

Age and Gleason's score in prostate cancer among Southern Nigerians: Is there any correlation?

ABSTRACT

Background: Prostate cancer (PCa) incidence and mortality are associated with age and African descent. African men are more likely to have aggressive disease, present late with complications and die from prostate cancer. Age is also an independent factor for consideration in the management of patients with PCa. The Gleason score is used both for risk classification, treatment stratification and prognostic purposes.

Objective: To determine the presence of a correlation between age and Gleason score in patients with histologically confirmed prostate cancer.

Materials and methods: This retrospective study was carried out on patients with histologically confirmed prostate cancer from August 2012 to July 2021. Their case records were retrieved, and the patient's age and Gleason grade were collated. Data collected were then analyzed using SPSS version 20. The data were collated using Microsoft excel 2016.

Results: There were 352 patients with histologically confirmed prostate cancer with a mean age of 68.88years±9.75, ranging from 48years to 117years. The modal age range was the 60-69year group. The commonest PCa grade is Gleason 8/Grade group 4 {27.8% (98)}, followed by Gleason 9/Grade group 5 {19.9% (70)} as shown in Figure 2. The Gleason score was associated with age as indicated in Table 2 (p=0.001). However, Pearson's correlation coefficient did not establish a statistically significant relationship (r=0.045; p=0.401). The high-risk Gleason's 8-10,

Grade group 4 and 5, was the most frequent among all the age groups. The low Gleason score cancers were commonest in the 40-49year age group.

Conclusion: There was an association between age and Gleason's score, even though it was not statistically significant. Gleason 8-10 /Grade groups 4 and 5 PCa was associated with older patients. It was also commonest among patients 80years and above.

Keywords: Age, correlation, Gleason score, ISUP, prostate cancer

INTRODUCTION

Prostate cancer (PCa) is the second most frequent cancer diagnosis in men and the fifth leading cause of death worldwide.¹ Evidence suggests the incidence is rising with higher reported prevalence in the developed countries.² Despite the absence of national prostate-specific antigen (PSA) based screening; prostate cancer is the most commonly diagnosed cancer in Nigerian men.^{3,4} The incidence and mortality are associated with ageing and African descent. African men are more likely to have an aggressive disease; ¹ present late with complications and die from prostate cancer.⁵

The original Gleason grading system was based on architectural patterns of prostate adenocarcinoma seen on haematoxylin and eosin staining on low power magnification rather than cellular features. With Gleason pattern 1 being the least aggressive and Gleason pattern 5 being the most aggressive.⁶ The International Society of Urological Pathology (ISUP) has issued guidelines for the **grading of prostate cancer based on a consensus conference held in 2014.**

Gleason scores 6 (Grade group 1), Gleason score 3+4=7 (Grade group 2), Gleason score 4+3=7 (Grade group 3), Gleason score 4+4=8 (Grade group 4), and Gleason score 9-10 (Grade group 5).⁶ Treatment of Prostate cancer depends on the stage and grade of the disease at presentation, the fitness of the patient, and the facilities available. Risk stratification is essential in patient management. Patients who are fit and present early with localized disease can be offered curative treatment such as brachytherapy, radical prostatectomy or radiotherapy. Different prognostic indicators for prostate cancer have been sought to aid the treatment of prostate cancer.⁷⁻⁹ The Gleason score is an essential tool in patient management.⁶ Several studies on the relationship between age and Gleason score have been carried out with varying observations.^{10,11,12}

OBJECTIVE

To determine the presence of a correlation between age and Gleason score in patients with histologically confirmed prostate cancer in Port Harcourt.

MATERIALS AND METHODS

A retrospective study carried out at the University of Port Harcourt Teaching Hospital, Rosivylle Clinic and Urology Centre Port Harcourt, Rivers State, Nigeria. Patients with histologically confirmed prostate cancer were evaluated from August 2012 to July 2021. Their folders were retrieved, and the patient's age and Gleason grade were collated. Data collected were then analyzed using SPSS version 20. The data were collated using Microsoft excel 2016.

RESULTS

There were 352 patients with histologically confirmed prostate cancer with a mean age of 68.88years±9.75, ranging from 48years to 117years. The modal age range was the 60-69years. The commonest PCa grade is Gleason 8 Grade group 4{27.8% (98)}, followed by Gleason 9/Grade group 5 {19.9% (70)} as shown in Figure 2. Gleason score was associated with age, as indicated in Table 2 (p=0.001); however, Pearson's Correlation Coefficient did not show a statistically significant relationship (r=0.045; p=0.401). The high-risk Gleason 8-10, ISUP 4&5, was the most frequent among all the age groups. It was also commonest among patients 80years and above. The low Gleason score cancers were most frequent in the 40-49year age group.

Table 1: Showing the age characteristic of the patients.

	Age (years)
N	352
Mean	68.88
Median	69.00
Mode	70.00

Std. Deviation	9.75
Variance	95.25
Youngest age	48.00
Oldest	117.00

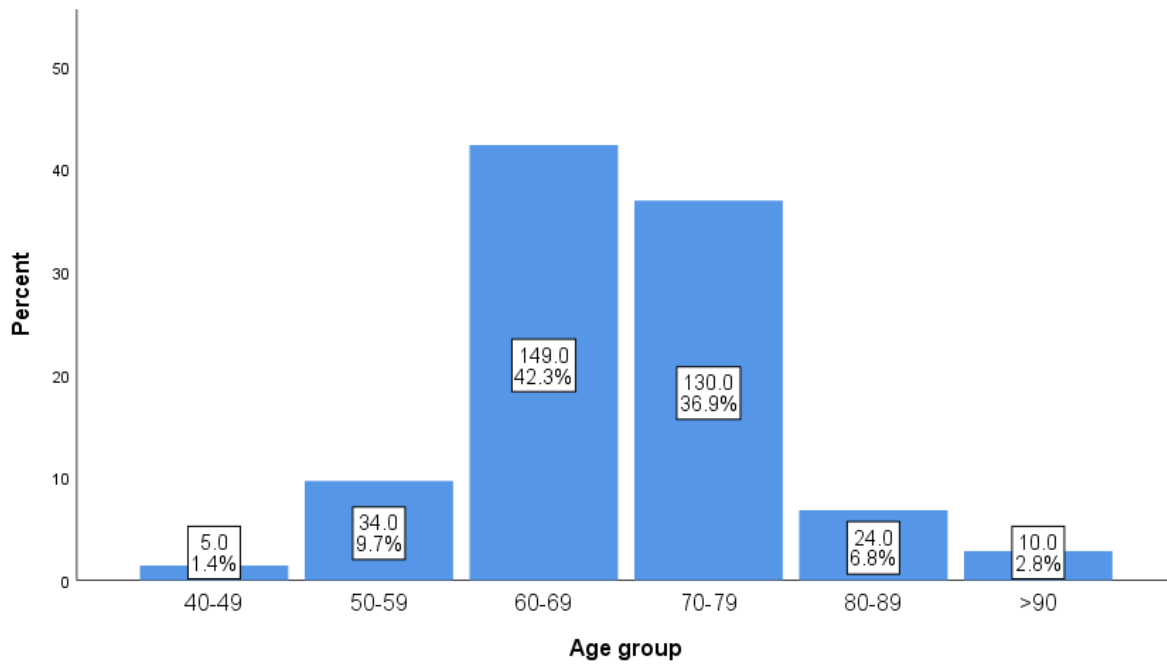


Figure 1: Showing the distribution of the patients' age groups

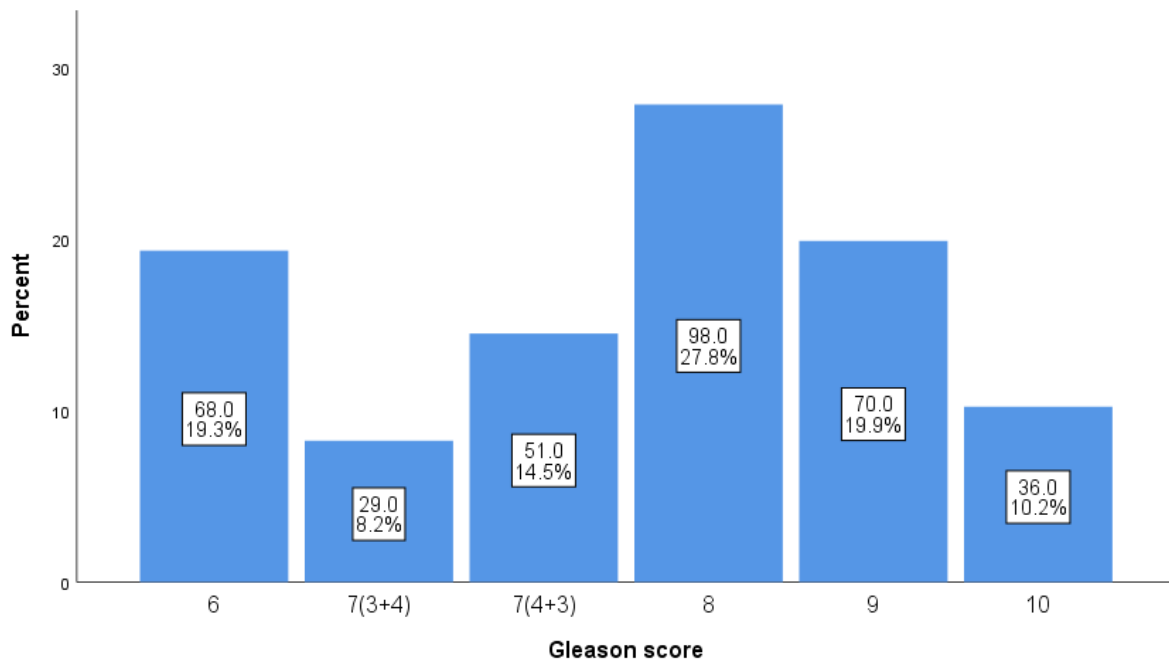


Figure 2: Gleason score distribution of the patients.

Table 2. The relationship between the age and the Gleason's score of the prostate cancer patients.

	Grading of Gleason score		
	Well differentiated (6)	Moderately differentiated (7)	Poorly differentiated (8-10)
	N (%)	N (%)	N (%)
Age group			
40-49	1 (20.0)	2 (40.0)	2 (40.0)
50-59	5 (14.7)	6 (17.6)	23 (67.6)
60-69	19 (12.8)	27 (18.1)	103 (69.1)
70-79	31 (23.8)	41 (31.5)	58 (44.6)
80-89	10 (41.7)	4 (16.7)	10 (41.7)
>90	2 (20.0)	0 (0.0)	8 (80.0)

*Chi square= 30.02, p-value= 0.001**

Table 3. Pearson correlation analysis between Age and Gleason score of the prostate cancer patients.

	Gleason score
N	352

P-value 0.401
R 0.045

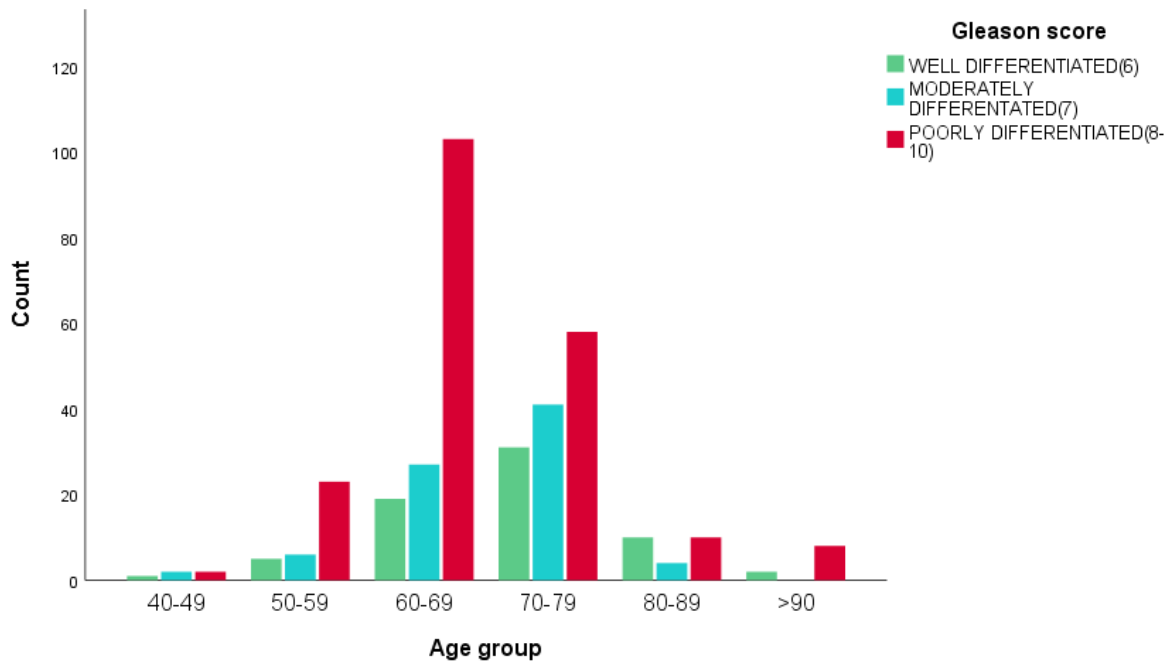


Figure 3. Gleason's score distribution among patient groups with prostate cancer.

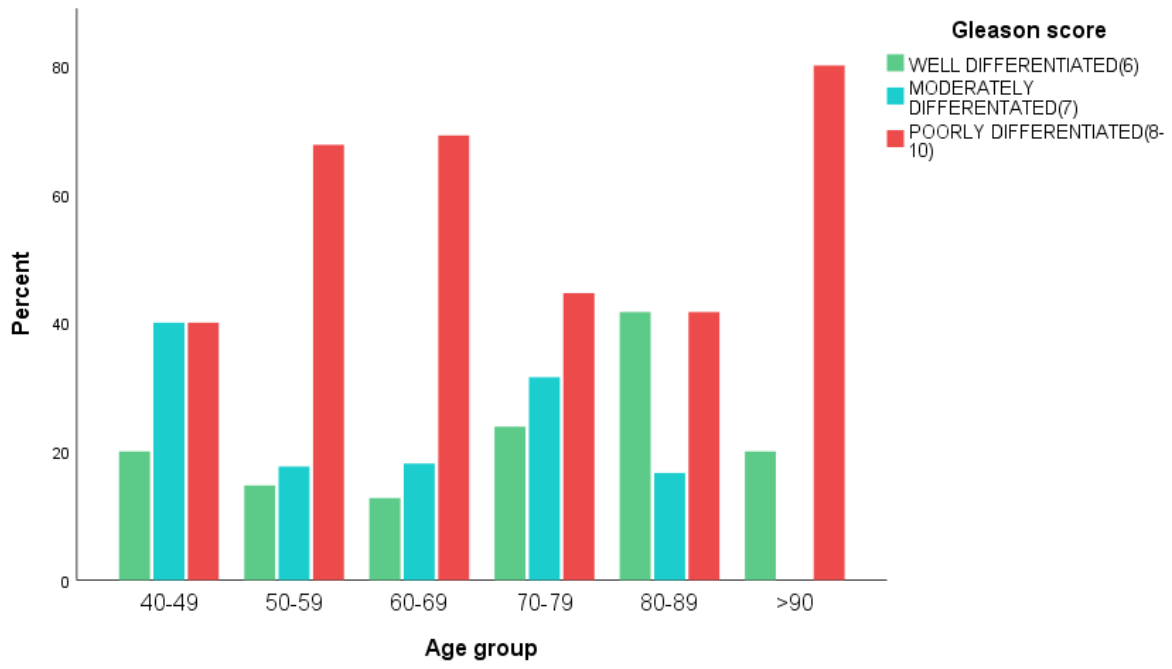


Figure 4. Percentage proportion of Gleason's score within the age groups.

Table 4. Linear regression analysis of Gleason score and age showing the model summary of the influence of age on the Gleason score

Variables	Unstandardized Coefficients B	P-value	95.0% Confidence Interval for B		
			Lower Bound	Upper Bound	
(Constant)	8.224		7.266	9.181	R = 0.045 R ² = 0.002
Age	0.006	0.401	-0.020	0.008	Adjusted R ² = 0.001 F (1,350) = 0.707, P = 0.401

DISCUSSION

Age, the black race and family history are well-established risk factors for prostate cancer.^{13,14,15} In this study, the mean age was 68.88years, with the youngest 48years and the oldest 117years, as shown in Table 1. Previous studies carried out in Port Harcourt, Nigeria by Eke et al.¹⁶ in 2002 and Ekeke et al.¹⁷ in 2012 had a mean age of 71.6years and 69.9years, respectively. This reduced mean age at presentation over the years could be a consequence of raised awareness, as screening tends to lead to earlier diagnosis and presentation the disease.

The mean age at diagnosis reported from different parts of Nigeria is similarly within our observed age range and at par with observations from other parts of the world. The mean age in Kano, Northern Nigeria, was 64.2years;¹⁸ in Lagos (Western, Nigeria), Zaria and Benin were 68.48, 64.5 and 68years, respectively;¹⁸ while in the United Kingdom, the United States and China, it was 72.3years,¹⁹ 68years,²⁰ and 66.84years²¹ respectively. In developed countries with high prostate cancer awareness, most patients are diagnosed at a relatively younger age and earlier stage,²² unlike in sub-Saharan Africa, where the majority still present with an advanced stage of the disease.⁵

Patients with high Gleason scores and Grade groups are associated with cancer-related complications and mortality. The osseous complication is one of the commonest because PCa is associated with early spread to the bone. A study in Japan found up to 6% of their study population of patients with advanced PCa, with a mean age of 77.3years had a bone fracture.²³ A

study carried out in Port Harcourt noted that high Gleason grades PCa was associated with a higher frequency of complications and skeletal-related sequelae.⁵ This finding is similar to observation by others.²⁴ Wenzel et al studied 17,263 patients with Grade group 5 cancer who underwent radical prostatectomy or external beam radiotherapy. They compared Gleason 9 (4+5, 5+4) with Gleason 10 (5+5) using the Surveillance, Epidemiology and End Results (SEER) database at biopsy, and found that PCa characteristics were increasingly unfavourable with increasingly aggressive Gleason pattern from 4+5 to 5+4 to 5+5.²⁵

The objective of treatment for early PCa is to achieve a cure. Treatment for localized prostate cancer includes brachytherapy, stereotactic radiotherapy, radical prostatectomy, active surveillance and watchful waiting.²⁶ In managing patients with PCa, differentiating clinically significant and potentially lethal cases from more indolent ones is crucial.²⁷ Gleason grade, serum PSA, and disease stage are important considerations for treatment selection and prognostication purposes.^{26,27} In our study, the most common Gleason's grade was 8 (Grade group 4) in 27% (98). Gleason 9 (Group grade 5) was next predominant with a frequency of 18.9% (70). The majority of the patient had high-risk aggressive carcinoma {57.95% (204)} with Gleason 8-10.

Our study also found the poorly differentiated cancers were more abundant in all age groups except the 40-49year age group, where moderately differentiated (Gleason's 7, Grade group 2&3) and poorly differentiated carcinomas (Gleason's 8-10, Grade group 4&5) were evenly distributed as shown in Table 2. and Figure 3&4. Several studies have shown that prostate cancer in black men may be more aggressive and likely to lead to mortality.¹ A high Gleason's score is associated with disease progression and benefits more from treatment.^{1,5} Watchful waiting and active surveillance are indicated for low-grade PCa (Gleason 6, ISUP 1), especially in older patients with life expectancy less than 10-15years. With younger patients, some circumspection is required because of the possibility of Gleason's score migration.

Our study revealed a weak correlation between age and Gleason's score, which was statistically significant. This entails that the higher the age, the worse the Gleason's grade and vice versa. As shown in Table 3, the model summary of the influence of age on the Gleason's score indicates a non-significant regression equation ($F(1, 350) = 0.707, P = 0.401$), with an adjusted R^2 of 0.002. This means that age explains 0.2% of the variance in the Gleason score. Gleason's score increased by 0.006% for every unit increase in age. Hence, age had no statistically significant impact on Gleason's score.

A retrospective study conducted by Shah et al.¹², which included 5,100 subjects, observed that septuagenarians with prostate cancer have a 61% frequency of Gleason 7-10 prostate cancer. They concluded that screening for prostate cancer should be carried out even for men above 70years. Hunyh-Le et al.¹¹ carried out a cross-sectional study in 20,356 men with prostate cancer in Norway. Their ages, stage and Gleason score were collated. The percentages of men with Gleason 8 to 10 disease among men aged 55-59, 65-69, 75-79, and 85- 89 years were 16.5%, 23.4%, 37.2%, and 59.9%, respectively ($p < 0.001$). The older our patients, the higher the Gleason grade/Grade group. Both Shah and Hunyh-Le et al. had a larger patient population in their study than ours. This high number of subjects could be a reason for the statistically

significant relationship between age and Gleason score. Muralidhar et al. ²⁸ studied 383,039 men diagnosed with prostate cancer from 2004-to 2011. They also observed that the prevalence of the high-risk Gleason score 8 to 10/ Grade group 4&5 PCa increased significantly.

Because of the diversity and heterogenous presentation of PCa, there is a need for larger cohort studies to characterize further the relationship between age and Gleason's score among Africans.

Conclusion

There was an association between age and Gleason's score even though it was not statistically significant. Our study could not exclude the presence of a correlation between age and Gleason/Grade groups of adenocarcinomas of the prostate. Gleason 8-10 or ISUP 4&5 PCa was associated with older patients. It was also commonest among patients 80 years and above. More extensive studies are required to validate the relationship between age and Gleason's score in prostate cancer patients.

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