ISSN 2073-9990 East Cent. Afr. J. surg

Assessment of DRE and PSA as Diagnostic and Screening Tools for Carcinoma of the Prostate in Rural Nigeria.

E. Irekpita[1], C. Owobu, E. Aigbe[3], G. Obasikene[3], A. Igbe[2].
[1] Dept of Surgery, Ambrose Alli University, Ekpoma, Nigeria.
[2] Dept of Histopathology, Irrua Teaching Hospital, Irrua, Nigeria.
[3] Dept of Surgery, Irrua Teaching Hospital, Irrua, Nigeria.
Correspondences to: Irekpita Eshiobo, Email: ieshiobo@yahoo.com

Background: ***Carcinoma of the Prostate is a major health burden globally. This study was aimed at assessing the value of digital rectal examination and prostate specific antigen as screening and diagnostic tools for carcinoma of the prostate in rural Nigeria***
Methods: ***Men who had abnormal digital rectal examination (DRE) findings, elevated prostate specific antigen (PSA) and prostatic histology within the period were included in the study. Data related to age, PSA value, DRE findings and histology were analyzed using SPSS and simple statistical methods.***
Result: ***The total number of patients was one hundred and fifty eight. The peak decade of occurrence of prostate cancer was the 61-70 years. When DRE findings was cross tabulated with histology, there was a significant correlation (P=.000). The positive predictive value (PPV) of DRE was 96.15% while the negative predictive value (NPV) was 93.5%. For PSA, there was also a significant correlation (P=.000). The PPV of PSA was 64.9% while the NPV was 96.33%.***
Conclusion: ***The extremely impressive performance of DRE and PSA as diagnostic and screening tools may be due to the limitation of the study to a cohort of patients who already hard lower urinary tract symptoms. There is need for community based studies.***

Keywords: Screening, DRE, PSA, Positive predictive value, Negative predictive value, Prostate cancer.

Introduction

Carcinoma of the Prostate Continues to be a major health burden worldwide[1]. According to Jason et al[2], the life time prevalence of the disease is 17 percent. In the United States of American, 218, 890 diagnosis of the carcinoma of the prostate were expected in 2007 with corresponding deaths of 27,050. In most third world countries, such information are either scanty or nonexistent. In Nigeria, available information are from the Urban centers and are mostly on incidence of the disease; Port-Harcourt[3] 114/100,000, Lagos[4] 127/100,000.

The diagnosis of Carcinoma of the prostate when affected men present for evaluation, is based on history, physical examination and Investigation. In simple uncomplicated disease, the history is similar to that of benign prostatic hyperplasia (BPH), consisting essentially of Lower Urinary Tract Symptoms (LUTS)[5]. In advanced disease when there are metastases, additional symptoms present depend on the involved system. The hallmark of physical examination in carcinoma of the prostate is the digital rectal examination (DRE). Features on DRE which point to the presence of carcinoma of the prostate include enlarged prostate, lobar asymmetry, nodularity, suspicious nodules and a rubbery or hard prostate[6]. Argen et al[7] in a systematic review concluded that DRE is the oldest least invasive screening tool for Ca prostate with a high specificity and a high negative predictive value though its moderate sensitivity does not allow for conclusion. An abnormal DRE finding is an indication for biopsy of the prostate.

Prostate specific antigen (PSA), a protein serease produced only by the prostate, replaced acid phosphatase in 1986 as an investigating modality and has since become a reliable tumor marker and screening tool for carcinoma of the prostate[8]. PSA is not specific for carcinoma of the prostate as other diseases of the prostate such as BPH and prostatitis may lead to an elevated

ISSN 2073-9990 East Cent. Afr. J. surg

value. PSA is also considered a tumor marker that is not sensitive enough as it is normal in some patients with prostate cancer.[9] The universally accepted normal upper limit is 4ng/ml but it is also well know that at this upper limit of normal, some cancers are missed. Essentially, biopsy of the prostate is advised when the PSA value exceeds this upper limit. In order to improve the sensitivity of PSA, concepts such as age cut off, PSA velocity, free PSA and complex PSA were developed.

PSA is presently the most reliable tumor marker in carcinoma of the prostate with a higher predictive value than DRE and TRUS.[9] Available data indicate that the PSA level is as, or more effective than DRE for the detection of prostate carcinoma. Currently, for screening purpose, a combination of DRE and PSA is recommended as this approach yields up to 75% diagnostic sensitivity for prostate carcinoma though, in the American Cancer Society updated screening guidelines for prostate cancer, DRE is optional[10].

This study was done in Irrua Teaching Hospital, a Nigeria tertiary institution based in a semi urban setting and sub serving a population of 4 million people. To the best of our knowledge, the role of DRE and PSA in screening for prostate cancer has not been studied or documented in the rural Nigeria men. We therefore aim to add to available information on Ca prostate with particular reference to rural black Nigerian men. This study will assess the value of DRE and PSA as diagnostic and screening tools for Ca prostate in this group.

Patients and Methods

All men who presented at the Urology out patient, General outpatient and the Accident and Emergency unit of the hospital with LUTS BPH were included. However patients who were on treatment or have had treatment for prostatic disease before presentation at our hospital were exclude. Others excluded were LUTS due to Bladder diseases and Urethral stricture. All these men were assessed with DRE and PSA and those who's PSA exceeded 4ng/ml or had abnormal DRE findings were subjected to prostate biopsy.

Digital rectal examination (DRE) was done in the left lateral position. In very sick patients, the supine position was used while the knee-elbow position was preferred in men who presented with urinary retention though the DRE was repeated after the retention had been relieved. Factors such as obliteration of the median groove, presence of suspicions nodules, lobar asymmetry, generalized nodularity, tenderness and palpability of the seminal vesicles were assessed for .All the DRE were done by specialist Urologists.

The specimen for PSA measurement was obtained either before or at least fourty eight hours after the DRE. The specimen were centrifuged at three thousand revolutions per minute. The supernatant was stored at -2^{0}C-8^{0}C if the investigation was not done immediately. The DRG international Inc., USA enzyme-linked immunosorbent assay was generally used by this Center during the study period. The findings on DRE, PSA value, the histology report and patients age were recorded. The data so obtained was analyzed using the statistical programming for social sciences (SPSS-17) and simple statistical methods. Pearson chi square was used to compare age, DRE, PSA and histology.

Results

A total of One hundred and Fifty -Eight patients seen within the study period with complete data suitable for this study were included. The age distribution is shown in Table 1. Of these, 95 (60.1%) had CAP, 5 (3.2 %) had prostate intra-epithelial neoplasia and 58 (36.75%) had BPH on histological evaluation. The peak age at diagnosis of both BPH and CAP was the seventh decade of life amounting to 35.4% of the total. The minimum age at which the diagnoses of CAP and BPH were made was within the 5th decade of life (1.9%).

ISSN 2073-9990 East Cent. Afr. J. surg

Table 1. Age distribution of Patients

Age Range	Frequency	Percentage
41-50	3	1.91
51-60	17	10.80
61-70	56	35.40
71-80	53	33.54
Above 80	29	18.35

Of the 158 patients, 62 (39.2%) had a benign feel of the prostate on DRE, 24 (15.2%) had an obliterated median groove, 13 (8.2%) had a suspicious nodule, 53 (33.5%) had a hard and nodular prostate and 6 (3.8%) had asymmetrical lobes giving a total malignant feel of the prostate of 96 (60.8%). When DRE was cross examined against histology, a significant correlation was found (P = 0.000). Eighty (84.21%) of the ninety six patients who had a malignant prostate on DRE had a histologically confirmed CAP, while 43 (68.25%) of these who had a benign finding on DRE were confirmed to have BPH. When age was cross tabulated with histology, there was no significant correlation (P= 0.431). The positive predictive value (PPV) of DRE was 96.15% while the negative predictive value (NPV) was 93.5%.

Table 2 shows the PSA distribution side by side the findings when PSA is cross-tabulated with histology. All the patients who's PSA were above 100ng/ml were histologically confirmed as having CAP. Below this PSA value, a variable number of patients had histologically confirmed CAP. Interesting is that between values of 0 - 4nglml, two of the seven patients had histologically confirmed CaP. Chi square test showed a significant correlation between PSA and histology (P= 0.000). When PSA was cross tested with Gleason score, there was no statistically significant relationship (P= 0.106) .Figure iii shows the relationship between PSA and histology. PSA had PPV of 64.9% while the NPV was 96.33%.

Table 2. PSA Histology cross tabulation

	Histology			
	BPH	**PIN**	**CAP**	**Total**
PSA	1	0	1	2
0-4	5	0	2	7
4.1-10	4	1	6	11
10.1-20	19	1	8	28
20.1-20	6	1	4	11
30.1-50	14	1	13	28
50.1-70	5	0	12	17
70.1-100	4	1	27	32
Above 100	0	0	22	22
Total	58	5	95	158

Of the Ninety One Patients who had histologically confirmed CAP, and who's Gleason scores were recorded, 17 (18.68%) had well differentiated tumors, 33 (36.26%) had moderately well differentiated tumors while the remaining 41 (41.06) had poorly differentiated tumors. When Gleason score was tested against histology, there was a statistically significant correlation (P= 0.000). Between Gleason score and PSA, there was statistically significant relationship (P=

ISSN 2073-9990 East Cent. Afr. J. surg

0.002). This was different for age and histology (P= 0.431).

Discussion

Prostate cancer is the leading non cutaneous cancer in the United States of America with a disease related death reaching 29,720 in 2013.[11] The highest prostate cancer incidence and mortality rates are reported in black African American men (AAM) living in the United States.[12] This is exceeded only by Jamaica with an incidence of 304/100,000[13]. Data available also indicate that the peak age for prostate cancer is a decade earlier in black African American men in the United States. In this study, the peak decade was 61-70 year group.

Little is known of the disease in Sub Saharan Africa, the poorest Countries of the world[14] and the origin of the black African American men. Available data are mostly from GLOBOCAN and are often unreliable because they are derived mostly from registries covering hospitals, small sub national areas or only major cities.[15] Apart from the paucity of data in this region, late presentation in the advanced stage of the disease implies that the mortality rate may be higher than in the AAM currently.[16]

The introduction of screening programs in the developed world revolutionized the management of prostate cancer. This was aimed at early diagnosis at a stage the disease is curable.[17] Currently, in these fortunate areas, concern now centers on issues of over diagnosis and over treatment.[18] Such screening programs are presently either erratic or unavailable in centers like where this study was done and in shot, most of Sub Saharan Africa. Several reasons such as lack of awareness, ethical implication of diagnosis and lack of resources have been documented as responsible for this [19]. These factors are remarkably at play in this centre with significant influence on the outcome of this study.

The two most commonly used variables for screening for prostate cancer are digital rectal examination (DRE) and prostate specific antigen (PSA). DRE is the oldest and least invasive method though a few patients are averse to it. DRE findings are considered as abnormal when the prostate is enlarged, the median groove is obliterated, the lobes are asymmetrical, there are (is) suspicious nodules, the seminal vesicles are palpable or the prostate is hard and or nodular.[20] The positive predictive value (PPV) and the negative predictive (NPV) values of DRE of 96.15% and 93.5% in this study, seemingly quite high, are explained by the extremely late presentation[21] by this rural dwellers. Factors such as poor health care regulation, the claim by complementary and alternative medicine (CAM) practitioners in the state media of their ability to cure several diseases, poverty and ignorance account for this late presentation[22]. In this late stage of presentation, even the Urology registrar is able to predict prostate cancer based on DRE alone.

Prostate specific antigen (PSA) was introduced into clinical practice in the 1986s for the purpose of prostate cancer screening.[23] Since then, the percentage of patients who present with late disease has reduced remarkably in developed communities[24]. Percentage free PSA is most useful and helpful in deciding on biopsy though in our centre, this decision is usually based on total PSA, the upper limit being 4ng/ml. This upper limit has been considered imperfect as according to Thomson et al[25] at this upper limit, significant number of cancers at lower PSA are missed. In our study, of the seven patients with PSA of 4ng/ml and below, who had prostate biopsy done based on DRE finding, two (28.57%) were positive for prostate cancer indicating that this upper limit may be too high for this community. However, local factors such as the source of the kit, storage facilities and efficiency of the laboratories may affect the PSA value [16].

Studies have shown higher PSA values in AAM than CAM [26]. However, some studies have pointed to factors such as large tumor burden, presence of undetected metastasis rather than more aggressive tumor biology, as a cause. Ikwuerowo et al[3] in their study indicated that the

ISSN 2073-9990 East Cent. Afr. J. surg

common association of prostatitis may be responsible for the higher PSA in our environment. The overall positive predictive value of PSA above the cutoff of 4ng/ml falls within the often documented. In the work of several authors[27,28,29] above the cutoff of 4ng/ml, the PPV was 30% while at the cutoff of greater than 10ng/ml, PPV was 42-60%. The prostate cancer prevention trial which biopsied men with normal PSA levels estimated NPV of 85% for PSA value < 4ng/ml, a figure fairly lower than the 96.3% obtained in this study. This is still explainable by the late patient presentation with higher PSA values. For instance, patients who presented with PSA value of >100ng/ml were all positive for prostate cancer on biopsy. This may mean that in our low resource environment, such patients could be spared prostate biopsy and diagnosis based on PSA if other features are present.

This study was hospital based, assessing the value of DRE and PSA as tools for screening for prostate cancer in patients who already have lower urinary tract symptoms. This to a large extent, may have influenced their remarkable performance as screening tools as most of the patents presented in the advanced stage. There is a need for community based studies in these rural areas to assess these variables and establish community based predictive values in preparation for properly regulated screening programs in sub Saharan African countries. This will help to avoid unnecessary prostate biopsies

References

1. Reckler F. Prostate Specific antigen in the diagnosis of organ confined treatable prostate cancer. Sch Weiz Med Wochen sch 1996; 126 (44): 1881 -1890
2. Jason Wilbar, Roy J, Lucille A. Prostate cancer screening: the continuing controversy. Am Fam Physician 2008; 78(12): 1377-1384
3. Stephen Odunayo Ikuerowo, Olufumilade Akinfolarin Omisanjo, Muftao Jimoh Bioku, Micheal Olawale Ajala, Victor Patrick Nonylim Mordi, Julius Olusanmi Eshio. Prevalence and characteristics of prostate cancer among participants of a community based screening in Nigeria Using serum prostate specific antigen and digital rectal examination. The Pan African Medical Journal 2013; 15: 129
4. Eke N, Sapira MK. Prostate Cancer in Por t-Harcourt, Nigeria: features and outcome. Nig J Surg Res. 2002; 4: 34-44
5. Ezenwa E, Tijani K. Jeje A, Ogunjimi , Ojewola R. Prevalence of prostate cancer among Nigerians with intermediate Total Prostate specific Antigen levels (0-4nglml): Experience at Lagos University Teaching Hospital. The internet Journal of Urology 2012; 9:3
6. Arjen Hoogendam, Frank Buntinza, Henrica CW Velb. The diagnostic value of digital rectal examination in primary care screening for prostate cancer: A meta-analysis. Family Practice 1999; 16:621- 626.
7. Mohammed El Imam Ahmed, Nawal Zarong Higazi, Daffalla O Abdulidris, Ali Ahmed Idris, khaled El Tahir khaled, Mustapha Omran, et al. Prostate specific antigen versus digital rectal examination as screening for ca prostate in Sudanese patient. Sudanese Journal of Public Health 2009:4(2): 278-281
8. Catalona WJ, Richie JP, Ahmann FR et al. Comparison of digital rectal examination and serum prostate specific antigen in the early detection of prostate cancer: results of a multicenter clinical trial of 61,630 men. J Urol 1994;15: 1283-1290
9. Micheal R Cupp, Joseph E Desterling. Prostate specific antigen, digital rectal examination and trans rectal ultrasonography. Their roles in diagnosing early prostate cancer. Mayo Clinic Proceedings 1993; 68(3): 297-306
10. Manyahi JP, Musau P, Mteta AK. Diagnostic values of digital rectal examination, prostate specific antigen and trans rectal ultrasound in men with prostatism. East African Medical journal 2009;86(9):
11. Siegel R, Naishadham D, Jemal A. Cancer Statistics 2013 CA Cancer J Clin 2013; 63(1): 11-30

12. CF Heyns. Is prostate cancer more common and more aggressive in African men. African Journal of Urology 2008; 14(2): 66-74
13. DU XL, Fang S, Coker Al, et al. Racial disparity and socio economic status in association with survival in older men with local/regional stage prostate carcinoma. Findings from a large community based cohort. Cancer 2006; 106(6): 1276-85
14. Jalloh mohamed, Lamine Niang, Medina Ndoye, Issah Labon, Serigne M. Gueye. Prostate cancer in Sub Saharan Africa. Journal of Nephrology and Urology Research 2013; 1:15-20
15. Jedy-Agba EE, Curado MP Oga E, ta al. The role of hospital based cancer registries in low and middle income countries. The Nigerian case study. Cancer Epidemiology 2012; 36(5): 430-5
16. Aghaji Aloy. Prostate cancer: coping with the monster in a third world setting. 22nd inaugural lecture of the university of nigeria
17. Paquette El, Connely RR, Sesterhenn IA, et al. Improvements in pathologic staging for African American men undergoing radical retropubic prostatectomy during the prostate specific antigen era: implication for screening a high risk group for prostatic carcinoma. Cancer 2001; 92(10): 2673-2679
18. Draisma G, Efzioni R, Tsochkov A, et al. Lead time and over diagnosis in prostate specific antigen screening: importance of methods and context. J Natl Cancer Inst 2009; 101(6): 374-83
19. Ajape AA, Babata A, Abiolu OO. Knowledge of prostate cancer screening among native African urban population in Nigeria. Nig QJ Hosp. Med. 2009; 19(3): 145-7
20. Ekwere PD, Egbe SN. The changing pattern of prostate cancer in Nigerians: Current status in the Southeastern states. J Nalt Med. Assoc. 2002; 94:619-627
21. Badmus TA, Adesunkanmi AR, Yusuf BM, et al. Burden of prostate cancer in south western Nigeria. Urology 2010; 76(2): 412-416
22. Reynolds D. Prostate cancer screening in African American men; barriers and methods for improvement. Am J Mens Health 2008; 2(2): 172-177
23. Payne H, Cornford P. Prostate specific antigen: an evolving role in diagnosis, monitoring and treatment evauation in prostate cancer. Urol Oncol 2010
24. Cooperberg MR, Moul JN, Carroll PR. The changing face of prostate cancer. J Clin Oncol. 2005; 23(32): 8146-8151
25. Thomson IM, Pauler DK, Goldman PJ, et al. Prevalence of prostate cancer among men with a prostate specific antigen level < or = 4.0ng/ml. N Engl J Med. 2004; 350(22): 2239-2246
26. Moul JN, Douglas TH, McCarthy WF, McLeod DG. Black race is an adverse prognostic factor for prostate factor recurrence following radical prostatectomy in an equal access health care setting. J Urol 1996; 155(5): 1667-1673
27. Brawer MK, Chetner MP, Beatie J, et al. Screening for prostatic carcinoma with prostate specific antigen. J Urol 1992; 147:841
28. Catalona WJ, Smith DS, Ratliff TL, Basler JN. Detection of organ confined prostate cancer is increased through prostate specific antigen based screening. JAMA 1993; 270:948
29. Schroder FH, van der Cruijsen I, De Koning HJ, et al. Prostate cancer detection at low prostate specific antigen. J Urol 2000 163:806