Original

Gleason Score as a Diagnostic Tool in Prostate Cancer Assessment: Findings from a Tertiary Health Care Center in Southwest, Nigeria.

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Abstract

Background: Prostate cancer is the second most common cause of death from cancers in elderly males. Gleason score has been used to evaluate patients with abnormal serum levels of prostate-specific antigen, and digital rectal examination. We assessed prostate cancer patients' Gleason scores and pathological findings.
Method: A retrospective assessment of the data of 149 patients with the diagnosis of prostate cancer from the anatomic pathology laboratory between 2017 and 2021 was conducted. Retrieved variables included findings on Gleason score, symptoms, inflammation, corporea amylacea, and digital rectal examination findings.
Result: Prostate cancer was more common in the 70-74 years' age group, and least common between 50 and 54 years. A Gleason score from 6 upwards was associated with low back pain, and common between 55 and 59 years, and 64 and 69 years. Most of the diagnoses were made through tru-cut biopsy. Both irritative and obstructive symptoms were present across the population age groups. A significant proportion of participants (p=0.0494) had higher tumour grades (4 and 5). There was a significant presence of enlarged and nodular masses and, involvement of the median groove, p=0.1029. The presence of corporea amylacea is not a significant feature of prostate cancer, p=0.0013.
Conclusion: The Gleason score is a useful diagnostic criterion in symptomatic and asymptomatic patients with abnormal digital rectal examination and prostate-specific antigen. It could streamline and guide treatment modalities for prostate cancer patients in our environment.

Keywords: prostate cancer, Gleason score, inflammation, corporea amylacea, Prostate cancer (PCa), prostate-specific antigen (PSA), digital rectal examination (DRE), transurethral resection of the prostate (TURP), International Society of Urological Pathology (ISUP).

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Introduction

Prostate cancer (PCa) is one of the leading cancers in elderly males in the United States and Europe and is documented to be the second most common cause of cancer death in elderly males. [1] Gleason score has remained the most widely used diagnostic criteria to evaluate patients older than forty years following an abnormal prostate-specific antigen (PSA) value. [2] It has remained an established prognostic indicator in prostatic adenocarcinoma, and it is entirely based on the histologic pattern of arrangement of the cancer cells in haematoxylin and eosin (H&E) stained prostatic tissue sections. It contains five basic grading patterns used to generate a histologic score from 2 to 10. In cases where there are more than two histologic patterns on a core needle biopsy, the Gleason score should be the sum of the predominant and the highest-grade pattern. [3] Tumours with higher grades are more common in prostatectomies. [4]

The cancer grade is dependent on the size of the histologic sample and the size of the tumour in the whole gland, and it is quite evident by comparing sample grades from radical prostatectomy, transurethral resection of the prostate (TURP), and tru-cut needle biopsies. [2]

Gleason grading should routinely be reported for all prostatic adenocarcinomas samples, and the pathologist and physicians should collaborate on the application modalities of the principles and practice of the system. [5] This is our understanding in Bowen University Teaching Hospital, but unfortunately, this collaboration is sometimes hampered in a resource-challenged setting like ours, due to low manpower availability. Moreover, this is coupled with the fact that in recent times, we have received prostatectomy specimens without an initial Gleason score. In addition, more prostate biopsy specimens were being submitted for histopathological examination without any result of Prostate-specific antigen (PSA) assay. Thus, we would like to determine the best practice in a resource-challenged setting like ours. We, therefore, set out to assess the Gleason score of prostatic cancer patients over five years in Bowen University Teaching Hospital and determined the grading patterns, the symptoms, the presence of inflammation, corporea amylacea, and the affectation of the median groove by prostate cancer. This will help to improve diagnostic acumen, contribute to knowledge, and foster increased collaboration with the clinicians and surgeons for a disease that is increasingly being diagnosed in our centre.

Methodology

Setting: The study was conducted at Bowen University Teaching Hospital, Ogbomosho, Southwest Nigeria, a missionary hospital, which serves as a referral facility for primary and secondary healthcare centres around the region and private hospitals.

Study design: It was an observational, retrospective cross-sectional study involving patients who had a histologic diagnosis of prostate cancer (through tru-cut biopsy or prostatectomy) between 2017 and 2021 in the anatomic pathology laboratory of the hospital.

Inclusion and Exclusion criteria: All middle-aged male adults with a histologic diagnosis of prostate cancer were included in the study. Participants with incomplete data on their histologic reports or request forms and those whose slides or formalin-fixed paraffin-embedded blocks were unavailable were not included in the study.

Study population: One hundred and forty-nine patients who were diagnosed for prostate cancer were involved in the study.

Sample size calculation: This was not determined.
Sampling method: The medical records and histopathologic findings of 149 patients were retrieved from the archives and critically analysed for details that will meet the research objectives. The convenience sampling method was employed in recruiting participants for the study at the anatomic pathology laboratory within the specified time. The full details of the participants on well-filled and signed result sheets and request forms were included.

Study variables: The variables that were retrieved and analyzed included the socio-demographic features, the staging criteria and the histologic grading, Gleason score, symptom pattern (irritative or obstructive), presence of inflammation, presence of corporea amylacea and findings from the digital rectal examination were retrieved.

Data collection: Data was collected by a well-trained staff of the medical records department from passworded computers at the Anatomic Pathology laboratory. Participants' biodata and their diagnosed Gleason score, symptom pattern (irritative or obstructive), presence of inflammation, presence of corporea amylacea, and findings from the digital rectal examination were retrieved. The slides of the corresponding reports were retrieved and those available were re-examined by two attending pathologists (AEG

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& AAO) to confirm the diagnosis. Participants with incomplete data and unavailable slides were not included in the study

Data analysis: The data obtained was analysed using the statistical packages for social sciences (SPSS) 25.0 and R- programming version 4.4.1. Proportions and frequencies, as categorical variables were compared using the Chi-square or Fisher's exact test. The P-value <0.05, was considered statistically significant. In the multivariate model

Ethical consideration: The study was conducted in compliance with the Helsinki Declaration on biomedical research on human subjects. All the data obtained were stored in a password-protected computer thereby maintaining patients' confidentiality. Ethical clearance approval was obtained before the commencement of the study from the Ethics Committee of Bowen University Teaching Hospital, Ogbomosho. BUTH Research Ethics Committee, Registration number: NHREC/12/04/2012. Approval number: BUTH/REC-2148.

Results

The prostatic tissues of 149 men were studied. The mean age of the population was 72.56. The 70-74 years' age group had the highest prevalence of prostate cancer (26.17%) while the 50-54 years' group had the least prevalence (2.01%), (Table 1 & fig. 1**)**. A Gleason score of 6 and above was more common in the 55-59 and 64-69 age groups. The majority (96%) of the diagnosis was made from tru-cut biopsy, which accounted for most of the samples under review (Table 2**)**. Low back pain was a common feature in patients who had Gleason scores above 6, p=0.432 **(**Table 3). Both irritative and obstructive symptoms were present across all the age groups. The number of individuals with a higher-grade tumour (4 and 5) was significantly higher p-0.0494 (Table 4). Inflammation was a common feature in tru-cut biopsies (15.44%).

There was a higher frequency of enlarged, nodular tumours with involvement of the median groove, though statistically insignificant, p=0.1029 **(**Table 5). The presence of corporea amylacea was not a significant feature of prostate cancer, p=0.001**.** The presence of cancer with Gleason scores 6 and below was less common in men 80 years and older (Figure 1).

Table 1: frequency of cancer among the age groups

Age (Years)	Frequency (n = 149)
50-54	3 (1.5)
55-59	5 (2.5)
60-64	10 (5.0)
65-69	30 (15.0)
70-74	39 (19.5)
75-79	33 (16.5)
80-84	14 (7.0)
85-89	9 (4.5)
>90	6 (3.0)

Table 2: Frequency of Gleason scores by specimen nature

Gleason category	Specimen nature	Frequency
≤6	Biopsy	23
> 6	Biopsy	120
≤6	Tissue	4
> 6	Tissue	2

Table 3. Clinical Presentation and Gleason score

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Variable	BOO/BPH (N=11)	Irritative & Obstructive (N=37)	Back Pains (N=11)	LUTS (N=38)	None (N=27)	Urinary Retention (N=25)	Total (N=149)	p-value
Age (years) (Mean)	76.6	74.3	69.5	71.3	71.6	72.4	72.6	0.2625
Gleason Score								0.4325
6 and below	2 (7.41%)	7 (25.93%)	0 (0%)	6 (22.22%)	8 (29.6%)	4 (14.81%)	27 (18.12%)	
Above 6	9 (7.38%)	30 (24.59%)	11 (9.0%)	32 (26.23%)	19 (15.5%)	21 (17.21%)	122 (81.88%)	

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Total	11 (7.38%)	37 (24.83%)	11 (7.3%)	38 (25.50%)	27 (18.1%)	25 (16.78%)	149 (100.0%)

BOO-bladder outlet obstruction, BPH-benign prostatic hyperplasia, IS-irritative symptoms, OS-obstructive symptoms, LBP-low back pain, UR-urinary retention

Table 4. Gleason score and prostate cancer grade

	6 & below (N=27)	Above 6 (N=122)	Total	P-value
Mean	69.6	73.2	72.6	0.0494
Grade				0.0001
1	20 (100.00%)	0 (0%)	20 (13.42%)	
2	0 (0%)	14 (100.00%)	14 (9.40%)	
3	0 (0%)	28 (100.00%)	28 (18.79%)	
4	1 (3.33%)	29 (96.67%)	30 (20.13%)	
5	1 (1.92%)	51 (98.08%)	52 (34.90%)	
Total	27 (18.12%)	122 (81.88%)	149 (100.00%)	

Table 5: Inflammation, DRE and corporea amylacea features in the participants

	absent (N=126)	present (N=23)	Total	P-value
Specimen nature				0.0014
Biopsy	124 (83.2%)	19 (12.8%)	143 (96.0%)	
Tissue	2 (1.3%)	4 (2.7%)	6 (4.03%)	
Total	126(84.56%)	23 (15.44%)	149 (100.00%)	
DRE				0.1029
Enlarged	5 (55.56%)	4 (44.44%)	9 (6.04%)	
Enlarged/nodular	41 (89.13%)	5 (10.87%)	46 (30.87%)	
Media groove	40 (86.96%)	6 (13.04%)	46 (30.87%)	
None	40 (83.33%)	8 (16.67%)	48 (32.21%)	
Total	126 (84.56%)	23 (15.44%)	149 (100.00%)	

Presence of corporea amylacea

	absent (N=137)	present (N=12)	Total	P-value
No of Fragments				0.0013
8	2 (100.00%)	0 (0%)	2 (1.34%)	
5	35 (92.11%)	3 (7.89%)	38 (25.50%)	
4	23 (92.00%)	2 (8.00%)	25 (16.78%)	
7	2 (100.00%)	0 (0%)	2 (1.34%)	

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6	11 (61.11%)	7 (38.89%)	18 (12.08%)
3	14 (100.00%)	0 (0%)	14 (9.40%)
2	1 (100.00%)	0 (0%)	1 (0.67%)
Total	137 (91.95%)	12 (8.05%)	149 (100.00%)

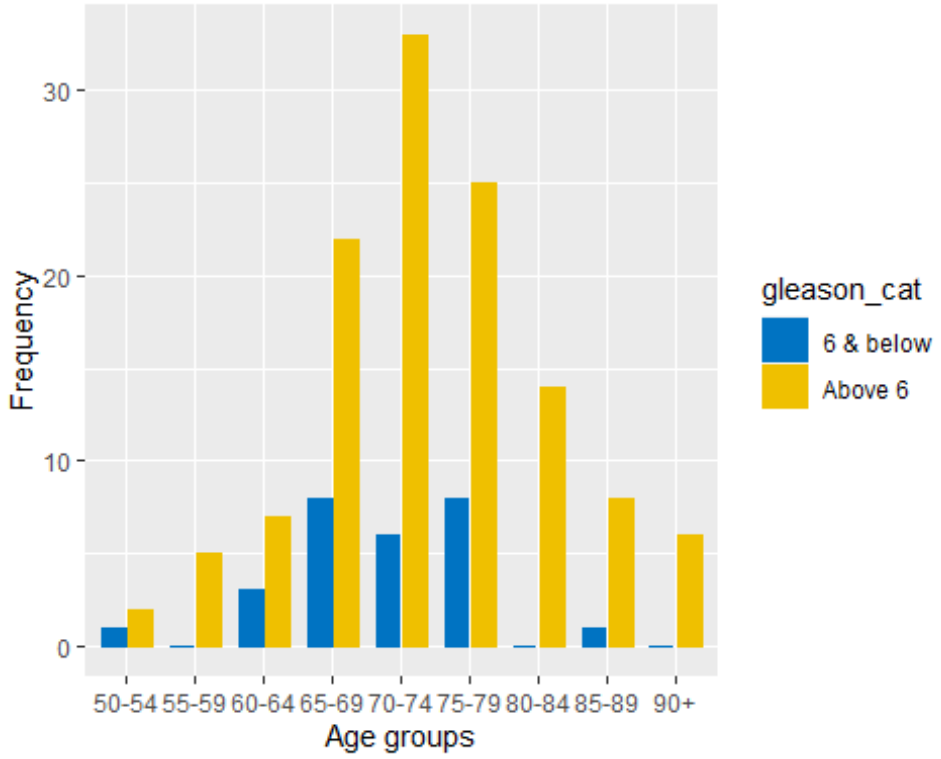

Figure 1: The relationship between the age of the men and the Gleason score.

Discussion

The relationship between the histologic pattern of prostate cancer and its outcome in patients is well documented. There is a correlation between the histologic pattern of prostate cancer on biopsy with the malignant potential of the cancer and the outcome for the patient. [1] The Gleason grading system in its original form was based on the architectural pattern of prostate adenocarcinoma on H&E-stained sections, rather than the cellular features. [2, 5] In the updated Gleason score system, reporting of higher grades on tru-cut biopsy by most pathologists have become the norm.[5] Moreover, the Gleason grading system is an important predictor of PCa outcome, with an emphasis that a Gleason score of 2-5 should be made with extreme caution on tru-cut biopsy samples. [6, 7] We classified prostate cancer cases into two groups based on the Gleason score of 6, following the recommendations of the 2005 International Society of Urological Pathology (ISUP) consensus conference (low-grade group with Gleason score ≤ 6, and high-grade group with Gleason score >6).[8]

The higher incidence of PCa with a Gleason score above 6 (81.89%) in this study agrees with the findings by Raphael et al. Similarly, the predominance of cases with Gleason scores above 6 in men of 70 years' upwards mirrors findings by Raphael and Abhulimen who found a positive relationship between the age of men and their Gleason scores. [8, 9] The commonest grades seen in this study were the higher prostate cancer grades (4 and 5) being predominant at (55.03%). This is like the findings in a previous study. [9] The higher incidence in this study could also be attributed to factors associated with resource-challenged settings where access to healthcare delivery is limited by several factors like socioeconomic status, educational and cultural beliefs, and practices whereby the elderly tend to have lesser drive to seek

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healthcare compared to the younger ones resulting in their late presentation at higher grades.[10]

Although, inflammatory changes and corporea amylacea were significantly rare on tru-cut biopsies and prostatectomies. Their presence in prostatic tissues should be recognized and reported. However, it has been postulated that there may be a weak association between prostatitis and prostate cancer. [11, 12]. Likewise, corporea amylacea has been reported to be common among men with prostate cancer that are associated with pro-inflammatory factors, markers of less aggressive disease, and those that lack TMPRSS2: ERG fusion. [13] Thus, specimens with moderate to severe chronic inflammation were more likely to have corporea amylacea, which may be a physiologic response to early cancers that acts to consolidate inflammatory debris, thereby, preventing more aggressively mutated tumours.[12, 13] A recent study has linked inflammation from unhealthy dietary foods with risk of prostate cancer grade reclassification. [14] This presupposes that inflammation has a role to play in the pathogenesis of prostate cancer and more research is needed to establish a true correlation. In addition, corporea amylacea has been reported in prostate cancer patients with higher body mass index (BMI). [13] Thus, further buttressing the recommendation that when it is seen on histological slides of patients with PCa, pathologists should include it in their report. Furthermore, our study shows that in cases of tru-cut biopsies, where a higher number of biopsied fragments submitted by the urologists were greater than 4, there was a higher chance of reporting the presence of corporea amylacea. This further strengthens the ISUP recommendation that urologists should take 12 tru-cut needle biopsies.

Most of the patients in this study had lower urinary tract symptoms and irritative symptoms. Also, the prostate glands were mostly enlarged and nodular, with the median groove affected, agreeing with findings by Loeb and Catalona et al [15], who reported the obliteration of the median groove in cases with a Gleason score of > 7. Asymptomatic discoveries at medical checks following an abnormal PSA as was seen in a few of our patients mirror findings by Gosselaar et al who reported higher chances of malignancy with suspicious DRE than normal DRE. [16] They reported that a PSA of $\geq$3.0 ng/ml with a suspicious DRE resulted in more PCa's with a Gleason score>7. Thus, this will help in more selective screening procedures and decrease unnecessary biopsies and over-diagnosis. [16] Therefore, we suggest that late presentation by most patients with prostate cancer in our local setting as reported by Ojewola et al in 201,[17] be discouraged. The time to make advocacy to churches, religious settings, and communities nearby is now. This may help to reduce the scourge.

We recommend that: (i) Attending pathologists should endeavor to grade inflammation as mild, moderate, and severe on reports of tru-cut biopsies. (ii) The presence of corporea amylacea should be indicated in reports. (iii) If possible, urologists should take about twelve cores for histopathologic examination. (iv) There is a need to train more anatomic pathologists in urologic pathology, establish new pathology centres, and modernize existing ones. In addition, we must widen the scope of information dissemination to the general population.

Strengths and limitations of the study

The strength of this study is the finding of both inflammation and corporea amylacea in the prostatic biopsies, which are being proposed as possible causal factors of prostate cancer. In addition, higher-grade cancers were recorded more in elderly participants. Some of the limitations encountered in this study included its retrospective design and the period of study which is five years. It is possible that with a much longer study period, more participants would have been included, and our statistical analysis would have been more robust. In addition, if the study involved multiple centres, it would have given us a clear idea of the trend in our region. Furthermore, the retrospective cross-sectional design didn't allow the institution of follow-up that could have positively impacted the disease outcome. Finally, resource-constrained setting, like ours needs adequate funding to conduct prospective research into prostate cancer that is becoming an epidemic among middle-aged and elderly men in our society.

Conclusion

This study emphasizes the significance of the Gleason score in evaluating prostate cancer patients in a southwestern Nigerian setting. The findings align with previous research, demonstrating a correlation between older age and higher Gleason scores. Inflammation and corporea amylacea were prevalent, and we need to emphasize them in our reports. There is a need for early detection through regular PSA screening and digital rectal examinations, coupled with the use of the Gleason score to guide appropriate management strategies.

Declarations

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