Research Article

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Archives in Cancer Research
ISSN 2254-6081

2020
Vol.8 No.1:3

DOI: 10.36648/2254-6081.8.1.3

Initial Prostate Specific Antigen (PSA) Test can be used to Reduce the Burden Associated with Prostate Cancer Screening in High Risk Populations

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Citation: Folasire A, Bamgboye E, Ntekim A (2020) Initial Prostate Specific Antigen (PSA) Test can be used to Reduce the Burden Associated with Prostate Cancer Screening in High Risk Populations. Arch Cancer Res. Vol.8 No.1:3

Abstract

Background: There is high mortality from prostate cancer in Nigeria. Lack of awareness and low screening uptake are associated with this poor outlook. There is need to develop strategies to improve uptake of screening to ensure early diagnosis for men with prostate cancer in our environment.

Objectives: The objective of the study was to determine the proportion of men with initial PSA values ≥ 2.5-4 ng/mL who will be eligible for yearly follow up screening in high-risk prostate cancer population.

Methods: This was a cross sectional study carried out among men from two worship centres in Ibadan Nigeria (A church and a mosque). Participants were educated on prostate cancer and the characteristics of PSA based screening before consent was obtained from individuals for participation. Self-administered questionnaires were completed before blood samples were obtained for PSA analysis. Digital rectal examinations were carried out among participants.

Findings: All the 97 participants aged between 40 to 72 years who turned up for the exercise gave consent to participate. Complete data was available for 81 participants included in the final analysis. Five (6.25%) out of the 81 participants analyzed heard about prostate cancer and PSA testing but none has ever undergone PSA based screening. Total PSA values ranged from 0.064 ng/mL to 41.427 ng/mL with one outlier having a value of >100 ng/mL. Sixty-nine (86.25%) participants had PSA values < 2.5 ng/mL, 7 (8.75%) had values ≥ 2.5-4 ng/mL while 4(5%) had values greater than 4 ng/mL.

Conclusion: Low number of participants (9%) had PSA values ≥ 2.5-4 mg/ml requiring yearly follow up screening. Sorting of men based on initial PSA results can reduce the number of those for yearly screening leading to the reduction in the burden associated with PSA based screening.

Keywords: Prostate cancer; Screening; PSA

Received: May 02, 2019; **Accepted:** January 23, 2020; **Published:** January 30, 2020

Introduction

Cancer of the prostate is on the increase in sub-Sahara African (SSA) countries. Lack of screening programs for men at susceptible age in addition to poor treatment facilities as well as low access to treatment have been implicated in the high mortality associated with this disease in LMICs. Screening using prostate specific antigen (PSA) which was introduced in the late eighties was considered to be responsible for low mortality from prostate cancer in high income countries (HICs) compared with LMICs [1]. However, in 2008, there were recommendations for the abolition of PSA based screening with claims that the benefits did not outweigh the harms citing unnecessary biopsy, over-diagnosis and over-treatment with attendant complications as harms associated with PSA based screening for prostate cancer [2]. Following these assertions, PSA testing especially in the United States and other high-income countries such as Sweden where screening were practiced were on the decline. However, in an analyses of data on prostate cancer between 1995 and 2012 using Surveillance, Epidemiology, and End Results

(SEER) data base (which includes period of active testing and period of decline in PSA based screening), it was reported that there was temporary decline in incidence of localized and loco-regional disease but the incidence of metastatic disease was on the increase especially among young patients [3]. Among the elderlies, other investigators also reported that the decline in PSA screening significantly changed the pattern of how prostate cancer now presents as 12 percent of men over 75 were diagnosed with metastatic prostate cancer in 2013, compared with 7.8 percent in 2011. Besides, the proportion of men diagnosed with aggressive cancer increased from 68.9 percent to 72 percent over the same period. Following these observations, several groups have recommended PSA based screening on selected age groups of men. The American Urological Association (AUA) and American Cancer Society (ACS) currently recommend that PSA testing be offered to asymptomatic men aged 55–69 years (AUA) or men older than 50 years with a minimum 10-year life expectancy (ACS) after patients receive information about the harms and benefits associated with screening [4]. These positions confirm that PSA testing is still a very relevant screening modality for early detection of prostate cancer especially in the absence of any other preferred screening method.

The American Cancer Society recommends screening at following age groups: Age 50 for men who are at average risk of prostate cancer and are expected to live at least 10 more years, age 45 for men at high risk of developing prostate cancer. This includes African Americans and men who have a first-degree relative (father, brother or son) diagnosed with prostate cancer at an early age (younger than age 65) and age 40 for men at even higher risk (those with more than one first-degree relative who had prostate cancer at an early age) [5]. The screening should be undertaken after the men have made informed decision to take part in the screening procedure. This follows receiving information on the uncertainties, potential benefits and risks of the screening exercise.

In Nigeria and other LMICs, routine screening practices were not available from the era of accepted routine screening till now. These were due to several reasons such as poor infrastructure, poor funding and low rate of public awareness on prostate cancer and the importance and acceptance of screening [6]. Even when PSA based screening is offered, the level of acceptance of testing in the Nigeria population has been reported to be 8-10% [7]. Several strategies have been used to improve the participation of men on prostate cancer education and testing. These include population-based activities and use of barbing saloons as sites where men could be reached [8]. These have yielded low success in acceptance rates. In this study we chose worship centres as likely places to engage a good proportion of men for prostate cancer education, and instant PSA based screening.

Data on the pattern of PSA levels among different age groups in Nigeria is scarce. This is not acceptable especially now that sporadic PSA testing is being favoured and the values used as baseline data to determine the frequency of further testing in order to reduce the frequency of PSA based testing [9]. There is also needed to design strategies to improve screening for prostate cancer in Nigeria in order to improve survival from this disease through early diagnosis and management. This is in line with a previous report that the usefulness of PSA as a tool for screening for prostate cancer has not been exploited maximally towards early prostate cancer diagnosis in Nigeria [10]. The goal of this study was to improve the uptake of PSA based screening for prostate cancer among Nigerians classified as high-risk group for prostate cancer. To achieve this goal, this study was conducted with the following objectives:

1) To determine the proportion of Nigerian men who will require yearly PSA based screening for early detection of prostate cancer;

2) To determine the proportion of men with previous PSA tests in the study population and

3) To determine the proportion of participants with elevated serum prostate-specific antigen in the study population. The outcome of the study indicated a great reduction in the number participants requiring yearly PSA testing.

Materials and Methods

This was a cross sectional study carried out among men aged forty years and above in two worship centers (one church and one mosque) in the city of Ibadan, Nigeria. The two worship centers were chosen based on high membership and proximity to the University College Hospital Ibadan where the samples were processed. Worship centers were used because of ease of getting access to eligible male participants. Ethical approval was obtained from the Institutional Ethics Committee for the study. Men aged from forty years and above were recruited into the study. The lower age group of 40 years was selected based on previous reports of elevated PSA of 4.8 ng/mL and diagnosis of adenocarcinoma of the prostate in males of 40 years of age [11]. This age group is also the recommended age for screening in high risk men such as those with family history and men of African ancestry (American Cancer Society). Following announcements to the congregations during regular worship sessions, eligible men turned up at the identified venue and time as announced. Information on prostate cancer including the need for PSA testing for early diagnosis as well as the possible risks and benefits of PSA testing was given to the participants with opportunities to ask questions of which answers were provided. The participants were then requested to sign informed consent for participation in the screening exercise. A self-administered questionnaire was distributed to those who agreed to participate. The questionnaire included questions regarding age, demographic details, medical, dietary and family history of prostate and other cancers, history of alcohol and tobacco use and physical measurements (height and weight), knowledge and previous information on prostate cancer and the usefulness of PSA test. Five ml of venous blood samples were obtained by phlebotomists (members of the study team) using vacutainer bottles. The samples were transported to the diagnostic laboratory of the University College Hospital within 3 hours of collection. The blood samples collected were centrifuged for 15 min after standing for a minimum of 30 min. Serum was pipetted into 2 mL microvials and stored at 4°C for Total PSA analysis which was done using microparticles enzyme immunoassay technology [12]. Participants were contacted individually by text messages to give appointments for digital

rectal examination (DRE) at the University College Hospital Ibadan. Phone calls were made to remind the participants a day to their appointment dates.

The PSA results were handed to the participants individually when they came for DRE. Those whose results were not ready as at the time of DRE or who did not turn up for DRE received their results through members of the worship centers who were part of the study team. Follow-up advice were also given to the participants. Those with abnormal results were directed to see Urologists at the Hospital for further investigations and management. Participants with PSA values ≥ 2.5-4 ng/mL were advised on the need to undergo yearly PSA based screening and were give appropriate appointments. Few participants who could not be reached had their results sent by text messages with follow up call to explain the results and follow up advice.

Data Analysis

Socio-demographic and other personal information were analyzed and presented as proportion and frequency counts. Mean and median PSA values were determined across various age subgroups. PSA was summarized as grouped data classified into three levels: < 2.5, ≥ 2.5-4 and > 4 ng/mL. The relationship between increasing age and PSA levels were determined using linear regression model. All calculations were conducted using SPSS 21.0, Windows version (SPSS, Chigaco, IL, USA).

Results

A total of 97 participants were screened but only 81 participants completed the questionnaires properly and were included in the analysis. All the 97 participants consented to the screening exercise. Five (6.25%) out of the 81 participants analyzed heard about prostate cancer and PSA testing but none has ever under gone PSA based screening. The main reason cited by the five participants (with previous information) for not undergoing screening was lack of funds. There was no family history of prostate cancer among the participants. Five participants were known hypertensive patients with good control on medications while one was a known asthmatic. The age of the participants ranged from 40 to 72 years. Seventy-two ((74%) participants turned up for the DRE and 22 (30%) of them had abnormal DRE findings and one out of the 22 had abnormal PSA. The Total PSA values ranged from 0.064 ng/mL to 41.427 ng/mL with one outlier having a value of >100 ng/mL. The mean PSA levels within different age groups are represented in **Table 1** and it shows similar mean values for ages 50-59 years and 60 years and above.

A simple linear regression was calculated to predict the relationship of age based on PSA. A significant relationship was found at age 50 years and above ($p<0.05$). Participants predicted age was 50.717 + 1.818 (PSA) years when PSA is measured in ng/mL **(Table 2).**

Sixty-nine (86.25%) participants had PSA values <2.5 ng/mL, 7 (8.75%) had values ≥ 2.5-4 ng/mL while 4(5%) had values greater than 4 ng/mL. Using a PSA cut of value of 4 ng/mL, four participants had values above 4 ng/mL. This includes the participant with value > 100 ng/mL. The distribution of the abnormal values based on age groups is presented in **Table 3.**

Discussion

Mortality from prostate cancer is still high in Nigeria and other countries of sub-Sahara Africa. In 2014 WHO Cancer Report, out of 30,400 deaths attributed to cancer in Nigeria, 30% was due to prostate cancer [13]. While close to 70% of the patients die from the disease in low- and middle-income countries, only about 30% die from the disease in high income countries even with their higher incidence of the disease. The high mortality in our environment is due to late presentation of the disease, inadequate facilities for proper diagnosis and optimal management as well as poor access to treatment due to lack of funds. PSA based screening is associated with early presentation

Table 1 The mean PSA levels within different age groups (Excluding value for the participant with PSA >100 ng/mL).

PSA Level (ng/mL)				
Age Recoded	**Mean**	**N**	**Std. Deviation**	**Median**
40-49 yrs	0.762935	31	0.6015717	0.622000
50-59 yrs	1.266395	38	1.0756536	0.974500
60 yrs and above	1.259636	11	0.9397733	1.182000
Total	1.070375	80	0.9228653	0.765000

Table 2 The mean PSA levels within different age groups (Excluding value for the participant with PSA > 100 ng/mL).

Coefficients[a]							
Model	**Unstandardized Coefficients**		**Standardized Coefficients**	**t**	**Sig.**	**95.0% Confidence Interval for B**	
	B	**Std. Error**	**Beta**			**Lower Bound**	**Upper Bound**
Constant	50.717	1.066		47.562	0.000	48.594	52.839
PSA Level	1.818	0.757	0.263	2.403	0.019	0.312	3.324
[a]Dependent variables: Age							

Table 3 The relationship between age group and PSA level after categorization into normal (≤ 4 ng/mL) and abnormal values (>4 ng/mL).

Age (Years) PSA Re-coded into 2 categories					
Variables			PSA Re-coded into 2 categories		Total
			Normal	Abnormal	
Age Recoded	40-49	Count	31	0	31
		% within Age Recoded	100.0%	0.0%	100.0%
		% of Total	38.3%	0.0%	38.3%
	50-59	Count	37	1	38
		% within Age Recoded	97.4%	2.6%	100.0%
		% of Total	45.7%	1.2%	46.9%
	60 and above	Count	11	1	12
		% within Age Recoded	91.7%	8.3%	100.0%
		% of Total	13.6%	1.2%	14.8%
Total		Count	79	2	81
		% within Age Recoded	97.5%	2.5%	100.0%
		% of Total	97.5%	2.5%	100.0%

but most susceptible men in our environment are not aware of the disease as well as the availability of screening methods that can lead to early diagnosis when management outcome can be better [14]. There are sporadic public education activities going on through radio, television and some face to face discussions but sometimes these do not reach wide audience and are not accompanied by actual testing. Some listeners may therefore not know where to go and access the services and some may not be able to pay for such. Most people undergo PSA testing as a diagnostic procedure ordered by their physicians following clinic presentation. Poor attitude towards screening for prostate cancer still persists leading to late diagnosis [7]. In this study, we found that only 6% of the participants had knowledge of prostate cancer and screening and they were all willing to be screened. This finding is similar to a previous report from Nigeria where out of 147 respondents, only 9 (5.8%) had previous knowledge about screening for prostate cancer and all 147 respondents were willing to be screened [10].

The choice of worship centers for this study enabled the successful and timely recruitment of participants as we had sufficient number as expected and all participants consented to the exercise. As Nigerians attend worship activities in large numbers and we took the PSA based screening activities to the vicinity of the worship centers which they attend regularly, this strategy enabled us to reach large audience easily instead of going from house to house or waiting for them to come to the clinics. We also think that the information having been passed to them by their spiritual leaders assisted in assuring them of the benefits of such exercise. In addition, the screening was free, and this would have also encouraged people to come especially as the few who had knowledge of screening for prostate cancer complained of lack of funds to access the services. Availability of free screening programs can therefore improve the uptake of screening exercises in Nigeria.

The percentage of participants with abnormal PSA values (>4 ng/mL) in this study was 5%. This is comparable to a value of 7.5% reported among 128 participants aged 40-79 years screened in Edo state in Southern Nigeria [15]. The slight difference may be due to the age of participants. In our study, the highest age was 72 years while in the cited report, it was 79 years.

One of the observations against population PSA-based screening for prostate cancer was the high rate of harm including high economic costs compared with benefits. It is however observed that men of African ancestry usually have very aggressive tumours with associated high mortality. Men with these characteristics carry a higher incidence of prostate cancer and could be at higher risk of dying from the disease. At present, even with the controversies surrounding PSA test for prostate cancer screening, there is uncertainty whether the impact of screening is similar in higher risk men such as Blacks in comparison to men at lower risk (Caucasians) [16]. We are of the opinion that some form of screening should be offered to men with high risk of developing prostate cancer in order not to miss aggressive cancers that would probably benefit from early diagnosis and treatment. The recent streamlining of screening tests by the American Cancer Society based on longitudinal studies will greatly reduce the frequency of testing as well as expenditure in this aspect. This can be demonstrated using the data from this study. The American Cancer Society recommends that 'at first screening, if no prostate cancer is found as a result of screening, the time between future screenings depends on the results of the PSA blood test:

a) Men who choose to be tested who have a PSA of less than 2.5 ng/mL may only need to be retested every 2 years;

b) Screening should be done yearly for men whose PSA level is 2.5 ng/mL or higher [5]. It follows from this study that 86% of the participants with PSA <2.5 mg/mL can do screening every two years thus saving huge amount of resources. On the other hand, only 8% will have to undergo annual PSA based screening which is quite manageable. This position has been supported by Luque et al. [8] who reported that using PSA at early age to stratify prostate cancer risk will enable a large number of men to have screening less frequent while few men of high-risk status will have more frequent testing [9].

Some workers attest that a single PSA measurement early in life before age 50 can identify a small group of men at increased risk of advanced prostate cancer diagnosed up to 30 years later determined by their first PSA level (if ≥ 2.5 ng/mL). Careful monitoring is warranted in these men. Based on available data on the risk of death using PSA value at age 60, it has been suggested

that three lifetime PSA tests (mid to late 40s, early 50s, and 60) are probably what at least half of men need [17-19]. Using this strategy can identify men with limited need for PSA screening in our environment thereby allowing a focus on the few that will need regular surveillance.

Conclusion

Very few eligible men had previous knowledge about screening for prostate cancer, but none had previous screening due to lack of funds. The proportion of participants with abnormal PSA values was low. The adoption of PSA stratification methods can limit the number of screening exercises with concentrations on high risk groups thus improving the effectiveness of the exercise in our environment. This will also reduce the clinical and economic burden associated with PSA based screening. This should be adopted in high risk populations especially as it is not yet clear whether the impact of screening is similar in higher risk men such as Blacks in comparison to Caucasians with lower risk.

Limitations of the Study

The sample size was low, and this was guided by the limited budget available for the study. Nevertheless, the outcome especially with respect to the low proportion of participants that required yearly follow up was noteworthy. It also highlighted the fact that with availability of funding, most men will undergo regular screening exercises for prostate cancer in the population thereby improving the screening rate which is currently unacceptably low. The result will also guide planning and implementation of future screening activities.

Future Perspectives

We plan to carry out future follow up screening activities among the participants screened in this study (yearly for those who had PSA value ≥ 2.5 ng/mL and every two years for those with values < 2.5 ng/mL). In addition, there is need to undertake screening among more participants to have a larger sample size that can reflect the different sections of Nigeria. This will enable us have PSA cut off values for our population. Longer follow up is also needed to monitor those who will develop the disease and outcome of management in those with high values of PSA. This will lead to the assessment of the impact of PSA based screening in high-risk groups.

Authors Contributions

Ayorinde Folasire: Data acquisition and revision of the manuscript.

Eniola Bamgboye: Statistical design and writing of analysis section of the manuscript.

Atara Ntekim: Data acquisition and manuscript writing.

All the authors read and approved the final version of the manuscript before submission.

Funding

College Research and Innovation (CRIM), University of Ibadan Grant # CTR16B00-5.

Conflicts of Interest

Non declared by any of the authors.

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