland under TRUS guidance is the standard procedure in the diagnosis of prostate cancer in the case of abnormal

digital rectal examination and/or elevated prostate specific antigen (PSA) (1,2).

Although, the lack of sufficient specificity and sensitivity of the classic sonographic findings of prostate cancer has been observed by numerous investigators, research results seem to indicate that majority of cancers are represented by hypoechoic peripheral zone (PZ) lesions on TRUS imaging (3). However, the diagnostic yield of additional lesion directed biopsy is the subject of debate.

On the other hand, the majority of prostate cancers arise in the PZ. However, detailed studies have suggested that up to 24% of prostate tumors originate in transitional zone (TZ) (4). However, the role of routine application of TZ biopsies is not clear.

The aim of this study was to define the diagnostic contribution and significance of TRUS guided biopsies from hypoechoic PZ lesions, and systematic TZ biopsies in diagnosing prostate cancer.

MATERIAL AND METHODS

A total of 271 patients initially being evaluated for lower urinary tract symptoms subsequently underwent TRUS guided prostate biopsies due to either elevated PSA (> 4 ng/ml) and/or abnormal digital rectal examination findings. The histopathological results were retrospectively analyzed.

All patients diagnosed as having prostate cancer through TRUS (Bruel & Kjaer 1849 or 1846 ultrasound units, Bruel & Kjaer, Naerum, Denmark; with a 7.5 = MHz multiplane endosonic transducer) guided biopsy using an 18-gauge needle with the Bard Biopty® gun (CR Bard, Covington, GA, USA). All biopsies were done as an outpatient procedure under antibiotic prophylaxis starting the day before the biopsy and continued for 3 days. Additionally, a single operator who is an urologist specially trained in uroradiology with an experience of 5 years performed all biopsies.

All biopsies were achieved with a systematic approach (3 specimens taken from the base, midgland, apex of the right and left sides of PZ) and hypoechoic lesion directed biopsies plus systematic TZ biopsies (one core taken from each side). However, we inserted needle into the PZ thoroughly to increase amount of tissue as a slight modification, so that laterally placed parasagittal biopsies were performed. Hypoechic lesions were identified as areas which had less reflection of the sound images than the normal PZ initially noticed as a uniform midgray image.

RESULTS

Prostate cancer was detected in 89 patients (32.8%) undergoing biopsy. The sonographic appearance of hypoechoic PZ lesions was observed in 120 patients (one in each patient). All these hypoechoic lesions were separately sampled.

Of the patients with carcinoma, 66.3% (59/89) had hypoechoic PZ lesions (Table-1). Among the patients hypoechoic PZ lesions on TRUS 49.2% (59/120) revealed carcinoma on histopathological examination, whereas 33.7% of patients (30/89) harboring cancer demonstrated no sonographic abnormalities. In contrast, among the men (151/271) who had no hypoechoic PZ lesions on TRUS, 20% (30/151) had cancer.

The histopathological results of lesion directed biopsies revealed cancer in 15.8% (19/120) of the cases (Table-2).

Only 3 patients had their cancer found uniquely in the biopsy sample taken from the hypoechoic

Table 1 *- The ratio of hypoechoic lesions on TRUS and subsequent percentage of prostate cancer after the biopsy in 271 patients with lower urinary tract symptoms.*

	Positive	**Negative**	**Total**
Hypoechoic lesion (%)	120 (44)	151 (66)	271 (100)
Subsequent prostate cancer (%) (after histological confirmation)	59 (66)	30 (44)	89 (100)

Table 2 - *Distribution of prostate cancer cases (n = 9) according to results of lesion directed biopsies.*

	Prostate Cancer Detection (%)
Lesion + systematic biopsies	16 (18)
Distinctly in systematic biopsies	70 (78.6)
Distinctly in lesion biopsies	3 (3.4)
Total	89 (100)

PZ lesion. Consequently, 3.4% of cancer cases would have been missed in the absence of the lesion directed biopsies.

On the other hand, the cancer detection rate on systematic biopsy within the TZ was 1.5% (4/271); in all of these cases, however, systematic biopsies from PZ were also positive.

DISCUSSION

The ability to guide the biopsy needle precisely into the regions of interest together with perfect separation of the areas sampled has resulted in performance of most prostate biopsies by TRUS guidance all over the world. Contemporarily, TRUS guided biopsy has become the gold standard method for prostate biopsy. Although limited in number, the studies regarding the comparison of the yield of digitally directed biopsy versus under TRUS guidance provided sufficient information on the superiority of the latter method. It was demonstrated that the ratio of cancer was 9% in men with negative digitally guided biopsies (5). In another study, carcinoma was detected by TRUS guided biopsies in each men who had positive digitally guided biopsy, whereas the cancer detection rate was 17.6% for digitally guided biopsy and 45% for TRUS guidance in men with palpable lesions on digital rectal examination (6). In addition, it is known that 25 to 50% of cancers would be missed if only hypoechoic lesions are biopsied (7).

Although, all these results confirm that TRUS guided prostate biopsy consisting of systematic PZ biopsies must be the standard approach in the diagnosis of prostate cancer, the diagnostic yield of hypoechoic PZ lesions and random TZ biopsies have been the subject of ongoing debate. This is mainly because there is no adequately specific appearance of prostate cancer on TRUS. Although, most commonly accepted appearance for prostate cancer is a hypoechoic lesion on PZ, it is known that the hypoechoic lesions are not cancer specific. Unlike sonographic images of other organs, such as liver and thyroid, hypoechoic lesions of the prostate do not always imply a specific pathological status. Although, majority of prostate adenocarcinomas is hypoechoic, other diseases may also reveal same appearance (2). Prostatic abscesses, cystic atrophy, some vascular structures, dysplasia, transitional cell carcinoma involving prostate, and even benign hyperplasia may also appear hypoechoic (8-11). These drawbacks of TRUS explained the insufficient specificity of hypoechoic lesions and importance of random systematic biopsies. The lack of specificity of TRUS appearance for prostate carcinoma has been observed by numerous investigators reporting that 20 to 40% of prostate cancers are isoechoic or nonvisible on TRUS (12,13). Carter et al. demonstrated that 50% of nonpalpable cancers more than 1 cm in greatest dimension are not visualized by ultrasound (14). Nevertheless, Lee et al. clearly demonstrated that the most common appearance for cancer is a hypoechoic PZ lesion (3). However, their study would be criticised as being performed in pre-PSA era and concerning larger lesions. On the other hand, the present study confirms that the most common appearance of prostate cancer is a hypoechoic PZ lesion found in 66.3% (59/89) of cancer cases. Among the patients with hypoechoic lesions on TRUS 49.2% (59/120) revealed carcinoma on biopsy, where as only 20% (30/151) of cases who had no hypoechoic lesions diagnosed cancer on biopsy. On the other hand, the ratio of isoechoic cancer was 33.7% (30/89). Also it was shown that histopathological results of lesion directed biopsies alone revealed cancer only in 15.8% (19/120) of the

cases. Consequently, most of the cancer cases (79%; 70/89) would be missed if only hypoechoic lesions were distinctly biopsied omitting systematic biopsies. On the other hand, only 3 patients had their cancer found uniquely in the biopsy sample taken from the hypoechoic PZ lesion. Subsequently, 3.4% of cancer cases would have been missed in the absence of the lesion directed biopsies. In a similar study, only 3 among 83 cancers would have been missed if no lesion directed biopsies were performed (1). Since, TRUS guided biopsy remains as an easy, rapid, and well tolerated procedure with considerably low morbidity, insertion of an additional needle for the lesion directed biopsy does not add further morbidity. In other words, since additional one or two biopsies bear very little infliction for the patient, it is justified to perform lesion directed biopsies in order to avoid at least 3% risk of missing cancer in the prostate.

Our study revealed the cancer detection rate by biopsy within the TZ as 1.5% (4/271); but, in all of these cases systematic biopsies from PZ were also positive. Bazinet et al. found cancer localized only to TZ in 1% of 847 patients undergoing routine TZ plus systematic biopsies (15). Similarly, Terris et al. reported cancer only in the TZ in 0.6% of 161 patients having routine TZ biopsies (16). They also stated that routine TZ biopsy is not warranted initially. Fleshner & Fair suggested the use of TZ biopsies in patients with previously negative TRUS guided biopsies (17).

In conclusion, in evaluation of a patient for prostate cancer, finding of a sonographic abnormality as a hypoechoic lesion on TRUS indicates lesion directed biopsy, since hypoechoic PZ lesion remains as the most common appearance of carcinoma and insertion of an additional needle bears almost no impairment for the patient. TRUS guided biopsy of hypoechoic lesions in addition to isoechoic regions in the sextant distribution improves the diagnostic yield of the procedure. In the absence of lesion directed biopsies and relaying on systematic biopsies would miss 3.4% of cancer cases according to our results. On the other hand, in our clinical settings performance of random TZ biopsies had no significant yield in cancer detection in patients undergoing systematic TRUS guided biopsy at first time.

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EDITORIAL COMMENT

The authors report the significance of prostatic biopsies directed to hypoechoic lesions and transitional zone in 271 patients that underwent TRUS guided sextant biopsies owing to elevated PSA and/or abnormal digital rectal examination findings.

The cancer detection rate on systematic biopsy within the TZ was 1.5%. However, in all of these cases, biopsies from the PZ were also positive. On the other hand, only 3 patients had their cancer found uniquely in the biopsy sample taken from the hypoechoic PZ lesion.

Systematic sextant biopsy of the prostate under TRUS guidance, introduced just over 10 years ago, has revolutionized our ability to detect carcinoma of the prostate. Prior to systematic sampling, prostate biopsies were usually performed under digital guidance and directed at palpable nodules.

The current knowledge of the published data and the results of this study do not support the use of only hypoechoic lesion biopsy. The authors showed that 60% of cancers would be missed if only hypoechoic lesions were biopsied.

Accordingly to the authors conclusion, routine TZ biopsies are discouraged, except in patients in whom negative sextant biopsies fail to reveal cancer but in whom there is indications for repeat biopsy.

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