ORIGINAL ARTICLE

A Pilot Study On Percent Free Prostate Specific Antigen As An Additional Tool In Prostate Cancer Screening

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Abstract

A cross sectional pilot study was carried out to look into the usefulness of percent free prostate specific antigen (fPSA) in the diagnosis of prostatic cancer in HUSM patients. All patients who attended surgical clinic and admitted to surgical wards with signs and symptoms of prostate problems during the study period were taken as the study subjects. Total prostate specific antigen (tPSA) was estimated by immunoassay technique and those values of 4 ng/mL or more were proceeded for estimation of fPSA. Using the cut-off value of less than 25% fPSA for diagnosing patients with prostate cancer, our study showed that majority of the prostate cancer patients have a ratio of fPSA:tPSA more than 25% and a significantly higher level of total prostate specific antigen (P<0.005) when compared with patients with benign prostatic hyperplasia (BPH). Unexpectedly, the fPSA values were high in patients diagnosed as prostate cancer compared to BPH. Ratio of percent fPSA to tPSA was found not to be sensitive and specific, in diagnosing prostate cancer at the cut-off value of 25%. In conclusion, total PSA is a more useful biochemical test for diagnosing prostate cancer in our patients.

***Keywords*:** *Percent free prostate specific antigen, total prostate specific antigen, prostatic cancer, medical sciences*

Introduction

Prostate Specific Antigen (PSA) is a protein manufactured solely in the prostate. The prostate glands manufacture this protein in large quantities. The PSA level in the blood can vary by about 20% from day to day (1). The Food and Drug Administration (FDA) in 1994 approved serum PSA to be used as an early detection of prostate cancer. Like so many serum tumour markers, it is produced by both normal and cancerous glands. In men with prostate cancer, the serum levels can be elevated in both localized and advanced or disseminated disease. PSA levels are generally proportional to the size of the tumour. However, there is a significant overlap between PSA levels found in cancer and benign prostatic hyperplasia cases (BPH) (2).

The introduction of free PSA (fPSA) testing has introduced a greater level of specificity in identifying early prostate cancer (3,4). In 1998, the FDA approved fPSA testing as a diagnostic aid for men with total PSA (tPSA) values between 4.0-10.0 ng/mL. In men without prostatic cancer, the ratio of fPSA / tPSA is more than 25%. A ratio of less than 25% is found in men with prostatic adenocarcinoma (5).

The usage of ratio of fPSA to tPSA as a tool for prostate cancer screening has not been introduced in this hospital. This could be due to lack of local evidence on the usefulness of fPSA as a screening tool for prostate cancer. This pilot study was thus, carried out to determine the benefits of introducing the test in HUSM.

Materials and Methods

A cross-sectional study was carried out beginning October 2006 until the end of December 2006 whereby all patients who attended surgical clinics and admitted to surgical wards with symptoms and signs of prostate problems were screened for PSA.

Patients' samples were initially analyzed for tPSA and results of tPSA of more than 4.0 ng/mL were further analyzed for fPSA. Total PSA and fPSA were measured using immunoassay method. The ratio of fPSA to tPSA (%fPSA) at a cut-off value of 25% was taken to suggest prostatic cancer (PCa). The clinical findings of these patients were noted and examined for correlation with the %fPSA. Statistical analyses using t-independent test were performed to investigate the potential utility of %fPSA or its combinations with tPSA in discriminating between BPH and PCa. PCa was confirmed by prostate biopsy.

Results

A total of 100 serum samples were analyzed for tPSA. The mean age of these patients were 68.2 and ranges from 45 to 90 years of age. Out of the 100 samples, 50 were noted to have serum tPSA results of more than 4.0 ng/mL. These samples which were further analyzed for fPSA had the percentage ratio ranging from 6% to 90% with a mean of 24.4% (Table 1).

Based on the 50 serum samples analyzed for fPSA, 8 samples were from patients diagnosed as PCa and 39 samples were from patients diagnosed as BPH. The other 3 serum samples were from patients diagnosed as other cancers. Table 2 shows the number of cases of PCa and BPH when 25% cut-off value of %fPSA was implemented.

Table 3 shows the means of tPSA, fPSA and %fPSA were significantly higher in patients with PCa as compared to patients with BPH ($p < 0.05$ for all the three assays), especially for the fPSA. Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) at 25% cut-off value of %fPSA were 50%, 41%, 14.8% and 80.0% respectively.

Discussion

Total PSA (tPSA) is comprised of free PSA (fPSA) and complex PSA. Although it has been used as an aid in early detection of prostate cancer (PCa), it is not an ideal tumour marker (6) as it lacks specificity to diagnose PCa. Because of this lack in specificity, many researchers have tried using free and complex PSA to improve the clinical value of PSA.

Different methods to differentiate PCa from BPH have been developed such as using human glandular kallikrein which displays a structural homology to PSA (7), PSA complexed to a1-antichymotrypsin (8) and the use of percentage fPSA (9,10).

Free PSA constitutes approximately 20% of the total PSA, and is found to be in abundance in patients with BPH (6). In PCa, fPSA:tPSA ratio has been recommended as an effective tool for screening (9). The ratio, expressed in the form of percentage, enhances the specificity of PSA testing

Table 1 : Range, median and mean of Prostate Specific Antigen measured in study samples

Group	Parameter	Mean ± SD	Median	Range
Total Serum Samples (N=100)	tPSA (ng/mL)	13.54 ± 21.95	4.00	1.0 — 101.0
Samples with serum tPSA > 4ng/mL (N=50)	tPSA(ng/mL)	24.84 ± 26.68	13.00	4.0 — 101.0
	fPSA (ng/mL)	6.24 ± 10.29	3.00	1.0 — 51.0
	%fPSA	24.46 ± 15.61	21.50	6.0 — 90.0

Note: tPSA = total prostate specific antigen
fPSA = free prostate specific antigen
%fPSA = the ratio of free to total PSA in percentage

Table 2 : Final diagnosis of the patients based on cut-off value of 25% fPSA [Benign prostatic hyperplasia (BPH), prostate cancer (Pca) and others cancers (Others)]

%PCa	No of Patients (%)			
	PCa	BPH	Others	Total
<25%	4 (8)	23 (46)	2 (4)	29 (58)
>25%	4 (8)	16 (32)	1 (2)	21 (42)
Total	8 (16)	39 (78)	3 (6)	50 (100)

Table 3 : The means of tPSA, fPSA and %PSA in prostate cancer (PCa) and benign prostatic hyperplasia (BPH) patients.

Parameters		Mean ± SD	Median	Range
tPSA(ng/mL)	**PCa**	49.50 ± 34.66	3.249	0.002
	BPH	19.26 ± 21.44		
fPSA (ng/mL)	**PCa**	19.75 ± 20.57	4.747	0.000
	BPH	3.67 ± 3.49		
%fPSA	**PCa**	37.38 ± 30.69	2.576	0.013
	BPH	22.36 ± 9.67		

for prostate cancer detection. A lower percent fPSA is associated with a higher probability of PCa (11). In our laboratory, percent fPSA is not used to aid the diagnosis of prostate cancer, perhaps due to lack of local evidence that support this notion.

This pilot study looked into the common biochemical tests used such as tPSA and fPSA and their usefulness in diagnosing and differentiating between PCa and BPH in our surgical patients.

In our study, tPSA which is used widely seems to be the most useful indicator in differentiating between PCa and BPH whereby the mean tPSA was significantly higher ($t = 3.249$, $df = 45$, $P<0.005$) in PCa compared to BPH.

Free PSA values in patients with PCa were also noted to be significantly higher ($t = 4.747$, $df= 45$, $P<0.001$) than in patients with BPH resulting in higher fPSA:tPSA ratio in PCa patients.

When the cut-off value of 25% fPSA was implemented to differentiate between PCa and BPH, %fPSA was found to be neither sensitive nor specific for diagnosing PCa. Free PSA and %fPSA failed to discriminate efficiently between PCa and BPH. An attempt to look at different cut-off value also failed to produce significant results. Other researchers, however, published contradictory results (6,12) whereby a cut-off value of fPSA below 25% was found to be associated with PCa.

In conclusion, the results of our study indicate that only tPSA is useful as an indicator of PCa. However, since many research found that a combination of tPSA, fPSA and %fPSA results could aid in diagnosis and provides an opportunity to reduce the demand for biopsy in doubtful cases of PCa, this study may need to be extended to include larger sample size involving other centers (9,11,13). It is recognized that the small sample size, especially the PCa patients involved in this study could be the main reason why the results were not significant. Although this study did not look at complex PSA, this option should be considered in future studies as an alternative tool in diagnosing PCa.

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