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Association of BMI and Age with Gleason Score and PSA in Patients with Prostate Cancer

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ABSTRACT

Background and Objective: Obesity has produced conflicting results on various indices of prostate cancer diagnosis. Since the effect of body mass index (BMI) on Gleason score and prostate specific antigen (PSA) as well as the overall classified risk of prostate cancer results is important, the present study was conducted to investigate the association of BMI and age with Gleason score and PSA in Patients with prostate cancer.

Methods: In this cross-sectional study, 310 prostate cancer patients referred to the affiliated hospitals of Babol University of Medical Sciences from 2011 to 2021 were evaluated in terms of age, height, weight, PSA and Gleason score. Based on BMI, the patients were divided into three groups: obese (BMI≥30), overweight (BMI=25-30) and normal weight (BMI<25) and according to the Gleason score into three low grades (G/S<7), medium grade (G/S=7), high grade (G/S>7) and were divided into three categories based on PSA: 4-10, 10-20 and more than 20. Then, the association of BMI and age with Gleason score and PSA was investigated.

Findings: The mean BMI of the patients was 26.3±3.77 kg/m^2. The mean PSA was 35.72±8.5 ng/dL and the mean Gleason score was 7.1±1.11. The mean Gleason score increased with increasing age (p<0.001, r=0.307). A higher Gleason score had a significant relationship with PSA increase (p<0.001, r=0.485). BMI had no significant association with Gleason score (r=0.072, p=0.102). PSA decreased slightly with increasing BMI (p=0.006, r=0.157).

Conclusion: The results of the study showed that increasing age is associated with a higher Gleason score. But the increase in BMI is not related to increased risk of prostate cancer and increased Gleason score.

Keywords: *Body Mass Index, Age, Gleason Score, Prostate Specific Antigen.*

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Introduction

Prostate cancer is the most common non-skin cancer in men in the United States in 2017 (1). Several factors including old age, race, ethnicity, various environmental factors, genetics and family history are related to the incidence and mortality of prostate cancer (1). Other factors associated with prostate cancer include diet, high consumption of saturated animal fat and red meat, less consumption of fruits, vegetables, vitamins, coffee, obesity and physical inactivity, inflammation, increased blood sugar, infections and exposure to chemicals or ionizing radiation (2). A study in Iran showed that the incidence of prostate cancer during 2003-2009 increased from 5.4 to 12.8 per 100,000 people, which indicates a continuous increase in incidence in recent years (3). The rate of prostate cancer increases with age. Although 1 in 350 men under the age of 50 are diagnosed with prostate cancer, the incidence increases to 1 in 52 men aged 50 to 59 years (4). The incidence rate in men over 65 years is approximately 60% (5). The incidence of prostate cancer varies significantly around the world, which seems to be related to the difference in screening in different countries (6). A study on immigrants from countries with a lower risk of this disease showed that adaptation, western lifestyle, probably due to obesity and inactivity, is a predisposing factor for prostate cancer (3, 7). Obesity can create a unique environment for the occurrence of endocrine and biochemical cancers that can affect any of the predictors of prostate cancer outcomes in a non-deterministic way (8). Some studies have shown that obese men typically show lower PSA concentrations. However, the value of PSA changes in higher BMI to predict the disease is questionable (9, 10).

Obesity is a serious health problem worldwide. The relationship between obesity and cancer has attracted less attention compared to its relationship with cardiovascular effects. But in many studies, obesity has been found to be associated with esophageal, kidney, colon, thyroid, liver, and prostate cancers in men and endometrial, esophageal, ovarian, postmenopausal breast, pancreas, and thyroid cancers in women (5, 11). By creating a carcinogenic, endocrinological and biochemical environment suitable for tumors, obesity can contribute to tumor development and expansion. In obese people, the secretion of insulin and IGF-1 increases, which especially increases the risk of prostate cancer (12). Prostate cancer mortality rates are steadily decreasing in most Western countries, including North America, as well as in Western and Northern Europe (13). Although the reason is not clear, it may be due to early diagnosis and improved treatment (14). The PSA test was first approved in 1986 as an inexpensive and effective tool for detecting asymptomatic cases of prostate cancer. Routine PSA test for all adult men has led to a rapid increase in the prevalence of prostate cancer in developed countries. After that, it had a decreasing trend, which is probably due to the change in the diagnostic guidelines of prostate cancer (15).

More than 20 different tools have been introduced to determine the risk of prostate cancer, mostly based on a combination of PSA before treatment, Gleason score and TNM (16, 17). Currently, the Gleason score (Gleason/Score = G/S) is the best predictive factor for prostate cancer outcomes (18, 19). The Gleason scoring system is currently used for both biopsy and radical prostatectomy samples. Although the Gleason score of radical prostatectomy determines the actual grade of prostate cancer (16), the use of the Gleason score in biopsy has recently been adopted as a suitable method to determine the type of prostate cancer treatment (17).

With PSA testing, the survival rate of prostate cancer can be significantly improved due to the earlier diagnosis of the disease, and the possibility of removal and local treatment before metastasis is provided (10, 15). However, routine PSA testing has been shown to be negative in low-risk individuals. Assuming that a higher BMI is also related to a higher Gleason score, which indicates a more aggressive tumor, it is necessary to investigate different BMI values on the overall risk of prostate cancer (4, 5, 20). Considering the high prevalence of obesity and the increasing growth of prostate cancer in Iran and considering the fact

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that no study has been conducted in Iran on the relationship between BMI and the Gleason score of prostate cancer, also considering the growing trend of prostate cancer in Iran, and since no study has been conducted in this region in Iran regarding the association of BMI and age with Gleason score and PSA in prostate cancer, this study was conducted with the aim of investigating the association of BMI and age with Gleason score and PSA.

Methods

After approval by the ethics committee of Babol University of Medical Sciences with the code IR.MUBABOL.REC.1399.395, this cross-sectional study was conducted on 310 patients who referred to the affiliated hospitals of Babol University of Medical Sciences to perform biopsy and radical prostatectomy or TUR-P from 2011 to 2021. The sample size was estimated 200 people based on the study of Zhou et al. (5) and the sample size formula. However, due to the availability of 310 samples, the study was conducted on all clients within 10 years.

Patients who had received hormonal treatment before sampling, drugs that affect weight such as corticosteroids, and patients who were unable to eat were excluded from the study. Variables including hospital records, age of patients, place of residence, height and weight, PSA before prostate biopsy, open surgery, TURP and FNB biopsy and pathological findings were collected through the study checklist. Based on BMI, patients are divided into three groups: obese (BMI≥30), overweight patients (BMI=25-30) and normal weight patients (BMI<25) and based on Gleason score were divided into three groups: low grade (GS<7), moderate grade (G/S=7), and high grade (GS>7) (8). Serveral studies divided BMI into two groups >25 and <25 (21, 22), yet in this research they were divided into three groups <25, 25-30 and >30 for more accuracy. Weight was measured with a Xiaomi digital scale and height was measured with a tape measure in the first visit, and to calculate BMI, weight was divided by the square of height. Also, in the first visit, a rectal examination was performed by an urologist and the PSA level was measured using a blood sample in an accredited laboratory. In order to evaluate the relationship between Gleason score and obesity, patients were separated according to PSA before prostate biopsy. Based on PSA, patients were divided into three categories: 4-10, 10-20, and more than 20 (15). The risk of prostate cancer was classified using the European Urology Society measurement tool for risk classification, based on rectal examination, PSA and Gleason score (5). Then, the association of BMI and age with Gleason score and PSA was investigated. Data were analyzed using SPSS statistical software version 23 and Chi-square, Spearman, ANOVA and Tukey's post hoc test, and $p<0.05$ was considered significant.

Results

A total of 310 patients with complaints of prostate cancer referred to centers affiliated to Babol University of Medical Sciences. The mean age of the patients was 70.87±8.94 years, the mean BMI of the patients was 26.30±3.77, the mean PSA of the patients was 35.08±72.5, and the mean Gleason score was 7.11±1.11 (Table 1).

As BMI increases, PSA decreases slightly ($p=0.006$ and $r=0.157$). The results showed that with increasing age, the mean Gleason score of patients increases ($p<0.001$ and $r=0.307$). Also, the mean concentration of PSA is different in different Gleason scores ($p<0.001$ and $r=0.485$). There was no significant relationship between BMI and Gleason score ($p=0.072$ and $r=-0.102$) (Table 2). Post-HOC analysis showed that the mean Gleason score increased with age. Also, Post-HOC analysis showed a significant relationship between those patients who had Gleason score less than 7 and patients with G/S=7

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and more than 7. In the case of PSA, patients with a Gleason score greater than 7 also had a higher initial PSA concentration, that is, with an increase in PSA, the Gleason score also showed a significant increase ($p<0.001$) (Table 2). In patients with PSA less than 20, there was no significant relationship between BMI and Gleason score. In the case of patients with PSA greater than 20, BMI and Gleason score showed an inverse and significant relationship ($p<0.05$). Also, no significant relationship was observed between BMI and Gleason score based on open surgery, TURP and FNB biopsy.

Table 1. Demographic characteristics of the participants

Basic values	Body mass index			Total n=310
	<25 n=121	25-30 n=141	>30 n=48	
Mean age	71.8±8.5	70.7±9.3	69.1±9.1	70.87±8.94
Mean body mass index	22.8±1.9	27.2±1.3	32.4±2.7	26.3±3.8
Type of surgery				
Biopsy	74	75	27	179
Radical prostatectomy	33	50	14	97
TURP	14	16	7	37
Residence				
Urban	76	93	31	200
Rural	44	48	18	110
Gleason score	7.2±1.1	7±1.1	7±1	7.11±1.11
PSA concentration				
4-10	38	66	17	121
11-20	24	33	13	70
>20	55	37	17	109
Total	117	136	47	300*

*It was unreliable in 10 patients and was not considered.

Table 2. Comparing the association of age, BMI, PSA and Gleason score

Variable and Gleason score	Number	Mean±SD	CI 95%	p-value*
Age				
<7	102	67.52±7.14	66.10-68.94[a]	
7	111	71.93±9.20	69.66-73.12[b]	<0.001
>7	88	74.10±9.14	72.17-76.04[c]	
Body mass index				
<7	104	26.74±3.65	26.03-27.45[a]	
7	111	26.32±3.71	25.63-27.01[a]	0.21
>7	92	25.79±3.94	24.97-26.61[a]	
PSA				
<7	99	10.94±7.97	9.35-12.53[a]	
7	111	32.37±80.37	17.25-47.48[b]	<0.001
>7	91	66.89±90.48	48.05-85.74[c]	

*ANOVA test

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The findings showed that patients in the TURP group had a higher Gleason score compared to patients who underwent radical prostatectomy or patients who only underwent biopsy. Also, the examination of patients of different risk groups based on the European Association of Urology based on their BMI did not show any significant relationship.

Discussion

In this study, a relationship between BMI and PSA concentration was observed. But there was no relationship between BMI and Gleason score based on the risk estimate of the European Society of Urology. As BMI increases, PSA decreases. These findings are consistent with the results of the study by Chamie et al., who noted that obese patients are not at higher risk and therefore do not need more aggressive treatment methods (8). In their research, Freedland et al. found that there is no relationship between BMI and PSA and the clinical stage of prostate cancer (23). The reason for PSA reduction in obese men can be attributed to blood dilution effect (24) and low serum testosterone level (25). Obese men have a higher volume of plasma, which dilutes the concentration of tumor markers such as PSA. Obesity is associated with low serum testosterone levels (24) and because the prostate gland is an androgen-dependent organ, low testosterone levels are expected to be associated with a decrease in prostate gland volume and PSA secretion. Since significant weight loss is associated with an increase in testosterone and PSA levels and a decrease in plasma volume (26), hormonal mechanisms and blood thinning are valid modifiers of PSA levels in the context of obesity.

Several studies found a positive correlation between BMI and Gleason score. In a meta-analysis by Bai et al., BMI was an independent risk factor for high Gleason score in biopsy specimens and radical specimens (11). In a study by Zhou et al., which was conducted on 290 patients suspected of having prostate cancer, it was shown that although BMI is not correlated with increased incidence of prostate cancer, it is related to higher stages of prostate cancer (5). Liang et al. found that high-grade prostate cancer increased with increasing BMI, so after adjusting for other factors, BMI provided independent predictive information about prostate cancer risks, especially high-grade prostate cancer (27). In a study on 4926 American patients, Kryvenko et al. found that overweight patients have higher glycation scores and more aggressive cancers (4). In this study, about 15% of patients were obese, while in study of Kryvenko, about 27% of patients were obese. Gioia et al. (20) and Liang et al. (27) also had similar findings. The strong contradictions of the results of this study with other studies can be caused by several factors, including the fact that the subjects under study are about 10 years younger. The mean age of 70.87±8.94 years and life expectancy of 74 years in Iranian men probably leads to lower BMIs compared to their counterparts in developed countries. Nwadi et al. found a significant relationship between normal BMI and low Gleason score and also between high BMI and high Gleason score (22). Jayachandran et al. observed that obesity is a risk factor for invasive prostate cancer and tumor recurrence regardless of race (28).

The findings of this study showed that there is no significant difference between BMI and Gleason score, even based on the method of obtaining Gleason score pathology (open surgery, biopsy and TUR-p). However, there is a significant relationship between low BMI and higher Gleason score in those patients with PSA greater than 20. This finding can be attributed to the late referral of patients. That is, referral is made when the progress of the disease leads to a decrease in the weight of the patients. For this reason, this finding is not a good indicator of the relationship between Gleason score and BMI. Furthermore, in the present study, it was observed that about 70% of patients are between 60-80 years old. Less than 20% of patients are over 80 years old. This issue can be related to the life expectancy of the studied population. This finding is consistent with the findings of Rafiemanesh et al. in Iran (29).

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One of the advantages of the present study is that only patients with prostate cancer were included in the study and suspected patients were not included. This means that we could not consider the incidence of prostate cancer as well as its progression, although we carefully excluded those who took weight gain drugs or had poor nutrition. Comorbidities or wasting conditions were not considered, and the addition of these two populations to our sample created a highly representative sample. Probably for this reason, no significant relationship between BMI and advanced prostate cancer was found in our study. Patients with a higher risk of prostate cancer did not have a higher BMI. However, PSA decreased with increasing BMI. A lower PSA threshold is suggested for obese men suspected of having prostate cancer. However, there is still insufficient evidence to make further predictions based on BMI alone.

The results of this study showed that increased BMI is not associated with a higher risk of prostate cancer, nor is it correlated with a higher Gleason score, however, it is negatively correlated with PSA. It is recommended to conduct a study with a healthy control group to determine the role of BMI as a predictive factor in deciding to treat prostate cancer.

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