IBOM MEDICAL JOURNAL
Vol.13 No.3 Sept. - Dec., 2020. Pages 156 - 163
www.ibommedicaljournal.org

Accuracy of digital rectal examination to diagnose prostate cancer confirmed by needle biopsy reports: A 3–year hospital-based study

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Abstract

Background: Digital rectal examination (DRE) is an indispensable tool for provisional diagnosis of prostate diseases. When abnormal prostate examination findings are elicited, a diagnosis of prostate cancer (Pca) is usually entertained and further tests to confirm or rule out the presence of Pca demands histological examination of biopsied tissue. A combination of DRE findings and serum PSA increases the predictive value for Pca diagnosis. In this study, we evaluated the degree of accuracy of DRE to diagnose Pca confirmed by histology reports of biopsy specimens.

Materials and Methods: Two hundred and six (206) patients were studied over a period of three years. Information retrieved from their case notes were entered into a well-structured protocol for management of prostatic diseases. Analysis of variables collated was performed with the statistical package for the social sciences (SPSS) version 20.0. Frequency table was used to analyze categorical variables while descriptive statistics was used for continuous variables. Level of significance was set at P<.05.

Results: 206 patients were studied with mean age of 68.23±8.71 years ranging from 48 to 91 years. Men in the Pca group were older than those in the BPH group. Abnormal DRE was associated with high grade tumours, and high level of aggressive tumour characteristics by WHO grade group standard.

Conclusion: DRE has a high level of accuracy in predicting a diagnosis of Pca which was confirmed by histology reports especially in prostates with abnormal findings.

Keywords: Accuracy, Digital rectal examination, Prostate biopsy reports.

Introduction

Digital rectal examination is indicated in patients with lower urinary tract symptoms (LUTS) especially in middle aged and elderly men who may harbour prostate diseases. It may also reveal other pathologies in the anal region and distal part of the rectum. It is non-invasive, simple and cost-effective although there may be some discomfort to the patient. Historically, DRE was the first and only diagnostic modality for the detection of Pca until the discovery of prostate specific antigen (PSA) in the mid 1980's[1]. Abnormal findings in the prostate by DRE usually prompt many clinicians to confirm its diagnosis by prostate biopsy and histological examination of the specimen[2]. However, for effective clinical assessment of the patient, it is mandatory to utilize the value of PSA assay before such decisions are taken. DRE when combined with serum PSA is said to increase or add significant information to Pca risk assessment[3]. Pca is commonly associated with middle aged men and the elderly. It is the second most frequently diagnosed

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cancer and fifth leading cause of death in men worldwide[4]. Pca is commoner in men of African ancestry with 50% increase in age-adjusted incidence than their white counterparts[5]. The cause of such wide discrepancy in incidence is unknown, but thought to be related to factors like genetic, hormonal, nutritional, socioeconomic status and behaviour[6].

Assessment of Pca starts with obtaining history of LUTS which may be non-specific with or without symptoms related to its complications. Further steps utilize the power of DRE for abnormal findings in the prostate which may comprise one or more of the following signs: a hard consistency, nodularity, fixity to the rectal mucosa, obliteration of the median groove and one or both lateral sulci and glandular asymmetry[7]. Absence of these findings define a normal DRE with the assumption of BPH as the diagnosis. DRE is limited by not being able to assess other parts of the prostate except the posterior surface.

Serum PSA is an important adjunct in the diagnosis of Pca. It is secreted by the ductal epithelial cells of the prostate and thought to be significant when serum levels of >4ng/ml are recorded[8]. It is presently the most reliable tumour marker for Pca detection and has a higher predictive value than DRE[9]. Detection rate is enhanced when both are used as indicators for further studies with TRUS and biopsy for histology[10]. Result of biopsy is usually reported based on the level of cellular and glandular differentiation from grade 1 to 5 as was popularized by DF Gleason in 1966[11]. A combination of the most predominant grade and the second most predominant grade gives a score ranging from 2 to 10. The international society for urological pathology (ISUP) conference held in 2014 adopted this system with slight modifications. This was later in 2016 incorporated by World Health Organization (WHO) into their Pca evaluation guidelines. In this guideline, grade groups 1 and 2 are designated as low grade tumours while grade groups 3 to 5 are regarded as high grade tumours. DRE has been reported to have the propensity to diagnose high grade tumours in notable abnormal prostate findings, but, the absence of these findings does not preclude a diagnosis of Pca[12]. In this study, we set out to determine the accuracy of DRE to diagnose Pca that was confirmed by biopsy reports in a cohort of men.

Materials and Methods: This was a retrospective study that covered a period of three (3) years from January 2017 to December 2019. A structured protocol was designed and used for data collection from patient's case notes. Information retrieved included bio-data, history, physical examination and DRE findings of the prostate. Relevant investigation results of full blood count, renal function test and urine cultures were also recorded. Results of imaging studies such as transrectal ultrasound scan (TRUS) and trans-abdominal ultrasound scan (TAUS) were also documented. Digital rectal examination was conducted following the standard technique in the left lateral position with thorough explanation of the procedure to the patient. Three urologists with more than 10 years of experience were involved in the examinations. With gloved hands, a well lubricated index finger was introduced into the rectum after inspection of the anal verge. The finger feels for the sphincteric tone and then assessed the prostate for evidence of enlargement, consistency which may be hard in Pca, nodularity, obliteration of the median grove and one or both lateral sulci, fixity to the rectal wall and asymmetry of the gland. TRUS-guided needle biopsy was done as indicated by abnormal DRE findings or a serum PSA of >4ng/ml or both. Prior to the procedure, bowel preparation was done with lukewarm saline enema a night before and morning of the procedure. Prophylactic antibiotic of intravenous ciprofloxacin 500mg stat is usually given and continued for five days post procedure with the oral form. In a left lateral position, about 10mls of 2% xylocaine gel was instilled into the rectum and after 5 to 7 minutes, an ultrasound probe was used to first scan the prostate areas and biopsy taken with the aid of a size 18G biopsy needle mounted on an automated spring loaded biopty gun. Ten (10) to twelve (12) needle cores were taken bilaterally from the apex, base and middle portion of the gland in addition to biopsies obtained at suspicious lesions. Specimens from each prostate were sent to the laboratory in a formalin containing bottle and examined for the presence or absence of malignancy. Exclusion criteria were patients with incomplete clinical and laboratory information and diagnosis of other lower urinary tract cancers.

Table 1: Descriptive Statistics for continuous variables

Prostate cancer	**Number**	**Mean std. Deviation**	**Min**	**Max**	**Mode**
Age	113	67.85 ± 8.63	48	91	65
PSA	113	55.94 ± 37.10	3.70	185.70	12.90
BPH					
Age	93	65.70 ± 11.20	53	90	50
PSA	93	13.28 ± 12.20	0.90	55.10	3.10
All patients					
Age	206	68.23 ± 8.71	48	91	65
PSA	206	36.68 ± 35.66	0.90	185.70	3.10

Table 2: Frequency Table for categorical variables

Variables	**Frequency (n)**	**Valid percent (%)**	**Cumulative percent (%)**
Abnormal DRE	121	58.7	58.7
Normal DRE	85	41.3	100.0
BIOPSY RESULTS:			
Prostate cancer:	113	54.9	54.9
BPH	93	45.1	100.0
Total	206	100.0	
Gleason Score:			
5	2	1.7	1.7
6	12	10.7	12.4
7	33	29.3	41.7
8	23	20.3	62.0
9	36	31.8	93.8
10	7	6.2	100.0
Total	113	100.0	
WHO grade groups: GG1 = (≤6)	14	12.4	12.4
GG2 (3+4=7)	17	15.0	27.4
GG3 (4 + 3 = 7)	16	14.2	41.6
GG4 (4 + 4 = 8)	23	20.3	61.9
GG5 (9&10)	43	38.1	100.0
Total	113	100.00	
Level of aggressiveness:			
High (GG 3 – 5)	81	71.7	71.7
Low (GG 1 & 2)	32	28.3	100.0
Total	113	100.0	

GG = Grade group

Table 3: Sensitivity and Specificity to diagnose prostate cancer by DRE

a = 98 (True positive)	b = 23 (False positive)
c = 15 (False Negative)	d = 70 (True Negative)

Note: a + c = All patients with prostate cancer
b + d = All patients without prostate cancer
Sensitivity = $^{a}/_{a+c} = {}^{98}/_{113} = 86.72\%$
Specificity = $^{d}/_{b+d} = {}^{70}/_{93} = 75.2\%$.

Table 4: Predictive Values

a = 98 (True positive)	b = 23 (False positive)
c= 15 (False negative)	d = 70 (True negative)

Note: a + b = All patients with abnormal prostate findings on DRE
c + d = All patients with normal DRE
Positive predictive value = $^{a}/_{a+b} = {}^{98}/_{121} = 81.0\%$
Negative predictive value = $^{d}/_{c+d} = {}^{70}/_{85} = 82.3\%$

Statistics Analysis: Data obtained were entered into spread sheets and analyzed using SPSS version 20.0. Continuous variables were summarized as means and standard deviations. Frequency table was used for categorical variables. Diagnostic accuracy of DRE as a predictor of positive prostate biopsy was assessed using sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV).

Results

Two hundred and six patients with histological diagnosis of prostate diseases were studied. They were aged between 48 and 91 years with a mean of 68.28±8.71 years. One hundred and thirteen (113) patients (54.9%) were diagnosed with Pca with mean age of 67.85±8.63 years while Ninety-three (93) patients (45.1%) had BPH with mean age of 65.70±11.20 years. Mean PSA for Pca patients was 55.94±37.10ng/ml (3.70 –185.70ng/ml), while that in the BPH arm was 13.28±12.20ng/ml (0.90 – 55.10ng/ml). Mean PSA in the study was 36.68±35.66ng/ml(0.90-185.70ng/ml) Table 1. Those with abnormal DRE were 121 (58.7%) and 85 (41.3%) had normal DRE findings. Patients with Gleason score (GS) of 9 formed the majority in the Pca group (table 2). WHO grade group 3 – 5 associated with high grade tumours were seen in 81 patients (71.7%) while 32 patients (28.3%) had low grade tumours (WHO grade groups 1 & 2). The sensitivity and specificity results were 86.72% and 75.2% respectively, while PPV and NPV were 81.0% and 82.3% respectively (tables 3 and 4). DRE findings correlated positively with histology reports, r (206) = .627, P< .05 (Table 5). Abnormal DRE was associated with 59.5% of high grade tumours but missed 10.6% of high grade tumours in prostates that had normal findings. Table 6(i-iv), shows comparison of DRE findings with other variables in the study.

Table 5: Correlative between DRE findings and prostate biopsy histology Reports:

		DRE	**Histology**
DRE	Pearson correlation	1	.627
	Sig (2 – tailed)		.000*
	N	206	206

*Correlation is significant at P < .05

TABLE 6: CROSS TABULATION OF VARIABLES

(i) Histopathology results versus DRE findings:

	DRE		
	Abnormal	**Normal**	**Total**
Biopsy histology **Pca** count	98	15	113
Within Histology	86.7%	13.3%	100.0%
Within DRE	81.0%	17.6%	54.9%
BPH Count	23	70	93
Within Histology	24.7%	75.3%	100.0%
Within DRE	19.0%	82.4%	45.1%
Total Count	121	85	206
Within Histology	58.7%	41.3%	100.0%
Within DRE	100.0%	100.0%	100.0%

(ii)PSA Values (categorized) versus DRE findings:

	DRE	
	Abnormal	**Normal**
PSA <4gn/ml Count	5	14
Within PSA	26.3%	73.7%
Within DRE	4.1%	16.6%
4 – 19ng/ml Count	9	29
Within PSA	23.7%	76.3%
Within DRE	7.4%	34.1%
11 – 20ng/ml Count	19	29
Within PSA	23.7%	76.3%
Within DRE	7.4%	34.1%
21 – 30ng/ml Count	11	12
Within PSA	47.8%	52.2%
Within DRE	9.1%	14.1%
31 – 40ng/ml Count	9	5
Within PSA	69.2%	27.8%
Within DRE	7.4%	5.9%
41 – 50ng/ml Count	13	5
Within PSA	72.2%	27.8%
Within DRE	10.7%	5.9%
>50ng/ml Count	55	2
Within PSA	96.5%	3.5%
Within DRE	45.5%	2.4%
Total Count	121	85
Within PSA	58.7%	41.3%
Within DRE	100.0%	100.0%

(iii)DRE Findings versus grade of tumours:

	WHO grade groups					
	≤6	3 + 4	4 + 3	4 + 4	9 & 10	Total
DRE; Abnormal count	12	13	13	21	39	98
Percent	12.3(%)	13.3(%)	13.3(%)	21.4(%)	39.7(%)	100(%)
DRE; Normal Count	2	4	3	2	4	15
Percent	13.4(%)	26.6(%)	20.0(%)	13.4(%)	26.6(%)	100.0(%)

(iv)DRE Findings versus Gleason Scores:

	Gleason Scores						
	5	6	7	8	9	10	Total
DRE; Abnormal							
Count	2	10	26	21	32	7	98
Percent	2.1 (%)	10.2(%)	26.5(%)	21.4(%)	32.6(%)	7.2(%)	100.0(%)
DRE; Normal							
Count	0	2	7	2	4	0	15
Percent	0.0(%)	13.4(%)	46.7(%)	13.3(%)	26.6(%)	0.0(%)	100.0(%)

Discussion

Digital rectal examination of the prostate was the first diagnostic modality for Pca before the discovery of PSA in the mid-1980s[1]. Diagnostic Sensitivity of DRE increases when it is combined with serum PSA in Pca evaluation[10]. DRE and PSA are valuable tools employed in the screening of patients for Pca[13]. Suspicious prostates with abnormal DRE findings, irrespective of the PSA level usually prompts the attending physician to obtain a prostate biopsy for histology. Biopsy results reported according to the Gleason system demonstrate prognostic significance to individual patients. Association between DRE findings of the prostate and final histological diagnosis had been widely studied with varying levels of concordance. Evidence suggests that an abnormal DRE is a good predictor for the presence of Pca on final histology[14]. These authors inferred that abnormal DRE was also an independent predictor of high risk disease[14].

In this study, 54.9% and 45.1% of patient had histological diagnosis of Pca and BPH respectively. This was in sharp contrast to other studies in Nigeria[15,16] and other parts of the world[17,18] which document BPH as the most common prostate disease in men past middle age. Our study demonstrates a selection bias as most of them were copted based on abnormal DRE findings coupled with raised PSA. This class of patients are most likely to harbor Pca rather than BPH. Overall, mean age was 68.28±8.71 years. In the Pca group, mean age was higher than in the BPH group. However, both peaked in the 7th decade of life. This had been a common finding in many studies across the globe[16,18,19]. Mean PSA was 36.68±35.66ng/ml. Mean and modal PSA were higher in the Pca group (Table 1). Other studies had demonstrated consistently higher PSA in Pca patients than those with BPH[20-22]. Experts opinion believe that PSA produced in the epithelial cells of Pca is released into the circulation when the basement membrane barrier layers of the cells are damaged by the tumour unlike in BPH where the cell membrane remain intact. This leads to high levels of serum PSA in Pca patients. However, it is of note that serum PSA in BPH patients may also rise above the reference range by reason of size[23].

The pathological characteristics of tumours in our study consistently demonstrate an aggressive pattern. Gleason score of 9 was most common, WHO grade group 5 was highest and high level of aggressive group also peaked (Table 1). This picture is a common occurrence especially in sub-Saharan Africa where patients present late for care[24]. It may not be unconnected to natural progression of undiagnosed tumours with age until quite late in the disease occasioned by inadequate screening programmes to diagnose early disease, poor compliance by patients due to ignorance and superstition and also poverty-driven mentality. Besides, it is of note that Pca in blacks usually display aggressive characteristics compared to caucasians by reasons of genetics, ethnics and environmental factors that influence the natural history of Pca development[24].

Diagnostic accuracy of DRE as a predictor of positive prostate biopsy in this study was assessed using sensitivity, specificity, PPV and NPV analyses. Sensitivity was defined as the percentage of biopsy-positive patients with abnormal DRE among all biopsy-positive patients. Specificity was defined as the percentage of biopsy-negative patients with normal DRE among all biopsy-negative patients. PPV was defined as the proportion of biopsy positive patients among all those with abnormal DRE, while NPV was defined as the proportion of cancer-free patients among all those assigned with normal DRE. A high sensitivity and specificity of DRE to diagnose and exclude Pca was noted in this study. This was not surprising as the abnormal findings in most of our patients are usually conspicuous due to their advanced nature and so difficult to miss by DRE. This was also supported by the fact that majority of them had advanced tumour characteristics (Table 2). Roberts et al[17] noted that DRE was the most sensitive method of detecting palpable prostatic abnormalities confirmed by biopsy, but lacked adequate specificity. There was an improved specificity in our study by reason of florid abnormal prostate features and long period of experience by urologists involved. PPV and NPV were also high indicating that a high percentage of patients who were assumed to have Pca by reason of abnormal DRE actually had it by biopsy, the reverse was true for NPV. There was a significant positive correlation between signs elicited on DRE of the prostate suggestive of Pca and biopsy reports: $r(206) = .627$, $P<.05$. From this

study, it is possible to make a provisional diagnosis of Pca based on abnormal DRE findings in combination with serum PSA and also to rule out Pca by same procedure with a high level of accuracy until proven otherwise by prostate biopsy.

The limitations of this study were as follows: being retrospective, it is subject to selection bias which may have influenced our results and again, DRE on its own may result in a high number of false-positives necessitating unnecessary prostate biopsies causing pain, rectal bleeding, urinary incontinence, haematuria and sepsis.

However, information drawn from this study can further strengthen our resolve to rely on DRE of the prostate as necessary guide for further evaluation of patients with LUTS.

Conclusion

DRE is an inexpensive, safe and simple procedure in the hands of urologists to provisionally diagnose Pca with some levels of certainty. However, definitive diagnosis is usually made by prostate biopsy and histological examination of the specimens. The concordance rate of both DRE and histology reports in this study was high. Comparatively, lower concordance rates have been reported internationally and we think our results was influenced by the cohorts of patients studied being hospital based.

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