Correlation of Digital Rectal Examination Findings with Findings on Histopathology of the Prostate in Patients with Suspected Prostate Cancer

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ABSTRACT

Introduction: Prostate cancer is the commonest malignancy affecting males worldwide and attempts at reducing the mortality of the disease are focused mainly on early detection. Digital rectal examination (DRE) and prostate specific antigen (PSA) test are preliminary modalities to identify patients who would require further study. Confirmation and grading of prostate cancer is currently done using histopathological analysis of prostate biopsy specimens. The aim of this study was to determine the correlation between digital rectal examination findings with findings on histology of the prostate in patients with suspected prostate cancer.

Material and Methods: Forty-five adult male patients aged 50 years and above with abnormal digital rectal examination findings had digitally-guided transrectal prostate biopsy done. Digital rectal examination findings were correlated with the histopathology findings. Data analysis was conducted using Statistical Package for Social Sciences version 16. Tests of correlation at 95% confidence limit, and p-value of ≤ 0.05 were conducted.

Results: The mean age was 68.1years (range: 52 – 93 years) with the age range for peak incidence being 61 – 70 years (42.2%). On DRE, 91.1% of patients were found to have enlarged prostate glands with 73.3% of the glands having a hard consistency and 51.1% being nodular. More patients (91.1%) had multiple DRE abnormalities. There was a statistically significant positive correlation between abnormal DRE findings and histologic diagnosis of prostate cancer (p<0.05). The prostate cancer detection rate for DRE was found to be 60%.

Conclusion: Abnormal findings detected using digital rectal examination correlated well with a histologic diagnosis of prostate cancer. Digital rectal examination remains a relevant tool in the diagnosis of prostate cancer.

Keywords: Correlation, Digital Rectal Examination, Histopathology, Prostate Cancer

INTRODUCTION

Prostate cancer is the second most frequently diagnosed cancer worldwide and the fifth leading cause of cancer deaths among men[1]. It has been the most common non cutaneous malignancy in males in the United States since 1984 accounting for one quarter of all such cancers[2,3]. African Americans are at a higher risk than whites and they tend to present at later stages of the disease. It has also been suggested that mortality from this disease may be higher for African Americans[4]. In Nigeria, prostate cancer is the number one cancer affecting men and it constitutes 11% of all male cancers in the country[5]. Studies from different parts of the country indicate that significant proportion of patients present with advanced disease[6,7,8]. It is thus a significant public health problem with associated high morbidity and mortality. Attempts at reducing the mortality of the disease are mainly focused on early detection of the disease[9]. Digital rectal examination (DRE) of the prostate is the oldest method of physically examining the prostate[10]. However it may have been deemphasized as a screening tool for prostate cancer by certain guidelines which have made it optional with emphasis rather placed on PSA[11]. PSA however, is not a specific test for prostate cancer as a considerable overlap between PSA levels exists in men with normal prostates, benign prostatic hyperplasia (BPH) and localized CaP[12]. Most cancers arise in the peripheral zone of the prostate, which comprises the posterior surface of the gland including the apical, lateral, posterolateral and anterolateral portions of the prostate. It is this part of the gland that is accessible by DRE[13]. Unfortunately, many cancers detected using DRE are either locally or regionally advanced but despite this limitation, DRE remains an important diagnostic procedure as up to 20% of cases of prostate cancer may be associated with a normal serum PSA and may be detected by DRE[13]. Contrary to the notion that DRE is highly subjective, it has been shown that little inter-observer variability exists when the prostate is properly examined in a systematic manner[12]. Considerable enhancement of detection rates is noted when DRE and PSA levels are used as indicators in patients that may require further study by transrectal ultrasound (TRUS) and biopsy[8]. Abnormal DRE findings usually leads the clinician to perform biopsy of the prostate to diagnose the disease[11,14]. Confirmation of the presence and the grading of prostate cancer is performed

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through histopathological analysis of biopsy samples and this is considered the reference standard[14,15]. This study was carried out to determine the prostate cancer detection rate of DRE using histology of biopsy specimens of the prostate.

MATERIAL AND METHODS

Study Design: This was a hospital-based, prospective, cross-sectional and descriptive study aimed at determining the correlation of digital rectal examination findings with histopathology of the prostate in patients with suspected prostate cancer.

Study Area: The study was carried out at the University of Calabar Teaching Hospital Calabar, a 410-bed hospital operating in Calabar Municipality Local Government area of Cross River State, Nigeria. It is a referral centre for hospitals in Cross River and the nearby states of Akwa Ibom, Benue, Abia, Rivers and Ebonyi states of Nigeria, as well as the Republic of Cameroon sub-serving an approximate population of over 8 million people.

Study Period: The study was carried out from May 2014 to April 2015.

Ethical Approval/ Informed Consent: Approval for the conduct of the study was obtained from the health research ethics committee of the hospital and informed consent taken from recruited patients.

Study Population: Forty five consecutive adult male patients aged 50 years and above were included in the study.

Method: A structured proforma was used to record details of patients' personal and clinical data as well as findings from relevant investigations. Consecutive adult male patients with lower urinary tract symptoms (LUTS) and other symptoms suggestive of prostate cancer seen by the Urology unit and in whom DRE finding(s) were suggestive of prostate cancer were included in the study. All patients who were on drug treatment with finasteride and dutasteride and those already on hormonal treatment for prostate cancer were excluded. A carefully performed clinical examination of each patient, with particular attention to DRE to assess the prostate gland for size, symmetry, presence or absence of median groove and lateral sulci, consistency, nodularity, induration, fixity and tenderness was conducted by the first author. Patients with abnormal DRE findings with or without total PSA elevation had digitally-guided automated transrectal prostate biopsy done under cover of oral Ciprofloxacin 500mg given thirty (30) minutes prior to the procedure. Patients were placed in the left lateral position and a well lubricated left index finger was used to guide a size 18G biopsy needle mounted on an automated spring loaded biopsy gun into the rectum to access the prostate. Six cores of prostatic tissue were obtained (2 each from the apex, mid-portion- lateral lobes and base of the gland), fixed in Bouin's solution and submitted for histology. Histological analysis of biopsy samples was carried out to determine the presence or absence of malignancy.

STATISTICAL ANALYSIS

Data obtained was analysed using Statistical Package for Social Sciences (SPSS) version 16. Data was summarized as frequencies, percentages, means, and standard deviations and presented in tables, bar and pie charts. Cancer detection rate was determined. Tests of correlation (logistic regression and Pearson's chi square) at 95% confidence limit, and p-value of ≤ 0.05 were conducted.

RESULTS

Sociodemographic data

A total of was 45 patients were studied with mean age of 68.1 years and age range of 52 – 93 years. The age range for peak incidence was 61 – 70 years which constituted 42.2% of the study population. The mean duration of symptoms was 11.7 months with range of 1 – 42 months. The duration of symptoms before presentation was greater than 6 months in 25 patients (55.6%), between 4 and 6 months in 8 patients (17.8%) and between 1 and 3 months in 12 patients (26.6%).

Symptoms and Complications

The most common lower urinary tract symptom was

	Frequency	Percentage (%)
Symptom		
Frequency	40	88.9
Nocturia	38	84.4
Incomplete bladder emptying	33	73.3
Urgency	18	40.0
Poor urine stream	17	37.8
Urge incontinence	10	22.2
Hesitancy	5	11.1
Interrupted urinary stream	3	6.7
Complication		
Low Back Pain	13	28.9
Acute Retention	11	24.4
Chronic Retention	7	15.6
Haematuria	3	6.7
Bone Pain	2	4.4
Perineal/Suprapubic Pain	2	4.4
Paraplegia	1	2.2
Paraparesis	1	2.2
Weight Loss	1	2.2
Swelling Of Lower Limbs	1	2.2

Table-1: Lower Urinary Tract Symptoms and Complications in the Patients

DRE Finding	Number	Percentage
Hard Consistency	33	73.3%
Nodules	23	51.1%
Obliteration Of Median Groove	16	35.6%
Firm Consistency	9	20.0%
Obliteration Of Right Lateral Sulcus	7	15.6%
Fixity	5	11.1%
Obliteration Of Left Lateral Sulcus	5	11.1%
Induration	2	4.4%
Discomfort	1	2.2%

Table-2: Characteristics of Prostate on DRE

Section: Urology

Isiwele, et al.   Digital Rectal Examination Findings with Findings on Histopathology of the Prostate

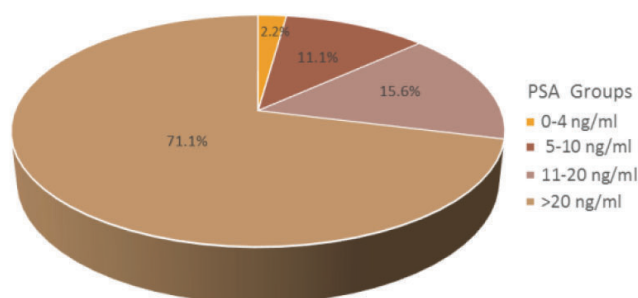| Correlation (Logistic Regression) Between Single/ Multiple DRE Abnormality And Histological Diagnosis							
DRE Abnormalities	Histologic diagnosis (CAP)	Total	Regression Coefficient (β)	95% Confidence Interval for β		Odds Ratio	p-Value
Constant			-0.6			3.0	0.08
1	1	4	1.8	0.5	61.8	5.7	0.15
2	5	9	0.4	0.3	6.9	1.5	0.58
≥3	21	32					
Total	27	45					
Correlation (Logistic Regression) Between Hard Consistency and Histologic Diagnosis							
Hard consistency	Histologic diagnosis		Total	Regression coefficient (β)	P-value	Odds ratio	95% confidence interval
	BPH	CAP					
Constant				-.9	.04		
No	4	8	12	-.4	.59	.7	.2	2.7
Yes	14	19	33				
Total	18	27	45				
Correlation (Logistic Regression) Between Nodularity and Histologic Diagnosis							
Nodularity	Histologic Diagnosis		Total	Regression Coefficient (B)	P-Value	Odds Ratio	95% Confidence Interval
	BPH	CAP					
Constant				-.2	.56		
No	10	12	22	.4	.46	1.6	.5	5.2
Yes	8	15	23				
Total	18	27	45				
Correlation (Logistic Regression) Between Fixity And Histological Diagnosis							
Fixity	Final Diagnosis		Total	Regression Co-efficient (B)	95% Confidence Interval For B		Odds Ratio	P-Value
	BPH	CAP					
Constant				-1.5			.2	.01
No	18	22	40	-19.7	-0.0	+0.01	.0	.9
Yes	0	5	5				
Total	18	27	45				
Correlation (Pearson's Chi Square Test) Between DRE and Histological Diagnosis							
Histological Diagnosis	Frequency		Percentage (%)		X²		P-Value
BPH	18		40.0				
CAP	27		60.0		45.0		0.00
Total	45		100.0				
Table-3: Correlation Statistics							

Figure-1: Prostate Specific Antigen (PSA) Results

urinary frequency experienced by 88.9% of patients, followed closely by nocturia seen in 84.4% and incomplete bladder emptying (73.3%) among other symptoms. Forty two patients presented with complications, with the most common being low back pain in 28.9% of patients, followed by acute retention of urine 24.4% and chronic retention of urine seen in 15.6% of patients (Table 1).

Digital rectal examination findings

On digital rectal examination (DRE), 41 patients (91.1%) were found to have enlarged prostate glands, 33 (73.3%) of the glands had a hard consistency and 23 (51.1%) were nodular. Of the 33 patients with a hard prostate, 19 had a histologic diagnosis of CaP (p = 0.59). Out of 23 patients with nodular prostates, 15 were found to have a histologic diagnosis of CaP (p = 0.46). Single DRE abnormality was seen in 4 (8.9%) patients while 41 (91.1%) had multiple abnormalities. Of the 4 patients with single DRE abnormalities, histology revealed 1 (25%) to have CaP, 5 of the 9 (55.6%) that had two prostate abnormalities were shown to have CaP while 21 of the 32 (65.6%) with three or more abnormalities were shown by histology to have CaP (p = 0.15). The five (5) patients who had fixity of the prostate all had a histologic diagnosis of CaP (p = 0.090) (Tables 2 and 3).

G14

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Isiwele, et al.   Digital Rectal Examination Findings with Findings on Histopathology of the Prostate

Section: Urology

Prostate Specific Antigen (PSA) Results

PSA was grouped as 0 – 4, 5 – 10, 11 – 20 and above 20 ng/ml. The modal PSA group was >20ng/ml which was seen in 32 patients (71.1%). (Figure 1)

DISCUSSION

Before the advent of PSA as a screening tool for prostate cancer, DRE was the most sensitive method of diagnosis. Earlier studies suggested that screening for prostate cancer with DRE was cost-effective and specific for detection of more aggressive tumour.[16,17] DRE is found to be particularly relevant in the detection of higher grade, clinically aggressive disease.[18] In this study, frequency of micturition (88.9%) was the most common lower urinary tract symptom in the patients studied, closely followed by nocturia (84.4%). Glasser et al[19] had noted that storage symptoms were more common than voiding symptoms in their own study. Similar picture was documented by Irwin and colleagues[20] in the EPIC study where they also discovered that storage symptoms were more common than voiding symptoms, with nocturia specifically being the most common symptom. The most common complication associated with LUTS was low back pain (28.9%) followed by acute retention of urine (24.4%). The low back pain may have been due to spinal spread of the disease knowing that the spine has been recorded to be most common metastatic site in prostate cancer in previous studies[21,22]. Ahmed et al[23] in Zaria found low back pain to be a very common complication in their study on patients with advanced prostate cancer, as well. Most patients presented with symptoms that had lasted for more than 6 months (55.6%). Late presentation to the hospital for evaluation of LUTS and subsequent treatment is a common feature with patients in this environment as has been previously documented in our centre by Bassey and colleagues[24]. The current study further buttresses this fact. The most common abnormality seen on DRE was a hard prostate seen in 73.3% of patients closely followed by nodularity of the prostate (51.1%). Ojewola et al[25] in Lagos had found nodularity (53.8%) to be most common in patients in a similar study which was followed by a hard prostate. Single DRE abnormality was seen in 8.9% of patients while 91.1% had multiple abnormalities. Twenty five percent (25%) of the patients with single DRE abnormalities, 55.6% of patients with two DRE abnormalities and 65.6% of patients with three or more DRE abnormalities had a final histologic diagnosis of prostate cancer. However, this finding was not statistically significant (p > 0.05). This shows that having multiple DRE abnormalities correlates directly with having a histologic diagnosis of CaP. Ojewola et. al[25] had reported findings following this same trend though with higher cancer detection rates of 40.1%, 83.7% and 100% for 1, 2 and ≥ 3 prostate abnormalities on DRE. Therefore, patients presenting with increasing number of abnormalities on DRE are more likely to have a histopathologic diagnosis of prostate cancer. Nineteen (19) of the 33 patients having hard prostate glands were found to have a histologic diagnosis of CaP (p >0.05). Nodularity of the prostate was found to correlate

positively with a histologic diagnosis of CaP as 15 of the 23 patients with nodularity had a histologic diagnosis of CaP (p>0.05). Fixity of the prostate also correlated directly with a histologic diagnosis of prostate cancer, as all the five (5) patients who had fixity on DRE had a final diagnosis of CaP. This also was not statistically significant. The fact that these findings were not statistically significant may be attributable to the relatively small number of patients studied. Twenty seven (27) out of 45 patients in this study who had suspicious DRE findings had a histological diagnosis of prostate cancer, giving a cancer detection rate of 60% which was statistically significant (p < 0.05). The detection rate for clinically organ-confined disease using DRE alone was found in a study by Babaian and colleagues to be only approximately 30%[26]. In another study by Lee et al[27] in Seoul, South Korea to assess the role of DRE and TRUS in the diagnosis of CaP, the cancer detection rate using DRE was found to be 43.8%. Cooner[8], in a separate study found the prostate cancer detection rate of DRE to be 32.6%. Thus the value obtained in our study was higher than the values obtained in these previous studies. More patients were found in this study to have multiple DRE abnormalities which had been shown to correlate well with a histopathologic diagnosis of CaP in an earlier study.[25] This explains the higher cancer detection rate found in our study. Overall, digital rectal examination remains an important tool in the diagnosis of prostate cancer especially when performed systematically and in a consistent manner. It is useful in detection of cancers even when PSA levels are within the normal range. A significant percentage of cancers would be missed if PSA alone were to be used for cancer detection. It however must be combined with other diagnostic modalities like PSA and TRUS to increase diagnostic accuracy and eliminate false positives.

CONCLUSION

Abnormal findings on digital rectal examination have been shown to correlate well with a histopathologic diagnosis of prostate cancer in this study (p<0.05). Specific DRE findings like hard consistency, nodularity and fixity of prostate as well as increasing number of prostate abnormalities were found to independently correlate positively with a histologic diagnosis of prostate cancer. The cancer detection rate by DRE was found to be 60%. Digital rectal examination remains a very relevant procedure in the prostate cancer detection protocol.

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G15

Section: Urology

Isiwele, et al.   Digital Rectal Examination Findings with Findings on Histopathology of the Prostate

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