Original Article

Correlation between Body Mass Index and Gleason Score in Men with Prostate Cancer in Southeastern Nigeria

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Abstract

Introduction: Prostate cancer has an increasing global burden. The clinical course varies from an indolent disease to a rapidly aggressive cancer. It is associated with higher mortality in less developed nations due to late presentation. The Gleason scoring system for prostatic adenocarcinoma has prognostic implications in diagnosed cases. Obesity has been associated with the evolution of many cancers including prostate cancer. There are conflicting reports on the relationship between obesity, as measured by body mass index (BMI), and prostate cancer aggressiveness, as measured by Gleason score. This study is aimed to determine if a correlation exists between BMI and Gleason score in men with prostate cancer. **Methodology:** This was a prospective, hospital-based, cross-sectional study involving consecutive patients with prostate cancer. Clinical evaluation including anthropometry, digital rectal examination, and relevant investigations were done for each patient and data collected with pro forma. This was followed by prostate needle biopsy and those diagnosed with adenocarcinoma of the prostate had their Gleason grades and scores obtained. Data were analyzed statistically using Spearman Correlation. **Results:** The mean age of the patients was 69.54 ± 8.61 years (range 47–83 years). The BMI ranged from 16.98 to 36.45 kg/m^2, with a mean of 27.03 ± 5.03 kg/m^2. Twenty-six of the patients (36.1%) were overweight and 34.7% were obese. The mean total prostate-specific antigen was 118.65 ± 84.43 ng/ml, with a range of 31–406 ng/ml. The modal Gleason score was 9 with a range of 4–10. There was a strong positive correlation between BMI and Gleason score (r = 0.817, P = 0.0003). **Conclusion:** The BMI of patients with prostate cancer correlated positively with their Gleason score.

Keywords: *Body mass index, Gleason score, Prostate cancer*

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Introduction

Difficulty with micturition is a common complaint in urology and is usually characterized by lower urinary tract symptoms (LUTS). Many men with LUTS have varying degrees of prostate enlargement often caused by prostate cancer, benign prostatic hyperplasia (BPH) and prostatitis as the most frequent pathologies.

Prostate cancer is the second-most common cancer among men and the fourth-most common malignancy worldwide.[1-4] It has a clinical course that varies from an indolent disease to a rapidly aggressive cancer that metastasizes quickly, leading to severe pain and untimely death.[5,6] Diagnosis is made through prostate biopsy and histology, which are prompted by clinical and/or biochemical features suggestive of the disease. The Gleason system is a histologic grading system for

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prostatic adenocarcinoma based on architectural patterns rather than cellular features.[7] In this system, histologic patterns called grades are defined. These range from Gleason grade 1, which represents the well-differentiated with the best prognosis to Gleason grade 5, which represents the poorly differentiated with the poorest prognosis.[7,8] The addition of the two most common Gleason grades in a field gives the Gleason score, which ranges from 2 to 10 and represents the level of aggressiveness of prostate cancer.[7,9]

High body mass index (BMI) is a major global health problem. The BMI is derived from the weight of the individual in kilograms divided by the square of the height in meters (i.e., kg/m^2).[10] Normal BMI ranges from 18.5 kg/m^2 to 24.9 kg/m^2, while overweight is defined as BMI ≥25 kg/m^2 <30 kg/m^2 and obesity is BMI ≥30 kg/m^2.[10,11]

Obesity has been shown by several studies to have a positive correlation with the more aggressive prostate cancers evidenced by high Gleason scores.[12-14] High BMI provides a favorable biological microenvironment for tumor onset and growth through some proposed mechanisms which involve alterations in the endocrine system, notably, the levels of testosterone, estrogen, and insulin-like growth factor-I.[14-20] However, this correlation was not found by some other studies. Gallina *et al*.[21] in a study of European men, and Chamie *et al*.[22] in California, the USA observed no relationship between BMI and high-grade prostate cancer.

With this disparity, it becomes necessary to ascertain if such a relationship exists in our environment where we have a high burden of the disease as well as obesity. The study, therefore, aims to determine the relationship between BMI and prostate cancer aggressiveness (Gleason score) in adult Nigerian males with histologically diagnosed prostate cancer.

Methodology

This was a prospective, cross-sectional study conducted at the Urology Clinics of Nnamdi Azikiwe University Teaching Hospital, Nnewi from July 2018 to July 2019 following approval by the hospital's ethics committee.

All-new adult male patients that attended the Urology Clinics with LUTS and consented were enlisted into the study. The exclusion criteria included patients that could not stand erect, history of bariatric surgery, those on the medical program for weight reduction, immunosuppressive illnesses (e.g., TB, AIDS), prostatitis, BPH, and those currently on treatment for prostatic adenocarcinoma.

Detailed clinical assessment, including digital rectal examination, weight, and height measurements, were taken for each patient on presentation. Investigations included full blood count, serum electrolytes, urea and creatinine, serum prostate-specific antigen (PSA), urinalysis with urine microscopy, culture and sensitivity, and abdominopelvic ultrasound scan. The data obtained were entered into predesigned pro forma.

Patients were stratified into underweight, normal weight, overweight, and obesity groups using the World Health Organization classification of BMI.[11]

Patients suspected to have prostate cancer based on clinical and/or biochemical findings were counseled and informed consent obtained before subjecting them to digitally-guided transrectal prostate biopsy using size 18G semi-automated Tru-Cut® biopsy needle after adequate lubrication with 2% xylocaine gel. Specimens obtained were sent to a designated pathologist for histological examination and reporting using the Gleason Scoring System. Those diagnosed with prostate cancer were then stratified into three groups: low (Gleason score 2–4), intermediate (Gleason score 5–7), and high (Gleason score 8–10).

Data collected were analyzed with a multi-purpose computer analysis program, Statistical Package for the Social Sciences version 23 (IBM; SPSS, Chicago, IL, USA). Results obtained were expressed as tables and figures where necessary. Data were subjected to Spearman correlation. An *r* - value (Correlation coefficient) of either ≥−0.7 or ≥+0.7 was considered a high/strong correlation, whereas an *r* - value (Correlation coefficient) that ranged either from − 0.3 to <−0.7 or from + 0.3 to <+0.7 was considered moderate correlation and an r-value of either <−0.3 or <+0.3 was considered low correlation. Value of $P \leq 0.05$ was considered statistically significant.

Results

A total of 159 patients were recruited during the study period; however, only 72 patients who satisfied the criteria for inclusion were analyzed.

The age range of the participants was 47–83 years with a mean age of 69.54 ± 8.61 years and the median age of 71.50 years. The peak incidence of prostate cancer was in the eighth decade [Figure 1].

Most (80.6%) of the men were married. Widowers and single men made up 18.06% and 1.39% of the patients, respectively.

The most common educational attainment was a secondary school (48.6%), followed by primary school (19.4%), postsecondary (18.1%), whereas 13.9% had no formal education.

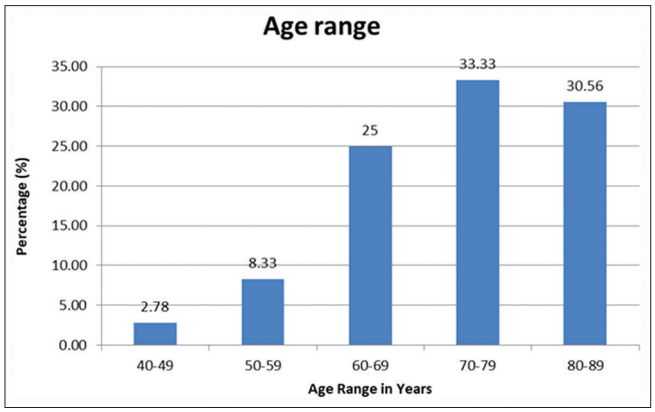

Figure 1: Age distribution of the patients

The patients generally had LUTS of varying degrees. In 38.9% of the patients, the symptoms were present for over 12 months before the presentation. The rest had their symptoms for 6–12 months (37.3%) and for <6 months (23.6%).

There was a family history of prostate cancer in 6 (8.3%) of the patients. This was seen in their fathers (2 patients), brothers (3 patients), and first cousin (1 patient).

The mean total PSA of the patients was 118.65 ± 84.43 ng/mL with a range of 31–406 ng/mL and a median of 85.86 ng/mL. The mean percentage Free PSA was 9.03% ± 6.23%, with a range of 0.52%–29.37%.

The mean weight of the participants was 75.75 ± 13.08 kilograms, with a range of 48–95 kilograms. The mean height of the participants was 1.68 ± 0.063 m, with a range of 1.56–1.78 m. The mean BMI was 27.03 ± 5.03 kg/m^2 with a range of 16.98–36.45 kg/m^{2}and a median of 27.85 kg/m^2. Twenty-six (36.1%) of the participants were overweight and 34.7% were obese (Class I obesity: 23 patients [31.9%]; Class II Obesity: 2 patients [2.8%]) [Table 1].

The mean, median, and modal Gleason Scores were 7.5 ± 0.80, 7.0, and 9, respectively, with a range of 4–10. Forty-one (56.9%) of the patients had Gleason Scores within the Intermediate group, whereas 29 (40.3%) of the patients had Gleason scores within the high group [Table 2].

There was a significant association between Normal BMI and Low Gleason score (χ^2 = 14.098; P = 0.003) after stratifying the patients into High (Gleason score >7) and low (Gleason score ≤7) Gleason Score groups [Table 3]. The obesity Class II patients had a low Gleason Score though not statistically significant (χ^2 = 1.547; P = 0.216), as shown in Table 3. On further analysis by stratifying the patients into high (≥25 kg/m^2), normal (18.5–24.9 kg/m^2), and low (<18.5 kg/m^2) BMI groups, there was a significant association between high Gleason score and high BMI (χ^2 = 4.771; P = 0.03), as shown in Table 4.

There was a strong positive correlation between BMI and Gleason Score (r = 0.817; P = 0.0003), as shown in Table 5.

Table 1: Distribution of body mass index of the participants

BMI group (kg/m^2)	Range	Number of patients (%)
Underweight (<18.5)	16.98	1 (1.4)
Normal (18.5-24.9)	19.4-23.7	20 (27.8)
Overweight (25-29.9)	25.9-28.2	26 (36.1)
Obesity Class I (30-34.9)	31.1-34.3	23 (31.9)
Obesity Class II (35-39.9)	35.7-36.45	2 (2.8)
Total		72 (100.0)

BMI: Body mass index

Table 2: Distribution of the Gleason scores of the participants

Gleason score	Nu mber of patients (%)
4	2 (2.78)
6	20 (27.78)
7	21 (29.16)
8	2 (2.78)
9	24 (33.33)
10	3 (4.17)
Total	72 (100.0)

Low score: ≤4; Intermediate score: 5-7; High score: 8-10

Discussion

Cancer of the prostate is a frequent diagnosis made at urologic consultations, and attempts at early diagnosis and prediction of prognosis using several patient parameters are usually made to institute aggressive but appropriate treatment. Several clinical and nonclinical parameters, including BMI, have been used to predict the aggressiveness of tumor and outcome of treatment. In this study, we have tried to establish if there is a correlation between BMI and the aggressiveness of prostate cancer.

The age distribution of the patients from this study is in keeping with the facts that prostate cancer is not commonly diagnosed in men <50 years and its incidence continues to increase with advancing age.[4,23] There is a slight drop in the frequency of the patients after the age group of 70–79 years, which could be attributed to the life expectancy of the study population. The mean age of 69.54 ± 8.61 years found in this study is similar to the findings of other Nigerian studies.[24-26] The age range of 47–83 years and the peak incidence of the 8th decade from this study compares fairly with 44–92 years found earlier by Nwofor and Oranusi[24] in the same centre.

Table 3: Relationship between body mass index and Gleason score of the patients

BMI (kg/m²)	Number of patients	High Gleason score group (%)	Low Gleason score group (%)	χ^2	*P*
UnderweighT (<18.5)	1	0 (0)	1 (2.32)	0.03†	0.935†
Normal (18.5-24.9)	20	2 (6.70)	18 (41.86)	14.098	0.003*
Overweight (25-29.9)	26	14 (48.28)	12 (27.91)	5.862	0.036
Obesity Class I (30-34.9)	23	13 (44.83)	10 (23.26)	4.547	0.043
Obesity Class II (35-39.9)	2	0 (0)	2 (100)	1.547†	0.216†

*Significant for low Gleason score, †Fischer's Exact test used, otherwise Pearson Chi-square test. High Gleason Score Group: Gleason Score >7, BMI: Body mass index

Table 4: Analysis of the relationship between high Gleason score and body mass index of the patients

BMI group (kg/m²)	Number of patients (%)	Low Gleason (≤7) score group (%)	High Gleason (>7) score group (%)	χ^2	*P*
High (BMI ≥25)	51 (70.83)	30 (69.77)	21 (72.4)	4.771	0.03
Normal (BMI 18.5-24.9)	20 (27.78)	12 (27.9)	8 (27.6)		
Low (BMI <18.5)	1 (1.39)	1 (2.33)	0 (0)		

BMI: Body mass index

Table 5: Correlation between body mass index and Gleason score

Parameters	Gleason score	BMI
Gleason score		
Correlation coefficient*	-	0.817
P	-	0.0003
BMI		
Correlation coefficient*	0.817	-
P	0.0003	-

*Spearman correlation. BMI: Body mass index

Secondary education was the most common highest educational attainment among patients. This may be attributed to the fact that Nnewi, Southeastern Nigeria, is a commercial hub with mainly traders as inhabitants.

Obesity and overweight have remained a global health concern. The global burden of high BMI is worse off in developing nations where there is attendant poor health facilities. Nigeria, the most populous nation in Africa, is one of such developing countries.[27] In Nigeria, prevalence ranges of 20.3% to 35.1% and 8.1% to 22.2% have been noted for obesity and overweight, respectively.[27] The mean BMI of 27.03 ± 5.03 kg/m² noted in this study compares well with the findings of Okafor *et al*.[28] who studied the relationship between obesity and blood pressure in Southeastern Nigeria and Goris-Gbenou *et al*.[29] who studied an American population. Furthermore, studies by Freedland *et al*.[20] in Europe and Su *et al*.[18] in an African–American population reported similar findings. The median BMI of 27.85 kg/m² in this study compares well with that of a European study (27.6 kg/m²) while it is at variance with a study in Asia (23.9 kg/m²).[20,30] As much as 36.1% of the participants in this study were overweight, while obesity was seen in 25 (34.7%) patients (Class I: 23 patients [31.9%]; Class II: 2 patients [2.8%]). This is similar to the findings by Bai *et al*.[30] who studied the association between BMI, Gleason score and risk of biochemical recurrence following radical prostatectomy in Chinese men.

The predominant Gleason score of 9 and the mean Gleason score of 7.5 ± 0.80 in this study are in contrast with the reported predominant Gleason score of 6 by Liang *et al*.[31] and a mean Gleason score of 5.87 ± 1.17 by Goris-Gbenou *et al*.[29] This could be due to early presentation of the patients used in those studies and thus, lesser tumor burden. Furthermore, it has been observed that men of African descent are more likely to have higher Gleason scores and present with more advanced disease.[32-35]

This study found a strong positive correlation between BMI and the Gleason score of patients with prostate cancer. The two patients with Class II Obesity had a low Gleason Score, though not statistically significant, this may have arisen as a result of a low number. Also found from this study was a significant association between high BMI and high Gleason score and between normal BMI and low Gleason score similar to the observations of Gioia *et al*.[14] in a study of Caucasian men, and Liang *et al*.[31] in a study using a cohort from Selenium and Vitamin E Cancer Prevention Trial (SELECT). They noted an association between high BMI and risk of high-grade prostate cancer, especially in men with a family history of prostate cancer. Similarly, Jayachandran *et al*.[19] observed in a retrospective analysis of 1,415 men treated with radical prostatectomy that obesity was a risk factor for aggressive prostate cancer and tumor recurrence irrespective of the race while high BMI was found to be independently associated with high-grade prostate cancer by Freedland *et al*.[20] in

their analysis of 2,302 men in America. There was a higher proportion (72.4%) of the patients with high Gleason score in the high BMI group, similar to the finding in the study by Zhou *et al*.[13] In another study by Kryvenko *et al*.,[12] 5118 patients who underwent robotic radical prostatectomy in America were analyzed and they observed that the Gleason score and the number of positive cores were higher in overweight and obese men.

In all, it seems that BMI correlates positively with the Gleason score.

Conclusion

There was a significant association between high BMI and high Gleason score as well as between normal BMI and low Gleason score from this study. The study showed a strong positive correlation between BMI and Gleason score in men with prostate cancer. Thus, the higher the BMI the higher the chances of aggressive disease.

Ascertaining the BMI of patients with prostate cancer should be encouraged and there is a need for more public campaign efforts to tackle high BMI through lifestyle and dietary modifications. Obese and overweight men should be encouraged to get screened for prostate cancer earlier than their normal-weight counterparts. Further, multi-center studies are necessary as these will be more representative of the picture in the general population.

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Conflicts of interest

There are no conflicts of interest.

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