Correlation between Prostate Volume and Gleason Score in Patients Diagnosed with Prostate Cancer. A 2-Year Hospital based Study

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ABSTRACT

Introduction: Prostate cancer (Pca) is a disease that commonly afflicts elderly male population especially those of African descent. Diagnosis is usually confirmed by microscopic examination of prostate tissue sample. Gleason system of grading Pca is widely adopted as a guide to selecting treatment modalities as an independent prognostic factor. In this study, we aimed at evaluating the relationship between prostate volume (PV) and Gleason score (GS) in prostate cancer patients.

Material and Methods: One hundred (100) male patients who were evaluated for Pca between January 2014 and December 2015 were studied. Information from their case notes were retrieved and entered into spread sheets for analysis using the statistical package for social sciences (SPSS) version 20.0.

Results: The mean age of the patients was 67.88 ± 8.83 years ranging from 48 to 91 years. Mean prostate volume was 95.97 ± 93.52mls, mean Gleason score was 7.89 ± 1.20 while mean PSA of 56.33 ± 38.99ng/ml was recorded. Most of the patients were in their 8th decade of life. Majority of them had PV in excess of 100mls and Gleason score of 9 was found in patients with mean PV of 120.98 ± 133.23mls.

Conclusion: Our work documented mixed results of high grade tumours observed in most patients, prostate size notwithstanding. This study predicts high grade disease in our cohort of patients irrespective of prostate size.

Keywords: Correlation, Prostate Volume, Gleason Score, Prostate Cancer.

INTRODUCTION

Prostate cancer is a disease associated with the aging male population and currently the second most common cancer and 5th leading cause of death from male dominated cancers worldwide.[1] Diagnosis is commonly made with a combination of digital rectal examination (DRE) findings of the prostate, elevated serum prostate specific antigen (PSA) and prostate biopsy for histological examination. A system pioneered by DF Gleason in 1966 classifies the cellular and glandular architecture of Pca and the degree of differentiation into five grades. Grade 1 is labeled as well differentiated tumour with gradual loss of differentiation capacity to anaplastic tumour in grade 5. A combination of the most predominant grade with the next most predominant grade gives scores ranging from 2 to 10. The Gleason system of grading of Pca is an independent prognostic factor in the evaluation of patients.[2] Older studies[3,4] as well as recent works[5,6] have clearly shown an association between prostate volume and Pca incidence. Important factors influencing optimal Pca detection in biopsy specimens have been widely discussed. The number of cores of needle biopsy taken and the size of the prostate are key factors. Hodges et al first described the sextant biopsy method which was widely used but lacked diagnostic sensitivity reported to be as low as 30 to 45%.[3] It was also observed that, the detection rate of Pca increased as the needle core biopsies increased[8], hence the current concept of extended sampling protocols recommending 10 to 12 cores of transrectal ultrasound scan (TRUS) guided needle biopsy.[9] Some authors speculated more core biopsies especially in larger prostates, however, a balance should be made between Pca detection rate, the adverse effects of several cores and cost effectiveness of such procedures. Uzzo et al[10] first documented the relationship between prostate volume and cancer detection rate. They observed that the sensitivity of Pca detection with sextant biopsy on large prostates was lower than in smaller prostates. Suggestions as to the possible causes of this were a greater probability of sampling errors as well as biopsy selection bias due to high PSA possibly caused by BPH.[12]

Studies on the relationship between PV and biopsy GS consistently showed that larger prostates associate with favourable GS[13] and smaller prostates harbor more of high grade Pca.[14] This discovery was made in both needle biopsy as well as radical prostatectomy specimens.[15,16] In this study, we set out to determine the relationship between PV and GS in needle biopsy specimens of our men diagnosed with prostate cancer.

MATERIAL AND METHODS

This was a two-year retrospective study of 100 patients who were evaluated for Pca between January 2014 and December 2015. All patients in the study had TRUS-guided systematic 10 to 12 cores of biopsy of the prostate. Prior to this procedure they all had bowel preparation with lukewarm saline enema a night before and morning of the procedure. Prophylactic antibiotic of intravenous ciprofloxacin 500mg stat was adminitered and then continued five days after

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with the oral form by all patients. Under TRUS guidance, suspicious lesions were targeted and biopsied. Specimens were transported to the laboratory in formalin containing bottles. Examination was done under low power microscope by the pathologists. Confirmed cases of Pca were included in the study. Exclusion criteria were patients with incomplete histologic information and a diagnosis of other lower urinary tract cancers. Other information from their case notes were retrieved including bio-data, history and physical examination with findings on DRE of the prostate. Relevant laboratory investigation results included full blood count, renal function test and urine cultures. Results of imaging studies were mainly TRUS and abdominopelvic ultrasound scan. Patient's age and serum PSA were grouped in intervals of 10. PV was also grouped. Gleason grading of Pca was copted and used.

Frequency table was made for categorized variables. Descriptive statistics was used to obtain means and standard deviation for continuous variables. Mean PV was compared with Gleason scores and also cross tabulated. Pearson correlation coefficient was used to determine the relationship between PV and GS. Statistical significance was set at P<.05.

RESULTS

100 men aged between 48 and 91 years were evaluated with a mean age of 67.88 ±8.83 years. Mean PV was 95.97 ± 93.52mls (10.74 – 597.20) while mean Gleason score was 7.89 ± 1.20 (5 – 10). Mean PSA was 56.33 ± 38.99ng/ml (6.90 – 185.70). Patients in their 8th decade of life were more in number (39.0%) Table1. Those with prostate volume in excess of 100 mls formed the majority (30%) Table1. Gleason score of 9 was observed in most patients (34.0%) and few of them (2.0%) had Gleason score of 5. Majority (47.0%) of them were observed to have PSA in excess of 50ng/ml (Table 1). Table-2 shows descriptive variables. Gleason score of 9 was also associated with the largest mean prostate volume and the least mean prostate volume with Gleason score of 5 (Table 3). In table 4, GS of 9 was observed predominantly in men with PV in excess of 100mls. Smaller glands (< 30mls) also harbored more of high grade tumours Gleason score 9. Correlation between prostate volume and Gleason Score was not statistically significant r (100) = .169, P > 0.05.

(i) Age category (yrs)	Frequency (n)	Valid percent (%)	Cumulative percent (%)
40 – 49	2	2.0	2.0
50 – 59	15	15.0	17.0
60 – 69	36	36.0	53.0
70 – 79	39	39.0	92.0
80 – 89	7	7.0	99.0
90 – 99	1	1.0	100.0
Total	**100**	**100.0**	
(ii) PV category (mls)			
<30	7	7.0	7.0
30 – 50	21	21.0	28.0
>50 – 80	26	26.0	54.0
>80 – 100	16	16.0	70.0
>100	30	30.0	100.0
Total	**100**	**100.0**	
(iii) Gleason Score			
5	2	2.0	2.0
6	12	12.0	14.0
7	25	25.0	39.0
8	22	22.0	61.0
9	34	34.0	95.0
10	5	5.0	100.0
Total	**100**	**100.0**	
(iv) PSA category			
4 – 10	4	4.0	4.0
>10 – 20	18	18.0	22.0
>20 – 30	8	8.0	30.0
>30 – 40	9	9.0	39.0
> 40 – 50	14	14.0	53.0
> 50	47	47.0	100.0
Total	**100**	**100**	

Table-1: Frequency Table for variables:

Variable	Mean	Range
Age (Years)	67.88 ± 8.83	48 – 91
PSA (ng/ml)	56.33 ± 38.99	6.90 – 185.70
PV (mls)	95.97 ± 93.52	10.74 – 597.20
GS	7.89 ± 1.20	5 – 10

Table-2: Descriptive Statistics for Continuous Variables.

Gleason Score	Mean	Std deviation
5	40.03	± 34.55
6	80.36	± 50.40
7	29.59	± 73.14
8	91.32	± 59.73
9	120.98	± 133.23
10	88.04	± 49.19
Total	**95.97**	**± 93.52**

Table-3: Comparing Gleason Scores with mean prostate volumes

DISCUSSION

Prostate cancer is a disease of the elderly male population and the number one cause of cancer related morbidity and mortality in men of African ancestry.[17] Age–adjusted incidence of Pca in African–American men is about 50% higher than their white counterparts and out-numbers other races the world over.[18] The cause of these racial differences is unknown, but suggested implicated factors are genetics, hormonal, socio-economic status, nutritional and behavioral.[19] Prostate biopsy remains the standard procedure for the diagnosis of prostate cancer.[20] For optimal detection of the disease, the extended biopsy protocol of 10 to 12 cores had been advocated with better results.[21] Gleason system of grading of Pca remains the best tool in the evaluation, treatment selection and prediction of disease outcome for individual patients.[2] The relationship between prostate volume and biopsy Gleason score has been well studied. Results consistently show presence of tumours with favourable Gleason score occurring in larger prostates and vice versa in smaller prostates.[13,14] This was observed in both needle biopsy and radical prostatectomy (RP) specimens.[15,16]

	Gleason Score Categories						
	5	**6**	**7**	**8**	**9**	**10**	**Total**
PV categories							
<30 Count	1	1	1	0	4	0	7
% of Total	1.0	1.0	1.0	0.0	4.0	0.0	7.0
30 – 50 Count	0	1	6	7	6	1	21
% of Total	0.0	1.0	6.0	7.0	6.0	1.0	21.0
>50 – 80 count	1	6	8	5	5	1	26
% of Total	1.0	6.0	8.0	5.0	5.0	1.0	26.0
>80 – 100 Count	0	2	6	4	3	1	16
% of Total	0.0	2.0	6.0	4.0	3.0	1.0	16.0
>100 Count	0	2	4	6	16	2	30
% of Total	0.0	2.0	4.0	6.0	16.0	2.0	30.0
Total Count	2	12	25	22	34	5	100
% of Total	2.0	12.0	25.0	22.0	34.0	5.0	100.0

Table-4: Cross tabulation between PV categories and Gleason score categories.

PV	Pearson correlation	1	.169
	Sig (2 – tailed)		.092*
	N	100	100
Gleason Score	Pearson correlation	.169	1
	Sig (2 – tailed)	.092*	
	N	1000	100
*Statistical significance set at P<.05.			

Table-5: Correlation between Prostate volume and Gleason Score.

Briganti A et al[16] in a large series of 4,277 RP specimens documented same findings and found the relationship more significant at PV < 45mls.

We evaluated men with a mean age of 67.88 ± 8.83 years. These were elderly men likely to harbor advanced disease due to natural progression of undiagnosed Pca with age and changes in hormonal status. Other studies also documented men in this age group among their Pca patient.[22,23] Mean PSA was 56.33 ± 38.99 and about half of them had PSA in excess of 50ng/ml. This picture portrays a likelihood of invasive disease being predominant in our cohort of men since most researchers had documented a direct and significant relationship between serum PSA and Gleason Score.[24,25]

A strong opinion of larger prostates conferring a protective effect on high grade Pca had been documented by Freedland et al[26], but the underlying mechanisms are not quite clear. BPH and Pca may coexist in the same prostate. Attempts to explain this hypothesis led to the phenomenon of "tumour mass effect" exerted by coexisting benign prostatic hyperplasia (BPH) due to accumulation of mechanical stress.[27,28] The benign tumour creates a compressive hydrostatic stress state within the prostate gland as well as an outward force that deforms the peripheral zone (PZ). In this state, BPH exerts an inhibitory effect on Pca growth rate directly by slowing down caner dynamics and also by deforming and collapsing the local blood supply in and around the tumour.[13,28] Kulkarni et al[15] studied both prostate biopsy and RP Specimen on this subject and reported lower incidence of high grade tumours in larger prostates. Other authors also documented similar findings.[6,30] Newton et al[31] further suggested that every 2cc increase in prostate volume decreases the rate of high grade Pca by six times. Researchers think this Scenario might also be due to sampling error in larger glands as well as elevated PSA induced prostate biopsy in BPH patients.[12]

We had mixed results in our study. The mean PV was 95.97 ± 93.52mls, meaning that majority of the patients harbored large prostates. As a follow up to this, Gleason Score of 9 (invasive tumour) was found associated in patients with mean PV of 120.98 ± 133.23mls (Table 3). This could, however, be explained by inherent attitude of late presentation to hospital with advanced tumours which actually may rule out sampling errors giving optimal sensitivity of needle prostate biopsy. We were also dealing with men in their advanced years forming the majority for which undiagnosed tumour may have progressed over the years with coexisting BPH involved in making the bulk of the prostate. On the other hand, table 4 shows that more than 50% of patients with PV < 30mls had high grade invasive (GS of 9) disease supporting other works mentioned above. The mixed report in this study is also demonstrated by lack of correlation between prostate volume and Gleason Score. Despite this mixed results, we are on point that, prostate size notwithstanding, a high index of suspicion of high grade tumor should be entertained in evaluating any patient presenting with findings suggestive of Pca in our locality. This notion will direct a good protocol for evaluation of patients, goal-directed treatment and prediction of outcome.

Limitations of this work are that of inherent flaws of a retrospective study, a relatively small sample size and the use of needle biopsy specimen alone without due comparison of final GS in RP Specimens. However, we are poised to undertake a prospective study on this topic to overcome the limitations listed above.

CONCLUSION

Globally, prostate volume and Gleason score have been shown to have an inverse relationship. Our study documents mixed reports. Smaller glands as well as larger glands harbor high grade tumours. This is a high point to note when evaluating new patients suspicious of Pca to deploy

aggressive assessment protocols and care aiming at a better outcome.

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