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Nomogram for predicting the probability of the positive outcome of prostate biopsies among Ghanaian men

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KEYWORDS
Nomogram;
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Abstract
Introduction and objectives: Several existing models have been developed to predict positive prostate biopsy among men undergoing evaluation for prostate cancer (PCa). However, most of these models have come from industrialized countries. We therefore, developed a prostate disease nomogram model to provide a basis for predicting a prostate biopsy outcome by correlating clinical indicators and diagnostic parameters among Ghanaian men.
Subjects and methods: The study was a hospital-based cross-sectional prospective one which was undertaken at the Department of Surgery (Urology Unit) Komfo Anokye Teaching Hospital (KATH) from December, 2014 to March, 2016. In all a total of 241 patients suspected of having a prostate disorder due based on an abnormal digital rectal examination (DRE) findings and, or elevated prostate specific antigen (PSA) level underwent Trans-Rectal Ultrasonography (TRUS) guided biopsy of the prostate. Stepwise logistic regression was used to determine the independent predictors of a positive initial biopsy. Age, prostate-specific antigen (PSA), digital rectal examination (DRE) status, prostate specific antigen density (PSAD),

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.

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history of alcohol consumption and history of smoking findings were included in the analysis. Two nomogram models were developed that were based on these independent predictors to estimate the probability of a positive initial prostate biopsy. Receiver-operating characteristic curves (ROC) were used to assess the accuracy of using the nomograms and PSA and PSAD levels for predicting positive a prostate biopsy outcome.

Results: Prostate cancer was diagnosed in 63 out of 241 patients (26.1%). Benign prostatic hyperplasia was diagnosed in 172 (71.4%) of patients and the remaining 6 patients (2.48%) had chronic inflammation. Significantly elevated levels of PSA and PSAD were observed among patients with PCa compared to patients without PCa ($p < 0.05$). Furthermore, it was observed that age, DRE, PSA, PSAD, history of smoking, and history of alcohol consumption were significantly independent predictors ($p < 0.05$) of prostate cancer. The area under the receiver operating characteristic curve (AUC) of nomogram I and II were 87.3 and 84.8 respectively which were greater than that of total PSA (AUC = 75.8) and PSAD (AUC = 77.8) alone for predicting a positive initial prostate biopsy

Conclusion: We conclude that, nomograms offer a better and accurate assessment for predicting a positive outcome of prostate biopsies than the use of traditional tools of PSA, DRE and PSAD alone.

Introduction

Prostate cancer has been the most commonly diagnosed cancer and the second leading cause of cancer-related death in men in the United States in 2011. It is the number one cancer in both incidence and mortality in Africa, constituting of 13% of all male cancer occurrence and 11.3% of all male cancer related mortalities [1]. In African countries where registers exist such as Nigeria, Uganda, South Africa and Zimbabwe, it has been observed that the incidence of prostate cancer is increasing between the ages of 40 to 70 years [1]. Rretrospective studies of all cancer cases have demonstrated that prostate cancer was the second leading cause of cancer-related mortality among male patients in Ghana [2–4].

Recently, controversy has arisen as to whether an early detection of prostate cancer through accurate determination of DRE, prostate specific antigen (PSA) screening and its derivatives is actually beneficial or not [5]. This diagnostic gap exposes men to intensive diagnostic screening and invasive management strategies that affect quality of life. Prostate biopsies give an absolute diagnosis though it is expensive and aggressive. Due to the pains and associated problems, the procedure should be circumvented in men with a low prostate cancer probability [6,7].

To improve the rates of prostate cancer detection and to reduce associated problems, predictive models for prostate cancer using laboratory, clinical and ultrasound parameters have been developed [8–10]. At present, numerous prevailing models had been developed to predict positive prostate biopsy outcome among men undertaking assessment for cancer of the prostate [11]. However, these models mostly come from industrialized countries. Moreover, prostate cancer is thought to differ epidemiologically and biologically between Western, American, African-American and Asian populations. Furthermore, nomograms developed for other populations cannot directly be applied to the Ghanaian population in Sub-Saharan Africa, where there is a higher incidence of prostate cancer compared to Asian and Western populations [12]. The existing evidence strongly suggests that, evaluation of prostate cancer risk should be tailored along racial lines [13–15]. Consequently, the development and use of a localized nomogram for given population is particularly pertinent. To our knowledge, no nomogram to evaluate the risk of prostate cancer in a Ghanaian population setting has been studied and published to date. It was against this background that this study was carried out to develop a prostate specific nomogram for predicting positive prostate biopsy among Ghanaian men.

Subjects and methods

Study design/setting

A hospital-based cross-sectional prospective study was used to assess the diagnostic accuracy of PSA, DRE and PSAD among men undergoing an initial Trans-rectal ultrasound guided (TRUS) prostate biopsy at Komfo Anokye Teaching Hospital (KATH) between December, 2014 and March, 2016. 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.

Study population/subject selection

Non-probability convenience sampling technique was used to recruit 241 patients visiting the Urology Unit at the directorate of Surgery, KATH. Indications for TRUS biopsy were an elevated total PSA, defined as > 4.0 ng/ml or an a digital rectal examination, which reveals an abnormal or suspicion of cancer, defined as the presence of a nodule, areas of induration or asymmetry in the size lateral lobes. A 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 at first

sexual intercourse, heart attack as well as rheumatoid arthritis were noted.

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 6.5 MHz 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 × transverse diameter × anterior posterior diameter × 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. All acquired specimens were placed in a formalin-filled container and sent for histopathologic examination. They were all examined by a board-certified pathologist at the department of Pathology, Komfo Anokye Teaching Hospital. All the pathologists were blinded from the clinical indicators of the patients

Statistical analysis

Data entry and analysis were performed using Stata version 12. Descriptive statistics was 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. Both univariate and multivariate logistic regression analyses were used to examine the association between predictive variables and biopsy outcomes. Crude or adjusted odds ratios and 95% confidence intervals (CI) were calculated. Univariate logistic regression analysis indicated that age, total PSA, DRE, PSAD, history of smoking and alcohol consumption were the six significant predictors for a positive prostate biopsy. A stepwise multivariate logistic regression analysis showed that the most significant of the six risk factors for detecting prostate cancer were total PSA, DRE PSAD and history of alcohol consumption. Based on the final model, the estimated probability of a positive biopsy was calculated and a nomogram was accordingly developed as a clinical tool. P-values less than 0.05 were also considered significant.

Results

Table 1 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

Table 1 Comparison of clinical, prostate related characteristics and diagnostic parameters of all participants, PCa and without PCa patients.

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 (14.9%	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
Prostate volume category				0.385
<40	24 (10.0%0	6 (9.5%)	18 (10.1%)	
40–80	89 (36.9%)	19 (30.2%)	70 (39.3%)	
>80	128 (53.1%)	90 (60.3%)	90 (50.6%)	
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 2 Univariate logistic regression analyses of diagnostic tools and identified risk factors for evaluating the risk of positive prostate biopsy outcome.

Variables	Patients	Positive biopsy	Odd ratio	95% CI	P-value
Age (years)					0.095
Age groups (years)					
50–69	105	20 (8.7%)	Ref		
≥70	136	43 (33.3%)	2.0	1.1–3.6	**0.038**
PSA(ng/ml)					**0.002**
PSA category (ng/ml)					
≤20.0	125	12 (19.1%)	Ref		
>20.0	116	51 (780.1%)	7.6	3.8–15.9	**<0.0001**
DRE findings					
Negative	102	44 (43.1%)	Ref		
Positive	139	19 (13.7%)	4.8	2.6–8.9	**<0.0001**
PSAD					**0.001**
PSAD category					
<0.15	111	10 (9.0%)	Ref		
≥0.15	130	53 (40.8%)	6.9	3.3–14.5	**<0.0001**
History of smoking					
No	174	52 (29.9%)	Ref		
Yes	67	11 (16.4%)	0.5	0.2–1.0	**<0.036**
History of alcohol consumption					
No	168	55 (32.7%)	Ref		
Yes	73	8 (11.0%)	0.3	0.1–0.6	**0.001**

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

(73.9%) did not have cancer. Out of the total studied subjects, 30 of them (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 aged of 70–79 years. Greater proportion (46.0%) of cancer subjects were in the PSA range of 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 subjects (84.3%) had PSAD ≥ 0.15 ng/ml/ml. Total serum PSA and PSA Density (PSAD) 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 difference in age groups, DRE findings, PSA categories and PSAD between subjects with and without cancer ($p < 0.0001$).

Table 2 shows the univariate analysis of diagnostic tools and identified risk factors for evaluating the risk of positive prostate biopsy outcome. The results of the univariate logistic regression analysis showed that age, prostate specific antigen (PSA), digital rectal examination (DRE), PSA Density (PSAD), history of smoking and history of alcohol consumption in men with initial positive prostate biopsy were all significantly different from those in men with negative biopsy ($p < 0.05$). Participants who were above 70 years recorded increased odds ratios of 2.0 (95% CI, 1.1–2.6). Moreover, increased PSA [OR = 7.6(3.8–15.9), $p < 0.0001$], PSAD [OR = 6.9(3.3–14.5), $p < 0.0001$] and abnormal DRE findings [OR = 4.8(2.6-8.9), $p < 0.0001$] were statistically significantly associated with increased odds of developing prostate cancer respectively.

Table 3 Multiple logistic analyses of diagnostic tools and identified risk factors for evaluating the risk of positive prostate biopsy outcome (Nomogram I).

Variables	Odd ratio	95% CI	P-value	Beta
Age groups (years)				
50–69	Ref			
≥70	1.6	0.8–3.1	0.188	0.46
PSA category (ng/ml)				
≤20.0	Ref			
>20.0	3.3	1.3–7.6	**0.014**	1.18
DRE findings				
Negative	Ref			
Positive	5.8	2.7–12.43	**<0.0001**	1.76
PSAD category				
<0.15	Ref			
≥0.15	3.1	1.1–8.20	**0.023**	1.12
History of smoking				
No	Ref			
Yes	1.7	0.6–4.6	0.737	0.16
History of alcohol				
No	Ref			
Yes	0.2	0.08–0.63	**0.005**	−1.5
Constant	0.0003	0.0002–0.049	**<0.0001**	−7.55

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

Table 3 shows the multiple logistic regression analysis of diagnostic tools and identified risk factors for evaluating the risk of positive prostate biopsy outcome. The results of the multiple logistic regression analyses showed that prostate specific antigen (PSA), DRE, PSAD and history of alcohol consump-

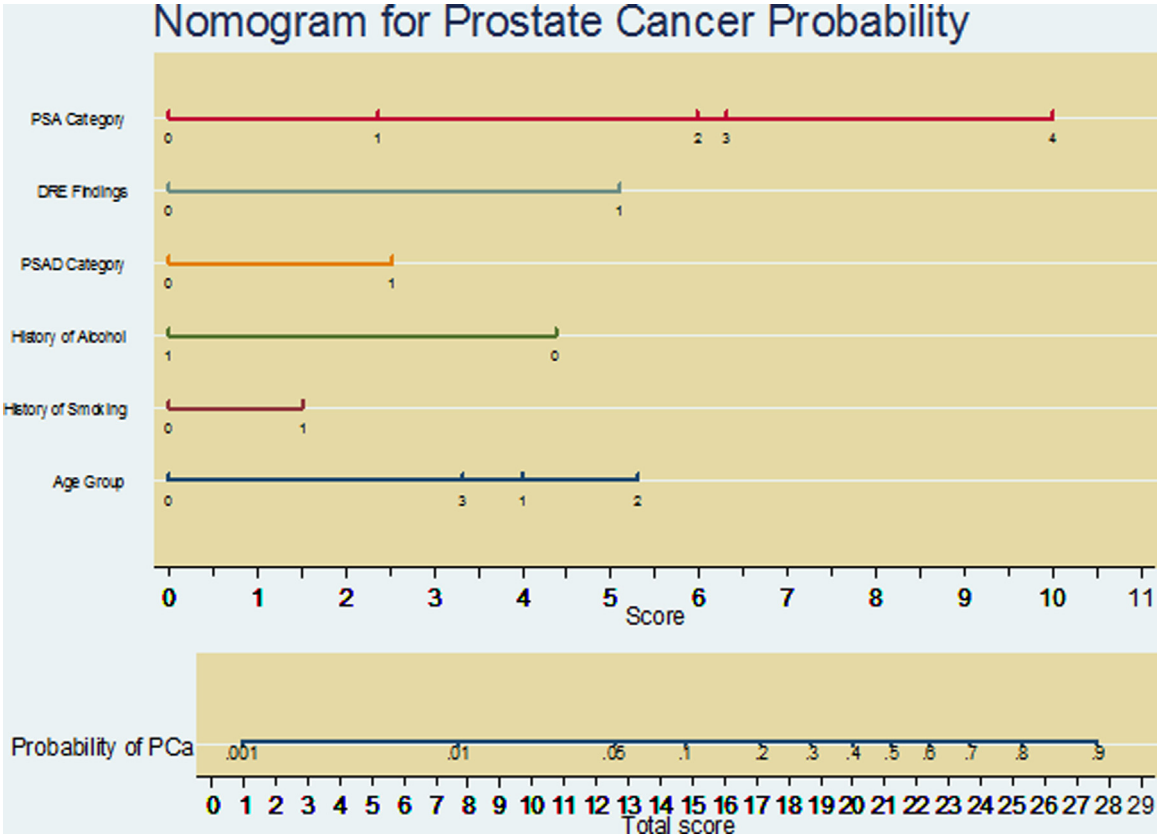

Figure 1 Shows nomogram I for predicting the probability of prostate cancer on needle biopsy using age, PSA category, PSAD category, history of smoking, history of alcohol consumption, and DRE findings. To determine the predicted probability of prostate cancer on initial biopsy, the patient's values are located on each axis. A vertical line is drawn to the '**Score**' axis is drawn to determine how many points are attributed to each variable. After summation of the points for all variables, the sum on the '**Total Scores**' is located on the total score axis to determine the individual probability of prostate cancer on initial prostate biopsy on the 'Probability of Prostate Cancer' line.

tion in men with initial positive prostate biopsy were all significantly different from those in men with negative biopsy ($p < 0.05$). Moreover, increased PSA [OR = 3.3(1.3–7.6), p = 0.014], PSAD [OR = 3.1(1.1–8.2), p = 0.023] and abnormal DRE findings [OR = 5.8(2.7–12.4), $p < 0.0001$] were statistically significantly associated with increased odds of developing prostate cancer respectively. The Hosmer–Lemeshow good of fit test showed that the model was well calibrated p equal to 0.325.

Table 4 shows the multiple logistic regression analysis of diagnostic tools for evaluating the risk of positive prostate biopsy outcome. In the multiple logistic regression analysis, PSA, PSAD and DRE in men were found to be significant independent predictors of initial positive prostate biopsy ($p < 0.05$). Increased PSA [OR = 3.0(1.1–7.8), p = 0.027], PSAD [OR = 3.8 (1.4–10.9), p = 0.010] and abnormal DRE findings [OR = 5.4(2.6–10.8), $p < 0.0001$] were statistically significantly associated with increased odds of developing prostate cancer respectively. The Hosmer–Lemeshow good of fit test showed that the model was well calibrated p equal to 0.283.

Table 4 Multiple logistic analyses of diagnostic tools factors for evaluating the risk of positive prostate biopsy outcome (Nomogram II).

Variable	Odd ratio	95% CI	P-value	Beta
PSA category (ng/ml)				
≤20.0	Ref			
>20	3.0	1.1–7.8	**0.027**	1.04
DRE findings				
Negative	Ref			
Positive	5.4	2.6–10.8	**<0.0001**	1.72
PSAD category				
<0.15	Ref			
≥0.15	3.8	1.4–10.9	**0.010**	0.94
Constant	0.01	0.001–0.08	**<0.0001**	−4.59

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

Discussion

Conventionally, prostate biopsy is often performed with caution, yet various invasive procedure-associated complications after prostate biopsy may occur. Each year, millions of men undergo prostate biopsy to detect PCa globally [16,17]. Recent studies have reported an increase in the occurrence of infections after trans-rectal prostrate biopsy [17,18]. It is therefore clinically imperative that, the decision to perform a prostate biopsy is carefully made, so as to avoid the risk of probable procedure-related complications. Although nomograms have been developed in some parts of the world, there is paucity of

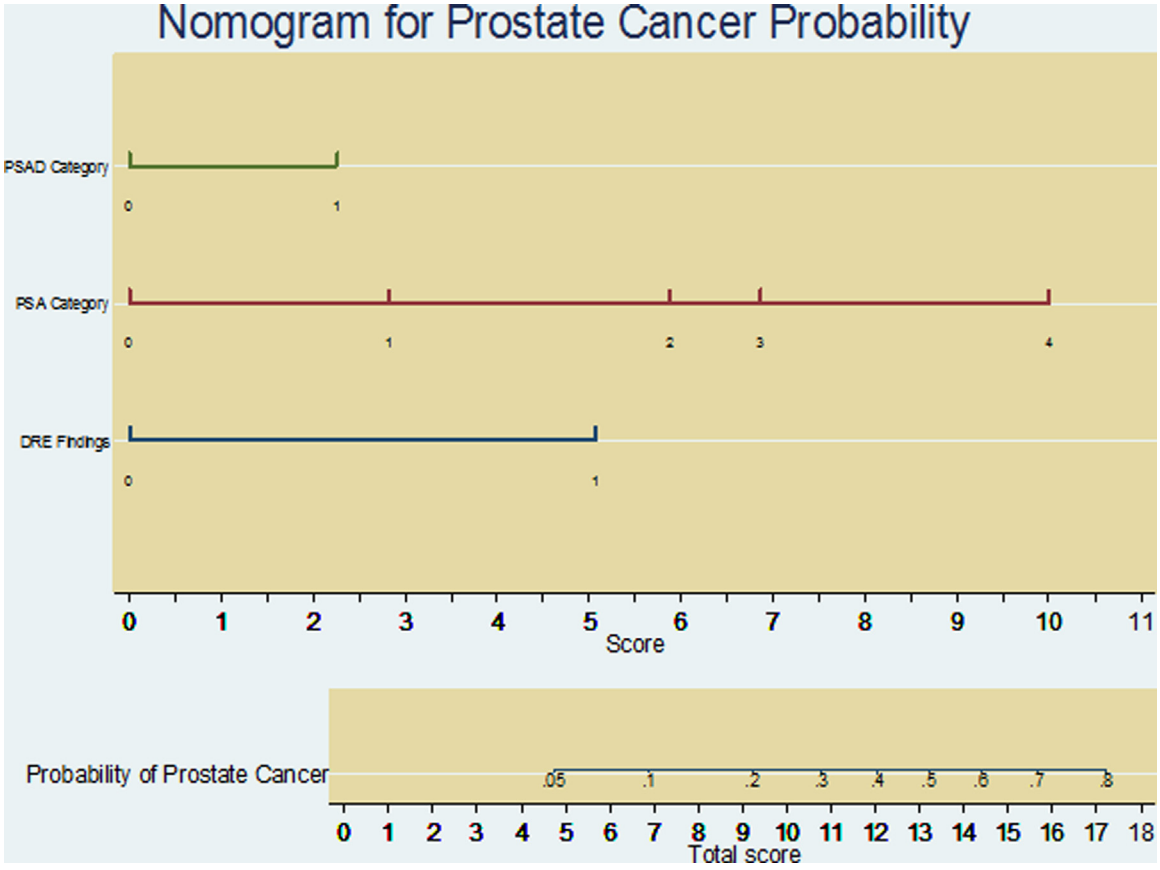

Figure 2 Shows nomogram II for predicting the probability of prostate cancer on needle biopsy using PSA category, PSAD category and DRE findings. To determine the predicted probability of prostate cancer on initial biopsy, the patient's values are located on each axis. A vertical line to the '**Score**' axis is drawn to determine how many points were attributable to each variable. After summation of the points for all variables, the sum on the '**Total Scores**' is determined by locating the individual probability of prostate cancer of the initial prostate biopsy on the 'Probability of Prostate Cancer' line.

information on the use on nomogram model to the clinical outcome of a prostate biopsy in Ghana. This study is the first to develop a predictive model that incorporates clinical and laboratory data from general practice and examine the accuracy of a nomogram for the prediction of the prostate cancer risk in a Ghanaian population (Fig. 1).

Reliable nomogram that can accurately predict and differentiate the presence of aggressive prostate cancer from benign conditions would be useful to urologists and patients to make relevant clinical decisions [19]. In the current dataset for nomogram development, we found that age, DRE PSA, PSAD, history of smoking, and history of alcohol consumption were significant independent predictors ($p < 0.05$) of prostate cancer and were used for the nomogram predictor variables. These findings are consistent with those in previous reports from systematic review and the prevention trial and European randomized study [20,21]. Furthermore, several factors such as age, prostate specific antigen, free PSA, family history, race and abnormal DRE findings have been used as a predictor of prostate cancer [11,19,22]. However, after multivariate analysis it was found that, age and history of smoking were not independent predictors of positive initial prostate biopsy ($p > 0.05$) in this current study. Previous studies among Americans and Canadian men by Nam et al., [18] and Optenberg et al., [22] reported a predictive value of 74% and 81.0% using clinical parameters and identified risk factors. We developed and internally validated two (2) nomograms in this present study that predicted the probability of PCa in men referred for prostate needle biopsy. Using clinical parameters such as DRE, PSA and PSAD, the predicting AUC of the nomogram was 84.8%. It was therefore observed that addition of the identified risk factors such as age, history of smoking, and alcohol consumption improves the AUC to 87.7%. Thus the two nomograms developed in our present study would appropriately predict 84.8% and 87.3% of patients with PCa in a set of one hundred randomly paired patients in which only 1 subject has cancer of the prostate on needle biopsy and the other does not. These observed values from the current study are higher compared to those previously reported regressions-based nomograms for patients with localized PCa [6,23–26]. The results from this study favorably relates to the nature of the predictor variables used in the employed nomograms; namely age, DRE, PSA, history of smoking, history of alcohol consumption and PSAD. Indeed these predictors in combination have been shown to be more informative and reliable in the diagnosis of prostate cancer (Fig. 2).

In the Ghanaian setting, there is a widespread use of the PSA, DRE and PSAD tests, thus Ghanaian men are more frequently referred for biopsy under these conditions. However, in the present study, we found that the accuracy of nomogram I and II for predicting

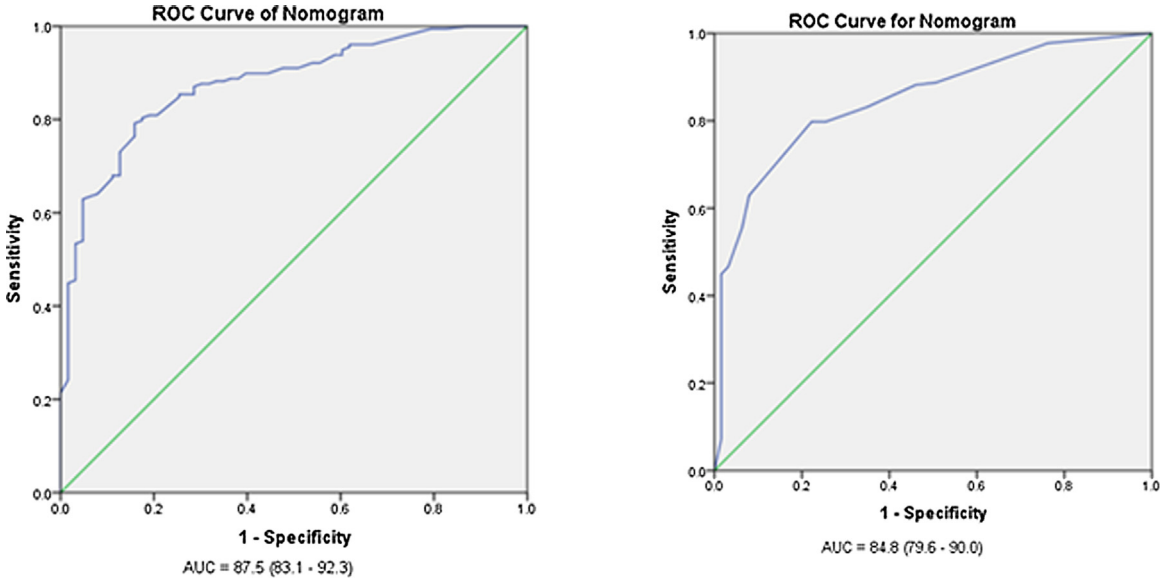

Figure 3 Shows the area under the receiver-operating characteristic curve (AUC) for showing the accuracy of nomogram I, nomogram II, PSA and PSAD for predicting a positive initial prostate biopsy. AUC was 87.3 (83.1–92.3) for nomogram I, 84.8 (79.6–90.0) for nomogram II, 77.8 (71.5–84.0) for PSAD and 75.8 (69.2–82.5) respectively with significant asymptomatic P-value (<0.0001).

a positive initial prostate biopsy was better than using PSA levels alone (AUCs were 87.3%, 84.8 vs. 75.8%, respectively) (Fig. 3). Similar trends were also shown between the PSAD, DRE and the two nomograms respectively (AUC were 78.9%, 68.6% vs. 87.3%, 84.8%). While these results are similar with those reported from previous studies from developed countries [19,27–29], this is the first time such findings are observed in a Ghanaian setting, using a Ghanaian cohort. Previous studies have not included PSAD in most prostate nomogram model, although PSAD has been shown in several studies to have a better accuracy than PSA and DRE [30–32]. A higher median PSAD value in our study was observed because PSAD testing is still not routinely used for early detection of prostate cancer in Ghana. Thus, the majority of prostate cancers are diagnosed at a later disease stage. PSAD, which was included in our predictive model, may also be a key factor in improving the accuracy of the nomogram.

Regression-based model needs to be calibrated and validated in patients with similar disease characteristics before usage since a generalized application of a model may various patient characteristics. In this study, the two nomograms developed were well calibrated by the Hosmer–Lemeshow good of fit test (p = 0.325 and = 0.283) and validated internally with 500 bootstrapped re-samples. Most of the predictors used in the development of the two nomograms were significant in the bootstrapped output. These internal validity estimates demonstrated less pronounced differences between development and internal validation samples than were observed for the prostate biopsy nomograms. These findings are consistent with to previous studies on internally validated regression-based nomograms by Tang et al., [27], Garzotto et al., [23] and Thompson et al., [26] in the Chinese and Western population though nomogram in these studies demonstrated minimal decrease in predictive accuracy relative to our nomograms. However, Hernandez et al., [25], Suzuki et al., [6] and Park et al., [24] failed to validate their models in their studies. The data in our study were obtained from a single, tertiary hospital, which may lead to partial results and our nomograms have not been validated externally. Whether it can be universally applied to Ghanaian populations must be confirmed, and further larger, prospective and randomized studies are necessary.

Conclusion

Nomograms offer a better and accurate assessment for predicting a positive outcome of prostate biopsies than the use of traditional tools of PSA, DRE and PSAD in predicting the prostate biopsy outcome such as presence of prostate cancer and benign prostatic hyperplasia. Furthermore, this study reflected a hospital-based screening population and validated internally for its accuracy. The study provides a base line for further studies probably using, a multi-institutional study with larger population is strongly recommended.

Ethical committee 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 written 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 could not continue with the study.

Authors' contributions

AYF contributed to the conception of the research idea, design data analysis and interpretation, paper drafting and revision. GSKC contributed to the conception of the research idea, design, data analysis

and interpretation, paper drafting and revision. AK contributed to the conception of the research idea, design, data collection, data analysis and interpretation, paper drafting and revision. EFL contributed to research design, patient recruitment, collection data analysis and interpretation, paper drafting and revision. CO contributed to data interpretation, paper drafting and revision. EA contributed to research design, patient recruitment data analysis and collection. TFB contributed to the conception of the research idea, design and data collection. GA contributed to the conception of the research idea, design, and data collection. ENB contributed to data interpretation, paper drafting and revision. EOA contributed to patient recruitment data analysis and collection BA contributed to data interpretation, paper drafting. All authors approved the final manuscript before publication and agree to be accountable for all aspects of the work.

Conflict of interest

Authors of this article have no competing interest.

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