Assessment of the Performance of Specific Prostate Diagnostic Tools in the Detection of Prostate Cancer among Ghanaian Men

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Authors' contributions

This work was carried out in collaboration between all authors. Author AYF contributed to the conception of the research idea. Author AK designed the study. Author GSKC contributed to the conception of the design, data collection and revision. Author LEF reviewed the drafted paper drafting and revision. Author AE manage recruitment and data collection and wrote the first draft of the manuscript. Author TFB contributed data collection. Author OAE contributed to the conception of data analysis. Author BNE contributed to data analysis and revision. Author AB contributed to data collection. All authors read and approved the final manuscript.

Article Information

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ABSTRACT

Aims: This study evaluated the individual and combined performances of specific prostate diagnostic tools in the detection of prostate cancer among Ghanaian men.
Study Design: A hospital-based cross-sectional prospective study.

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Place and Duration of Study: Department of surgery (urology unit) Komfo Anokye Teaching Hospital (KATH) from December, 2014 to November 2015.

Methodology: A total of 241 patients suspected of having prostate cancer (PCa) due to abnormal digital rectal examination (DRE) and, or elevated prostate specific antigen (PSA) level underwent Trans rectal ultrasonography guided biopsy of the prostate. Evaluation of PSA, Prostate Specific Antigen Density (PSAD), DRE, prostate volume was done using receiver operating characteristics curve analysis These four diagnostic tools were combined into a single score to improve the diagnostic performance.

Results: Prostate cancer was diagnosed in 63 patients out of 241 (26.1%). Significantly elevated levels of PSA and PSAD were observed among patients with PCa compared to patients without PCa. PSAD showed better accuracy (AUC= 78.9) followed by PSA (AUC=77.8) and DRE (AUC=68.6) respectively for the individual diagnostic tools. PSAD had sensitivity and specificity of 84.1% and 56.7% respectively. Among the different combination of diagnostic tools, bioscore combination of DRE+PSAD+PSA had better accuracy (AUC=80.6) followed by PSAD+DRE (AUC=78.1) PSA+PSAD+DRE+ Prostate Volume (AUC= 76.7), and for PSAD+PSA (AUC=71.5) respectively. PSA on its own had a sensitivity of 98.4% and specificity of 16.3% respectively. The best statistically significant (p<0.05) odds ratio (OR) for the combination of PSAD+DRE was 33.40 followed by PSA+PSAD at 19.52 and PSA+DRE at 13.67 respectively.

Conclusion: Combined diagnostic performance of DRE+PSAD+PSA poses a better diagnostic accuracy. Bioscores for the combination of the diagnostic tools were significantly associated with increasing odds of prostate cancer detection upon logistic regression analysis. Further studies are required to evaluate the combine diagnostic performance in larger population.

ABBREVIATIONS

PCa   : *Prostate Cancer*
PSA   : *Prostate Specific Antigen*
DRE   : *Digital Rectal Examination*
PSAD : *Prostate Specific Antigen Density*
BPH   : *Benign Prostatic Hyperplasia*
AUC   : *Area Under Curve*
KATH : *Komfo Anokye Teaching Hospital*
ROC   : *Receiver Operating:Characteristics*
TRUS : *Trans Rectal Ultrasonography*

1. INTRODUCTION

Cancer of the prostate (PCa) is the sixth leading cause of mortality and second most frequently diagnosed cancer among males globally [1]. The worldwide incidence rates vary considerably among different regions with the highest incidence noted among males from advanced countries which was attributed to the utilization of the prostate specific antigen (PSA) test as a screening tool [2,3]. The incidence and mortality rates in black American men is almost twice those of white American men and 5 times higher than those of Asian men living in Asia [4]. The discovery of PSA has revolutionized the management of PCa as it has immensely contributed to the early detection of the disease [5,6]. The presence of an abnormal digital rectal examination (DRE) or an elevated PSA level (>4.0 ng/ml) is currently used to select men for prostate biopsy [7,8]. Previous study conducted among the Ghanaian population observed that 83.6% of the subjects had their PSA levels above the upper limit of the reference range (4.0 ng/ml) with their ages ranging between 56 to 85 years [9]. Previous studies have also explored the sensitivity(21%) and specificity (86%) of DRE as a diagnostic tool in detecting prostate cancer [10]. Although, PSA is routinely used as a marker in assessing PCa and other prostate related conditions, various studies have indicated that, it lacks adequate specificity but has better sensitivity. Management of patients with increased levels seem to be controversial since it is elevated in benign pathologies like prostatitis and benign prostatic hyperplasia (BPH) [11,12].

In an attempt to reduce unnecessary biopsies and detect PCa, several methods have been employed to improve the accuracy of PSA test, including measurement of PSA density (PSAD), transitional zone PSA density, age specific PSA, PSA velocity, free-total PSA ratio, and PSA isoforms [13-15]. PSAD was introduced to correct PSA levels associated with prostate volumes, on the basis of the fact that prostate cancers release more PSA per unit volume into circulation than BPH [16,17]. The emerging use

of the combination of DRE, PSA and PSAD for diagnosis have been shown to be promising, however these studies have mainly come from the advanced countries. Previous studies have explored the accuracy of total PSA [9,18], and DRE [19] in the Ghanaian population, however combinations of these with PSAD have received little attention. It was against this background that we explored the individual and combined diagnostic performance of PSA, PSAD and DRE in the detection of prostate cancer among Ghanaian males.

2. MATERIALS AND METHODS

2.1 Study Design/Setting

A hospital-based cross-sectional prospective study was used to assess the diagnostic accuracy of specific prostate diagnostic tools among men undergoing an initial Trans rectal ultrasound guided (TRUS) prostate biopsy at Komfo Anokye Teaching Hospital (KATH) between December, 2014 to November 2015. Komfo Anokye Teaching Hospital is a tertiary referral teaching hospital located in Kumasi, the regional capital of the Ashanti region in Ghana with a total projected population of 4,780,380 according to the Ghana Statistical Service, 2010. It is the second largest Hospital in Ghana.

2.2 Study Population/Subject Selection

Non-probability convenience sampling technique was used to recruit 241 patients visiting the urology unit at Department of Surgery, KATH. Indications for TRUS biopsy were an elevated total PSA, defined as > 4.0 ng/ml or a digital rectal examination, abnormal or suspicion of cancer, defined as the presence of a nodule, areas of induration or asymmetry in the size lateral lobes. Structured questionnaire was used to elicit socio-demographics such as age, educational status, marital status and religion. Furthermore, various identified risk factors including smoking, family history of prostate cancer, number of sexual partners, alcohol, marriage duration, hypertension, diabetes, age of first sexual intercourse, heart attack as well as rheumatoid arthritis was noted.

2.3 Estimation of PSA, DRE and Trans Rectal Ultrasound Biopsy

Prior to ultrasonography, five millilitres (5 ml) of blood was collected into a vacutainer[(R)], and centrifuged to obtain the serum used for total PSA assay. The assay was performed using the electrochemiluminiscence method (Cobas e411 Analyzer, Roche Diagnostics, Germany). Trans rectal ultrasonography was performed using an endocavitary convex probe with a 6.5MHz transducer. Measures of the triaxial distances of the prostate were taken in its larger diameter and total volume was calculated using the formula; volume 0.52 x transverse diameter x anterior posterior diameter x longitudinal diameter. The PSAD was calculated as PSA (ng/ml) divided by the prostate volume (ml) and expressed as ng/ml/ml. Value of PSAD taken to be indicative of cancer was >0.15 ng/ml/ml. Digital rectal examination (DRE) was performed on each subject by an experienced urologist. Trans rectal biopsies of the prostate were also performed by an experienced urologist with an 18-gauge automatic Tru-cut biopsy needle (Sonocare, Shanghai P.R.C) trans rectal ultrasonography. Biopsy sections were reviewed histologically by a pathologist.

2.4 Statistical Analysis

Data entry and analysis were performed using IBM statistical package for social science (SPSS) version 20. Descriptive statistics were performed for demographic variables, expressed as mean and standard deviation in the case of continuous variables with normal distribution. In case of asymmetrical distribution, the median and inter quartile (IQR) values were used. Comparisons of variables (age, prostate volume, PSA and PSAD) between the patients with and without prostate cancer were done with t-test and Mann-Whitney u-test was used to compare non-parametric values. The positive predictive value, negative predictive value, sensitivity and specificity for the test were calculated for total PSA, PSAD, DRE and test combinations. Chi Squared was used to test the differences in frequency. For evaluation of PSA, PSAD and DRE, we used the receiver operating characteristics curve analysis and areas under the curve (AUC). To determine whether the combination of these four biomarkers into a single score could improve the diagnostic performance, individual data were scored as 0 or 1 whether they were below or above the threshold previously determined with the ROC curves. This constituted the bioscore, which therefore ranged between 0 (all four markers below their respective thresholds) and 4 (all four markers above threshold). Multiple logistic-regression analysis was used to select independent predictors. P-values less than 0.05 were also considered significant.

3. RESULTS

Table 1 shows the socio-demographic characteristics of study participants. Two hundred and forty-one (241) men participated in the study with a mean age of 70.27 years. Majority (43.2%) of the subjects were between the ages of 70 – 79 years. The study population was predominantly married men (88.8%). There were more Christians (88.0%) than Muslims (12.0%). Out of the 241 subjects, 132 (54.8%) were pensioners. The average number of children each participant had was five (5). Higher proportions of the participant were educated to the tertiary level (54.8%) and only 26.6% and 18.7% had secondary and primary education respectively.

Table1. Socio-demographic characteristics of Study participants

Variables	Frequency (n)	Percentage (%)
Age (years, mean±SD)	70.3±8.3	
Age groups (years)		
50 -59	23	9.5%
60 – 69	82	34.0%
70 – 79	104	43.2%
80+	32	13.3%
Marital status		
Single	15	6.2%
Married	214	88.8%
Widower	8	3.3%
Divorced	4	1.7%
Religion		
Christian	212	88.0%
Muslim	29	12.0%
Occupational status		
Unemployed	20	8.30%
Pensioner	132	54.8%
Formal	13	5.0%
Informal	76	31.5%
Educational status		
Primary	45	18.7%
Secondary	64	26.6%
Tertiary	132	54.8%
No of Children (median, IQR)	5.0(4.0-7.0)	
Age of Sexual First Contact (mean ±SD)	20.5±2.2	

SD, standard deviation, IQR, Inter quartile range

Table 2 shows comparison of clinical, prostate related characteristics and diagnostic parameters of all participants, PCa and without PCa patients. Of 241 patients, PCa was found in 63 (26.1%) and 178 (73.9%) did not have cancer. Out of the total participants, 30 patients (12.5%) had PSA < 4 ng/ml, 23.2% had their PSA between 4.1–10 ng/ml, 16.2% had PSA between 10.1- 20 ng/ml, 33.6% had PSA between 20.1 – 50 ng/ml and 14.5% had PSA >50.0 ng/ml. The positive DREs detected among subjects were 57.7%. Higher proportion (53.9%) of all participants had PSAD >0.15 ng/ml/ml. With regards to age, majority (57.1%) of participants with cancer were between the ranges of 70–79 years. Greater proportion (46.0%) of cancer subjects were in the PSA range 20.1–50.0 ng/ml followed by >50.0 ng/ml (34.9%). Of the cancer subjects 69.8% had positive DRE at the initial screening stage. Higher proportion of cancer participants (84.3%) had PSAD ≥ 0.15 ng/ml/ml. Total serum PSA and PSA Density were significantly higher (P <0.0001) in subjects with PCa than subjects without PCA. There was no significant difference in the mean age and prostate volume between subjects with and without prostate cancer (P > 0.05). There was a significant associations of age groups, DRE findings, PSA category and PSAD category between subjects with and without cancer (p<0.0001).

Table 3 shows the diagnostic yields of PSA based parameters, DRE and prostate volume using prostate biopsy as gold standard. Using a cut-off value of 4.0 ng/ml PSA had a sensitivity of 98.4% and specificity of 16.3% with negative predictive value of 96.7% and positive predictive value 29.4%. With PSAD, a cut-off value of 0.15 ng/ml/ml was used; this yielded a sensitivity of 84.1% and specificity of 56.7% for detection of prostate cancer with positive predictive value of 40.8% and negative predictive value of 91.0%. Digital rectal examination had a sensitivity of 69.8% and specificity of 67.4%. Prostate volume had a sensitivity of 90.5% and specificity of 10.11% with a cut off value of 40.0 ml.

Table 4 shows the diagnostic performance of bioscore in diagnosis of prostate cancer. Using prostate biopsy as gold standard, a bioscore of 4, i.e. where all the four combined parameters (PSA+PSAD+DRE+ Prostate Volume) have values above their normal threshold had the highest specificity 100% but the lowest sensitivity 0.1% in the diagnosis of sepsis. A score of 0 and 1 had the highest sensitivity of 100% each and lower specificities of 1.7% and 11.8%

respectively. Also a bioscore of 3 and 2 recorded sensitivities of 49.2% and 90.5% with specificities of 87.6% and 48.3% respectively. A bioscore of 3 for three combinations of PSA+DRE+PSAD had the highest specificity of 100% and lowest specificity of 0.1%. A bioscore of zero had the highest sensitivity of 98.4% and the lowest specificity of 7.3%. Also a bioscore of 1 and 2 recorded sensitivities of 95.2% and 57.2% with specificities of 45.2% and 89.3% respectively. A bioscore of 2 for two combinations of PSA+DRE, PSAD+PSA and PSAD+DRE had the highest specificity of 100% and lowest specificity 0.1% respectively. A Bioscore of 1 for combination PSA+DRE recorded a specificity of 76.4% and sensitivity of 65.1%. Combination of PSAD+PSA and PSA+DRE had the highest sensitivity of 98.4% each and lower sensitivities of 15.7% and 7.7% respectively.

Table 5 shows the binary logistic regression of parameters used in differentiating between patients with and without prostate cancer. Individual diagnostic tools and bioscore for the combination of the diagnostic tools were entered into the logistic regression model. When the bioscore was entered into the multiple logistic regression model its performance was shown to be far better than that of each individual biomarker taken individually A bioscore for the combination of PSA+DRE+PSA+ Prostate Volume showed increasing odds ratios with a score of 4 recoding the highest odd ratio of 24.4 (95% CI, 3.15 – 204.3) and it was statistically significant (p = 0.002). One of the diagnostic tools was omitted from the bioscore (PSA+PSAD+DRE; this score thus ranging from 0-3). A bioscore of 3 recorded a statistically significant (p=0.003) highest odds ratio of 24.6 (95% CI, 2.99 – 202.9) followed by score of 2 (OR =4.0, 95% CI 0.49 -32.2). The performances were modified when another diagnostic tool was removed from the bioscore (this score thus ranging from 0-2). The best odds ratio for the combination of PSAD+DRE at 33.40 (95% CI, 9.42 – 118.50) followed by PSA+PSAD at 19.52 (95% CI, 2.58 – 147.8) and PSA+DRE at 13.67 (95% CI, 1.72 – 108.7) and they were statistically significant (p<0.05) respectively.

ROC curve for combinations of the various diagnostic tools showing AUC are shown in Fig. 1. AUC was 76.7 for the bioscore combinaion of PSA+PSAD+DRE+ Prostate Volume, 80.6 for DRE+PSAD+PSA, 71.5 for PSA+DRE, 71.5 for PSAD+PSA and 78.1

PSAD+DRE respectively Fig. 2. Receiver operating characteristics (ROC) curve analyses for depicting the accuracy of Prostate Specific Antigen (PSA) Digital Rectal Examination (DRE) and PSA Density (PSAD ROC curve. Area under curve (AUC) was 78.9(69.3 – 82.4) for PSAD, 77.8 (71.6 – 83.96) for PSA, 68.6 for DRE and 52.2 for prostate volume (44.1 – 60.4).

4. DISCUSSION

Although PSA is the routinely used marker in assessing PCa and other prostate related conditions, various studies [11,12] have indicated that, this marker lacks adequate specificity and sensitivity for a clinical decision to be made in a suspected prostate disorder. This study therefore assessed the performance of individual and combination of specific diagnostic tools used in the detection of prostate cancer among Ghanaian men.

Results from the present study shows that, 26.1% of patients diagnosed with prostate cancer which concurs with a prospective study by Catalona et al. [8] among Americans. Among the patients with prostate cancer in our study, 69.8% had both abnormal DRE and PSA> 4.0 ng/ml which is comparable to a prospective study done by Hudson et al. [20]. The result of this present study showed that majority of patients diagnosed with prostate cancer had an abnormal DRE which is comparable to a retrospective study among Turkish by Akdas et al. [21]. This means that DRE should not be taken out from the physical examination of patients as it remains a key tool of PCa diagnosis.

This current study observed that higher proportion of the diagnosed prostate cancer patients were within the PSA range 20.1 ng/ml to 50ng/ml which corroborate with a retrospective study by Gerstenbluth et al. [22]. A similar trend was also reported in a population study among Iranians by Ghafoori and colleagues [23]. Our study showed that, higher proportion of prostate cancer patients had PSAD > 0.15 ng/ml/ml which is the traditionally accepted cut-off point. This means that the possibility of identifying patients with PCa is higher when PSAD is greater than 0.15 ng/ml/ml. Several authors have stated that PSAD could be a useful marker to distinguish patients with PCa from BPH more accurately [24,25].

Table 2. Comparison of clinical, prostate related characteristics and diagnostic parameters of all participants, PCa and without PCa patient

Variables	All participants (n=241)	PCa (n=63)	Without PCa (n=178)	P-value
Age (years, mean ±SD)	70.3±8.3	71.8±6.8	69.7±8.8	0.094
Age groups				
50 -59	23(9.5%)	2(3.2%)	21(11.8%)	0.036
60 – 69	82 (34.0%)	18(28.6%)	64(36.0%)	
70 – 79	36(34.6%	36(57.1%)	68(38.2%)	
80+	32 (13.3%)	7(11.1%)	25 (14.0%)	
PSA (ng/ml, Median IQR)	18.6 (6.9 - 28.0)	29.6(21.0 - 91.3)	12.9 (5.6 - 23.6)	<0.0001
PSA category (ng/ml)				<0.0001
≤ 4.0	30 (12.5%)	1 (1.6%)	29(16.3%)	
4.1 – 10	56 (23.2%)	4 (6.3%)	52 (29.2%)	
10.1 -20	39 (16.2%)	7 (11.1%)	32 (18.0%)	
20.1 50	81 (33.6%)	29 (46.0%)	52 (29.2%)	
> 50	35 (14.5%)	22 (34.9%)	13 (7.3%)	
DRE Findings				<0.0001
Positive	102 (42.3%)	44 (69.8%)	58 (32.58%)	
Negative	139 (57.7%)	19 (30.2%)	120 (67.41%)	
PSAD (ng/ml/ml, Median IQR)	0.17 (0.08 - 0.41)	0.40 (0.18 - 0.77)	0.12 (0.007 - 0.33)	<0.0001
PSAD category				<0.0001
< 0.15	121 (46.1%)	10(15.87%)	101 (56.7%)	
≥ 0.15	(130 (53.9%)	53 (84.3%)	77 (43.3%)	
Prostate Volume (ml, Median IQR)	83.1 (60.9 - 124.5)	86.9 (61.0 - 124.5)	80.65 (60.7 - 124.6)	0.600
Qmax	9.0(6.0 - 12.9)	6.0 - 10.5)	9.0 (6.0 - 14.0)	0.262
Vcomp	106.0 (88.2 - 127.0)	103.8 (92.5 - 126.0)	106.2 (85.0 - 136.8)	0.569
I-PSS Score	21.6±5.8	22.3±5.9	21.4±5.7	0.121

DRE digital rectal examination, PSA prostate specific antigen, PSAD, prostate Specific antigen, IQR interquartile range, SD standard deviation, IPSS, International prostate symptoms score

Table 3. Diagnostic yields for PSA based parameters, digital rectal examination (DRE) and prostate volume

Variable	Sensitivity (95% CI)	Specificity (95%CI)	PPV	NPV	TP	TN	FP	FN
PSA (ng/ml)	98.4(90.5 -100)	16.23 (11.6 -22.5)	29.4%	96.7%	62	29	149	1
DRE findings	69.8 (57.6 -79.8)	67.42 (60.2 - 73.9)	43.1%	86.3%	44	120	58	19
PSAD (ng/ml/ml)	84.1 (72.9 - 91.3)	56.7 (49.3 - 63.8)	40.8%	90.9%	53	101	77	10
Prostate Volume (ml)	90.5 (80.3 - 95.8)	10.1 (6.5 - 15.5)	26.3%	75%	57	18	160	6

PPV, Positive Predictive Value, NPV, Negative Predictive Value, CI = Confidence Interval, TP, true positive, true negative FP, false positive, FN false negative

Table 4. Shows the diagnostic performance of bioscore combination of diagnostic tool in diagnosis of prostate cancer

Variable	Specificity (95%CI)	Sensitivity (95% CI)	PPV (%)	NPV (%)	TP	TN	FP	FN
Bioscore (DRE+PSAD+PSA+ Prostate volume)								
0	100 (92.9 - 100)	1.7 (0.4 - 5.1)	26.5	100	63	3	175	0
1	100 (90.6 -100)	11.8 (7.8 - 17.5)	28.3	95.5	62	21	157	1
2	90.5 (80.3 - 95.3)	48.3 (41.1 - 55.6)	38.3	93.5	57	86	92	6
3	49.2 (37.3 - 61.2)	87.6 (81.9 -91.7)	58.5	82.9	31	156	22	32
4	0.1 (0 - 7.1)	100 (97.4 - 100)	0	73.9	0	178	0	63
Bioscore (DRE+PSAD+PSA)								
0	98.4 (90.6 - 100)	7.3 (4.3 -12..3)	27.4	92.9	62	13	164	1
1	95.2 (86.2 -98.8)	45.2 (38.1 - 52.6)	38.2	96.4	60	80	97	3
2	57.2 (44.9 - 68.6)	89.3 (83.7 - 93.1)	65.5	85.4	36	158	19	27
3	0.2 (0 - 7.1)	100 (97.4 - 100)	0	73.4	0	177	0	63
Bioscore (PSA+DRE)								
0	98.4 (90.6 - 100)	7.7 (4.7 - 12.9)	27.4	93.3	62	14	164	1
1	65.1 (52.7 - 75.7)	76.4 (69.6 - 82.0)	49.4	86.1	41	136	42	22
2	0.1 (0 - 7.1)	100 (97.4 - 100)	0	74.9	0	179	0	63
Bioscore (PSAD+PSAD)								
0	98.4 (90.6 - 100)	15.7 (11.1 -21.9)	29.3	96.6	62	28	150	1
1	(84.1 (46.4 - 70.0)	57.3 (49.9 - 64.3)	41.1	91.1	53	102	76	10
2	0.1 (0 - 7.1)	100 (97.4 - 100)	0	74.9	0	179	0	63
Bioscore (PSAD + DRE)								
0	95.2 (86.2 - 98.8)	36.5 (29.8 - 43.8)	34.5	95.6	60	65	112	3
1	58.7 (46.4 - 70.0)	86.5 (80.6 - 90.8)	60.7	85.6	37	154	24	26
2	0.1 (0 - 7.1)	100 (97.4 - 100)	0	74.9	0	179	0	63

PPV, Positive Predictive Value, NPV, Negative Predictive Value, CI = Confidence Interval, TP, true positive, true negative FP, false positive, FN false negative
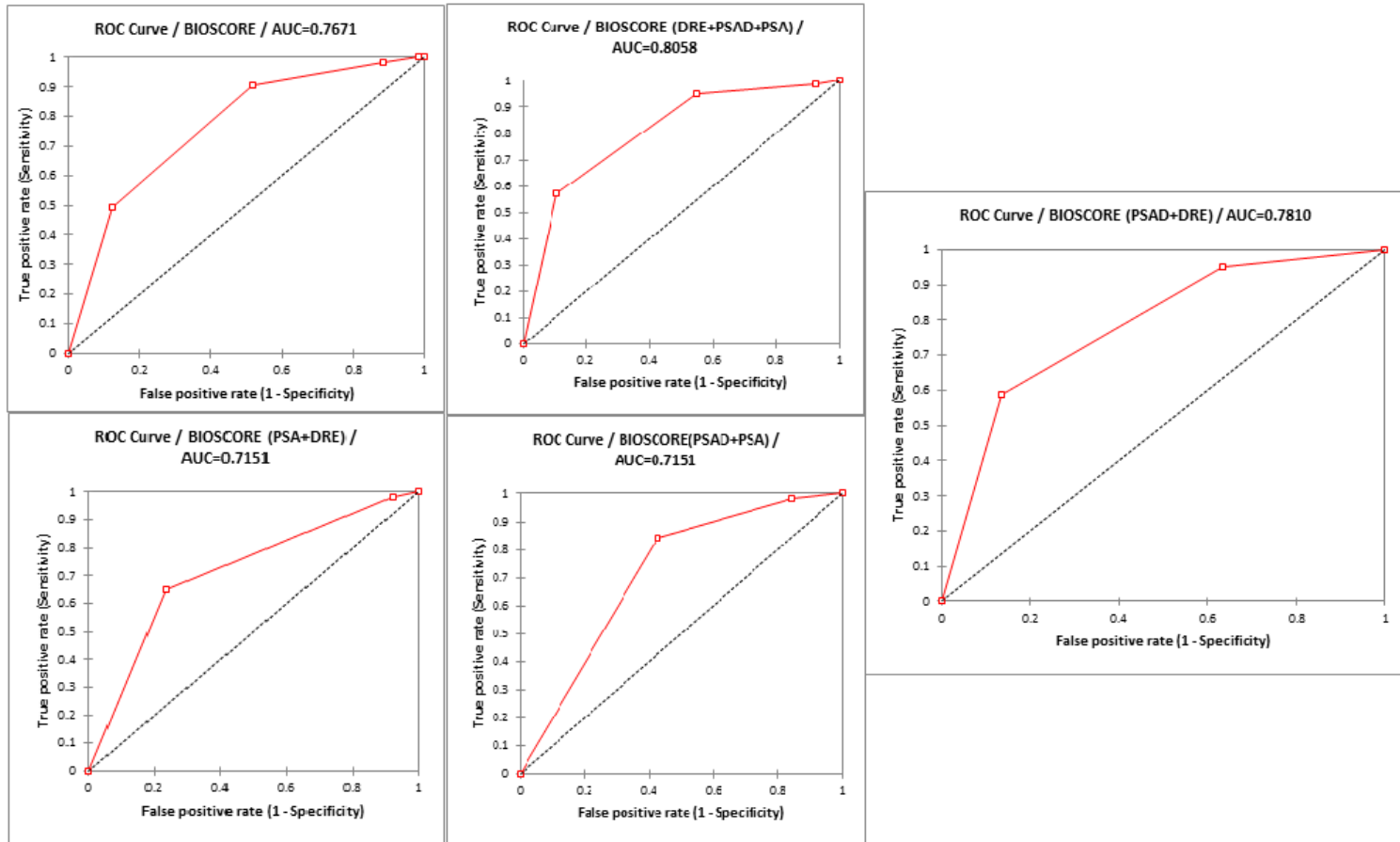
Fig. 1. Receiver operating characteristics (ROC) curve analyses for showing the accuracy of the bioscore for the various combinations of the diagnostic tools AUC = Area under Curve
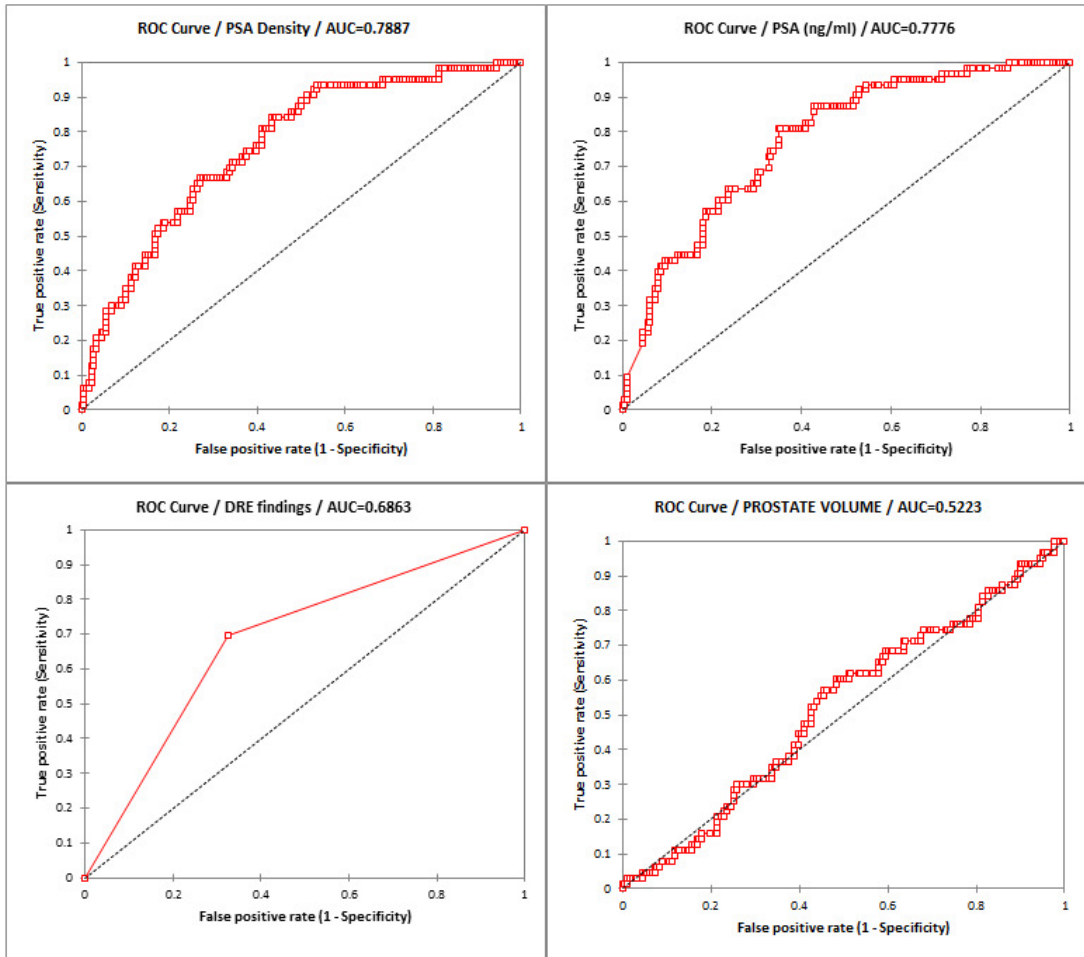
Fig. 2. Receiver operating characteristics (ROC) curve analyses for depicting the accuracy of Prostate Specific Antigen (PSA), Digital Rectal Examination (DRE) and PSA Density (PSAD)

The findings of this study indicate that PSA and PSAD were significantly higher (p<0.01) in comparison between patients with and without prostate cancer, and this is consistent with previous reports from some studies [23,26,27]. There was no significant difference in age between the patients with and without prostate cancer which agrees with a cross-sectional study by Sheik et al. [28] among Arab men. However, Stephen and colleagues [17] did find a significant difference in a retrospective study among Germans. A serum PSA threshold of 4 ng/ml is usually an indication for prostate biopsy and PSA level between 4 and 10ng/ml which is considered a gray zone are shown to have low sensitivity but values above 10 ng/ml have a high sensitivity for PCa. The sensitivity even reaches 100% if values higher than 15 ng/ml are considered [28, 29]. In our study the lower cut-off point of 4ng/ml

for PSA had a higher sensitivity and lower specificity which is in line with a study among Iranian population [23].

The result of this current study showed that, among the individual diagnostic tools, PSAD had better accuracy followed by the PSA, DRE and prostate volume respectively. Previous study by Deliveliotis et al. [24] have shown that PSAD is a useful marker in detecting prostate cancer which agrees with finding in our present study and that of a cross-sectional study among a Japanese population by Sasaki et al. [30]. To make this study more credible and very successful, bioscores were developed combining different tests (DRE, ultrasound, PSA assay and PSAD) in the diagnosis of prostate cancer. The combination of three tests (DRE+PSAD+PSA) yielded a higher better accuracy (AUC =80.6)

followed by combination of two test (PSAD+DRE) with AUC of 78.1 and an AUC of 76.7 for fours combinations respectively. These trends of accuracies have shown that combinations of diagnostic tools have high rate of detection of prostate tumors better than the use of a single diagnostic test that can evoke a low detection rate. Similar findings were reported in descriptive retrospective study conducted among Algerians by AB Kandouci [31]. Likewise, in Japan, Shimizu et al. conducted mass screening for PCa using PSA and DRE as indices without age limit and reported that there was high detection rate for PCa when these parameters were combined. However, they indicated that the detection rate was low % when PSA alone was examined [32].

Table 5. Shows the binary logistic regression of parameters used in differentiating between patients with and without prostate cancer

Variable	Odd ratio	95% CI	P-value
Model 1			
PSA	1.01	1.0 -1.1	0.545
PSAD	2.15	0.9–5.4	0.104
DRE	4.85	2.52–9.3	<0.001
Model 2			
Bioscore (DRE+PSAD+PSA+ Prostate volume)			
0			
1	1 (referent)		
2	1.40	0.2-12.6	0.773
3	6.70	0.9-52.6	0.071
4	25.40	3.2-204.3	0.002
Bioscore (DRE+PSAD+PSA)			
0	1 (referent)		
1	0.40	0.03 -4.6	0.453
2	4.10	0.5-32.2	0.192
3	24.60	3.0-202.9	0.003
Bioscore (PSA+DRE)			
0	1 (referent)		
1	2.40	0.3 -19.3	0.407
2	13.70	1.7-108.7	0.013
Bioscore (PSAD+PSAD)			
0	1 (referent)		
1	3.40	0.4-28.1	0.255
2	19.50	2.6-147.8	0.004
Bioscore (PSAD+DRE)			
0	1 (referent)		
1	5.60	1.6-19.4	0.001
2	33.40	9.4-118.5	<0.0001

CI confidence interval, DRE digital rectal examination, PSA prostate specific antigen, PSAD, prostate Specific antigen

Based on data from advanced countries [16,33] , PSA density of 0.15 ng/ml/ml has been widely used as a cut-off point value. Results from our study shows that PSAD had sensitivity of 84.1% and specificity of 56.7% which is comparable to findings from previous studies [25,34].

Positive predictive value is another parameter in the assessment for cancer detection. It gives vital clinical information. Higher values imply less redundant biopsies [8]. In our study, the positive predictive values for PSAD+DRE+PSA and PSAD+DRE were in the increasing order respectively. Similar findings pertaining to positive predictive values have also been reported by some previous studies [8,23,25]. In this study, sensitivity and specificity were done for the various combinations of the test methods which are common in clinical practice with combination of all four diagnostic tools having sensitivity of 90.5%. However, combinations of PSAD+DRE had the highest specificity. These findings obtained from these two different combinations agree with a retrospective study among Turkish population by Akdas et al. [21]. For the first time, we have shown that, the combination of diagnostic tools have a better diagnostic performance for detecting prostate cancer among Ghanaian men. The bioscore's calculation implies the measurement of three biomarkers clearly provides relevant information likely to strengthen the physician's decision in addition to clinical work-up.

Results from our study shows that bioscores for the combination of the diagnostic tools were significantly associated with increasing odds of prostate cancer detection upon logistic regression analysis [Table 5] which is in line with a retrospective study among Chinese population by Teoh et al. [35]. Another cross-sectional prospective study among Filipino males by Chua et al. [36] reported that increased PSA level, abnormal DRE were statistically (p <0.001) associated with prostate cancer with lower odd ratios in comparison to findings in our study. These low odd ratios are likely to be due to the lower incidence of prostate cancer among Asians compared to that of Africans, African Americans and European Caucasians [37].

It should be mentioned here that, there were some few limitations of the study. The inability to conduct a longitudinal cohort study among larger population which could have assessed the changes of these diagnostics tools over time and the use of elevated total PSA or abnormal digital

rectal examination as indicators for selections of participants. Notwithstanding, this study is a baseline for further studies to address this interest.

5. CONCLUSION

Serum total PSA and PSAD had a good sensitivity as a biomarker but lacks the clinical specificity for the definitive diagnosis of prostate cancer. On the other hand, DRE did not show adequate specificity and sensitivity in reaching a clinical decision of suspected case of prostate cancer. However, combined diagnostic performance of DRE+PSAD+PSA poses a better diagnostic accuracy. Bioscores for the combination of the diagnostic tools were significantly associated with increasing odds of prostate cancer detection upon logistic regression analysis. Further studies are required to evaluate the combine diagnostic performance in larger population.

ETHICAL APPROVAL

Ethical Approval (CHRPE/AP/243/15) for the study was obtained from the Committee on Human Research, Publication and Ethics of the School of Medical Sciences (SMS), Kwame Nkrumah University of Science and Technology (KNUST) as well as ethical review board of the Komfo Anokye Teaching Hospital (KATH). Participation was voluntary and verbal informed consent was obtained from each participant according to Helsinki declaration. Respondents were assured that the information gathered was to be used strictly for research and academic purpose only. In addition, respondents were given the freedom to opt out any time they thought they couldn't continue with the study.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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