PROSTATE CANCER DIAGNOSTIC METHODS IN KORLE BU TEACHING HOSPITAL, ACCRA, GHANA

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Abstract

Objective: The diagnosis of prostate cancer is based on a combination of digital rectal examination (DRE), serum prostate specific antigen (SePSA) estimation and trans-rectal ultrasound guided biopsy (TRUS-B) of the prostate, the latter being the gold standard for prostate cancer diagnosis. This study compared the diagnostic rate of prostate cancer in patients attending the urology clinic at Korle-bu Teaching Hospital, Accra, Ghana, using these methods.

Patients and Methods: One hundred and fifty male patients 45 years and older with abnormal DRE and raised or rising SePSA had TRUS biopsy done. The biopsies were processed routinely and all cancer positive slides were graded using the Gleason scoring system. DRE findings were comparatively analysed statistically against SePSA and histological findings.

Results: Of the 150 subjects, 71(47.3%) were diagnosed as benign and 79(52.7%) had cancer on TRUS-B. Cancer diagnosis rate using a combination of DRE and SePSA was slightly higher (66.4%) than using DRE (64.5%) or SePSA (53.7%) in isolation.

***Conclusion*:** DRE was found to have a high positive predictive value, probably due to the late presentation of majority of the patients in this study. SePSA alone is not very reliable, and results must be interpreted with caution due to significant false positive rates. Combining DRE and SePSA improves cancer diagnosis rates.

Key Words: DRE, SePSA, TRUS-biopsy, prostate cancer

Introduction

Prostate cancer is currently regarded as the most common cancer in men and the second leading cause of cancer related deaths in men in the United States of America[1, 2]. The diagnosis of prostate cancer is based on a combination of digital rectal examination (DRE), serum prostate specific antigen (SePSA) estimation and trans-rectal ultrasound guided biopsy (TRUS-B) of the prostate. DRE has been found to have a poor rate of early cancer detection, but is more useful in diagnosing and staging locally advanced cancer[3, 4]. SePSA estimation detects more tumours and at an earlier stage than DRE[5, 6]. However, an elevated SePSA is not necessarily specific for cancer, because SePSA has been found to be elevated in some benign diseases of the prostate also[7, 8]. In some cancers the SePSA is normal or lower than the traditional limit of 4ng/ml[5, 6,7]. TRUS-B is said to be the gold standard of diagnosis with a very high sensitivity[9], although a cancer may be missed by biopsy due to inadequate sampling[9, 10]. Because of these individual limitations, it is recommended that these three tests be used in combination in order to improve the diagnosis of prostate cancer[7, 11]. The objective of this study was to evaluate and compare the diagnosis rate of prostate cancer, using DRE or SePSA in isolation and also in combination, in patients attending the urology clinic at Korle-bu Teaching Hospital (KBTH), Accra, Ghana.

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SUBJECTS AND METHODS

The study was a prospective study involving male outpatients aged 45 years and older referred to the Korle-bu Teaching Hospital Urology Clinic and presenting for the first time. Many of the patients had been referred to the unit on account of lower urinary tract symptoms (urine retention, haematuria, infection). Others had been referred on account of an abnormal finding on DRE performed by a family physician, and/or an elevated total SePSA. The patients were assessed by one consultant urologist through a physical examination including DRE. Total SePSA assay was done in an accredited laboratory for all the patients. Patients were recruited into the study following the successful administration of informed consent. The study was approved by the Ethical and Protocol Review Committee of the University of Ghana Medical School and was carried out over a 4-month period. Detailed demographic and clinical data were collected on each patient including age, educational background, occupation, nature and duration of symptoms, and family history of prostate cancer.

Patients with abnormal DRE (abnormal being defined as the presence of hard, irregular, asymmetric, nodular or indurated areas), an elevated total SePSA or both underwent TRUS-B, performed by the urologist in an outpatient setting using a B&K ultrasound machine (Denmark), an 8.0 MHz end-firing transducer (BARD, USA) and an 18-gauge biopsy needle. A total of 12 biopsies were taken from the apex, mid-zone and the base of both sides of the prostate, with a minimum of two biopsies taken from each site. Any abnormal areas detected by DRE or TRUS, were incorporated into one of the six biopsy sites. The biopsies were fixed in 10% buffered formalin and processed into paraffin wax-embedded tissue blocks. The tissue was sectioned at a

thickness of 5µm. Three slides, with 3 sections on each, were prepared for each of the six biopsies. Step sections were taken at 3µm intervals to ensure adequate sampling. The sections were stained with haematoxylin and eosin and examined for the presence of cancer and other histopathological changes. All slides positive for cancer were then graded using the Gleason scoring system.

Data on age, DRE findings, SePSA results and TRUS-B results were analysed using the Statistical Package for Social Sciences (SPSS) version 10, and the results presented as simple frequency tables. PSA density and cancer diagnosis rate using each method were calculated using the following formulae:

PSA density = Total SePSA / Gland volume.

Cancer diagnosis rate = (number of malignancies/number of subjects) x 100.

RESULTS

A total of 150 patients were recruited into the study. The ages of the subjects ranged from 46 to 85 years with a mean age of 67.7 (SD 8.6) years. Majority of subjects (110, 73.4%) were between 60 and 79 years of age. Of the 150 subjects, 71(47.3%) were diagnosed as benign and 79(52.7%) had prostate cancer confirmed histologically. The ages of prostate cancer patients ranged between 49 and 84 years, with a mean of 68.2 (SD 8.6) years.

The recorded values of total SePSA in patients with prostate cancer showed a wide range between 8.3ng/ml and 6,305.0ng/ml with a mean total SePSA of 242.7ng/ml (SD 762.2). SePSA density values were obtained for 67 subjects out of the 79 with prostate cancer. The range was from 0.5 – 110.2, with a mean PSA density of 6.62(SD 17.5). The PSA density was found to be high (>0.15) in all patients with prostate cancer, and this finding was statistically significant (X^2 =5.245, p-value=0.022).

Table 1: Combined Gleason Scores in 79 prostate cancer cases

Gleason score	Frequency	Percentage
3+2 (5)	2	2.5
3+3 (6)	14	17.7
3+4 (7)	14	17.7
3+5 (8)	5	6.3
4+2 (6)	1	1.3
4+3 (7)	8	10.1
4+4 (8)	10	12.7
4+5 (9)	8	10.1
5+3 (8)	4	5.1
5+4 (9)	7	8.9
5+5 (10)	6	7.6
Total	**79**	**100**

The lowest combined Gleason score was 5 and the highest 10 (Table 1). The mean combined Gleason score was 7.61 (SD 1.23).

Only 2 subjects with prostate cancer had low grade malignancy (Gleason score 5, 2.5%). Half of the subjects with cancer had high grade malignancy (Gleason score 8-10, 50%). The remaining 37(47%) had moderate grade tumours (Gleason score 6 & 7). There was a positive relationship between the total SePSA and the Gleason score (ie, the SePSA was high in patients with a high Gleason score). However, the association was not statistically significant. (P-value = 0.053). Table 2 shows the cancer diagnosis rates using the DRE and SePSA individually and in combination. Seventy one (71) subjects out of 110 who had abnormal features on DRE alone were found to have cancer, giving a cancer diagnosis rate of 64.5%. Thirty nine (39) subjects with abnormal DRE did not have cancer on biopsy.

Table 2: Comparison of Cancer diagnosis rates using DRE and PSA

	Group	Number	Number of malignancies On TRUS-B	Cancer diagnosis rate (%)
DRE	Normal	40	8	20.0
	Abnormal	110	71	64.5
PSA	0-4	3	0	0.0
	4-10	22	2	9.1
	>10	125	77	61.6
Normal DRE				
PSA	0-4	0	0	0.0
	4-10	10	0	0.0
	>10	30	8	26.7
Abnormal DRE				
PSA	0-4	3	0	0.0
	4-10	12	2	16.7
	>10	95	69	72.6

Table 2 also shows that for a total SePSA above 10ng/ml, 77 cancers were diagnosed out of 125 subjects, giving a cancer diagnosis rate of 61.6%. However, for SePSA between 4 and 10ng/ml, the cancer diagnosis rate was found to be 9.1%. Forty eight (48, 38.4%) subjects who had SePSA elevated above 10ng/ml did not have cancer on biopsy.

Combining the two tests, no cancers were diagnosed in subjects with a normal DRE and SePSA below 10ng/ml. For those with a normal DRE and SePSA above 10ng/ml, (30 subjects) 8 cancers were diagnosed. However, in subjects with both abnormalities on DRE and an elevated SePSA, 2/12 were diagnosed with cancer and SePSA between 4 and 10ng/ml and 69/95 were diagnosed with cancer and SePSA above 10ng/m.

Table 3 shows that the cancer diagnosis rate using a combination of DRE and SePSA was higher (66.4%)

than using the DRE (64.5%) or SePSA (53.7%) in isolation.

Table 3: Cancer Diagnosis Rates in DRE and PSA

Variable	Total Number	Malignancies	Cancer detection rate
Abnormal DRE	110	71	64.5%
Elevated PSA>4ng/ml	147	79	53.7%
Both abnormal DRE and Elevated PSA>4ng/ml	107	71	66.4%

DISCUSSION

There has been great progress in the last few decades, in the investigation and treatment of prostate cancer. However, the basis for diagnosing early prostate cancer clinically remains dependent on DRE findings and elevated SePSA. Patients with abnormalities on DRE and/or an elevated SePSA are usually referred for TRUS-guided prostate biopsy.

The positive predictive value or cancer diagnosis rate of DRE in this study was 64.5%. Nwofor et al[12] also described a positive predictive value for DRE of 66.7%, in a study in Nigeria. The high positive predictive value in this study may be because many of the subjects in Ghana, as in Nigeria, present with high SePSA and abnormal features on DRE that suggest more advanced disease than subjects in other places where similar studies have been carried out[13]. DRE is therefore more useful in diagnosing late stage disease but its' usefulness in detecting early cancers is still unclear. Researchers in other settings studying the use of digital rectal examination as a screening tool have reported values of 20% and 37%[14] and in 1998 Schroder et al[15] reported that DRE has a poor predictive value for detecting early prostate cancer and should be replaced with a more sensitive test. Findings from this study which assessed the use of DRE in diagnosis of prostate cancer (and not in screening), may indirectly be in agreement with this position and suggest that DRE, though not so useful in detecting early cancers, has a reasonably good predictive value in late stage disease.

No cancers were diagnosed in subjects with SePSA below 4ng/ml. This may be due to the small number of subjects (3 out of 150, 2.0%) presenting with SePSA in this range. Other studies on prostate cancer diagnosis in men with a SePSA of 4-10ng/ml show diagnosis rates of 20-32%[16, 17]. The cancer diagnosis rate in the current study in this category of subjects was 9.1% and this low figure may again be because only 14.5% of the subjects had SePSA between 4 and 10ng/ml. The cancer diagnosis rate for subjects with SePSA above 10ng/ml, however, was 61.8%, and this compares with the findings of Ng et al[18] who reported a rate of 68% in this category of subjects in their study conducted in Sydney, Australia, and confirms that the higher the SePSA, the greater the likelihood of cancer being present. Overall, however, the cancer diagnosis rate using SePSA elevation above 4ng/ml alone was 53.7%, with an almost equal percentage of subjects with no cancer also having a SePSA above 4ng/ml. This suggests that the chances of a patient with an elevated PSA above 4ng/ml having prostate cancer, is roughly 50%. Thus, moderate elevation of SePSA may be due to benign disease of the prostate. Therefore, SePSA test results must be interpreted with caution, and patients appropriately counselled and referred for TRUS –B.

No cancers were diagnosed in subjects with normal DRE and SePSA below 10ng/ml, even though there were 10 subjects with normal DRE and SePSA in the 4–10ng/ml range. In a similar study, Ng et al[18] found that 248 out of 812 subjects with normal DRE and total SePSA less than 10ng/ml had prostate cancer. The subject population they used, as in this study, was not a screening population, but rather a highly selected group who were recruited from the hospital's urology clinic. Reasons for the negative yield in this study compared with theirs may be the small sample size and the presumed late presentation of the subjects in this study.

For subjects with abnormalities on DRE, no cancers were diagnosed in those with SePSA within the conventional normal range of 0-4ng/ml. Though this finding suggests that an abnormal DRE and a SePSA of less than 4ng/ml is not likely to be due to prostate cancer, it is difficult to draw such a conclusion as there were only three (3) subjects with these characteristics in this study. In their much larger study, Ng et al[18] found 26 cancers out of 98 subjects who had an abnormal DRE and SePSA below 4ng/ml. On the other hand, if a patient with an abnormal DRE also has a SePSA above 10ng/ml, then the likelihood of having cancer is much higher (72.6%) as shown in this study. Therefore a combination of abnormal DRE and elevated SePSA above 10ng/ml would be a strong indication for TRUS-biopsy.

In this study the cancer diagnosis rate using DRE alone was 64.5%; the rate using SePSA alone was 53.7%. When the two tests were combined, the cancer diagnosis rate increased to 66.4%. These figures indicate that more prostate cancers are diagnosed when DRE and SePSA are combined, and is in support of the findings of Ng et al[18].

CONCLUSION

The present findings suggest that DRE has a high positive predictive value in our patients, but this is probably due to the late presentation of majority of the patients. The use of DRE in detecting early cancers

remains controversial. SePSA alone is not reliable, and results must be interpreted with caution because of significant false positive rates. Cancer diagnosis rates increase when the DRE and SePSA tests are combined. These patients should be referred for TRUS-guided biopsy of the prostate and histological confirmation.

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