

CORRELATION OF BODY MASS INDEX AND SMOKING HISTORY WITH GLEASON SCORE OF PROSTATE ADENOCARCINOMA AT GATOT SOEBROTO ARMY CENTRAL HOSPITAL FOR THE PERIOD 2020-2023

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ABSTRACT

Background: Prostate adenocarcinoma is the fifth most common cancer incidence among males in Indonesia. Risk factors such as obesity and smoking contribute to the occurrence of prostate adenocarcinoma. Gleason score in prostate adenocarcinoma aims to assess the degree of tumor differentiation and determine the prognosis of patients. At RSPAD Gatot Soebroto, 70% of patients arriving are already detected with advanced-stage cancer. In previous studies, there were gaps in the relationship between Body Mass Index (BMI) and Gleason score, while research on the association between smoking and Gleason score is limited in Indonesia. The purpose of this study is to determine the relationship between Body Mass Index (BMI) and smoking with the Gleason score in prostate adenocarcinoma patients. **Methods:** This study employed an observational analytical design utilizing a cross-sectional approach involving 66 prostate adenocarcinoma patients at RSPAD Gatot Soebroto from January 2020 to October 2023, who met the inclusion and exclusion criteria. The data used are secondary data obtained from medical records using total sampling techniques and analyzed using the Spearman test. **Results:** Univariate analysis results indicate that the majority of patients have an overweight BMI (47.0%), a history of smoking (66.7%), and a Gleason score for prostate adenocarcinoma 8-10 (Poorly differentiated) (74.2%). Subsequently, the analysis of BMI with Gleason score in prostate adenocarcinoma shows a p-value of 0.017 with a correlation coefficient (r) of 0.294. Meanwhile, the analysis of smoking with Gleason score in prostate adenocarcinoma shows a p-value of 0.000 with a correlation coefficient (r) of 0.465. **Conclusion:** The majority of patients have a Gleason score for prostate adenocarcinoma of 8-10 (Poorly differentiated) with an average of 8.48 indicate a poor prognosis. Furthermore, BMI and smoking exhibit a relationship with the Gleason score in prostate adenocarcinoma.

Keywords : Prostate adenocarcinoma., BMI., smoking., Gleason score.

INTRODUCTION

Prostate adenocarcinoma is a malignancy of the urogenital system that is the most common cancer in men and the second most common in the world. Prostate adenocarcinoma is the fifth most common cancer in men in Indonesia. It is estimated that 42.772 people were diagnosed with prostate adenocarcinoma with 13.563 new cases in 2020. Deaths from prostate adenocarcinoma in Indonesia reached 4.863 or 2.1% of total deaths.¹ The highest incidence is found at more than 60 years old and rarely found at less than 40 years old.²

Risk factors that can lead to the development of prostate adenocarcinoma include age, race, obesity, smoking, and family history.² The prevalence of obesity in Indonesia is 21.8%.³ The relationship between prostate adenocarcinoma and obesity remains unclear. However, the risk of mortality is higher in prostate adenocarcinoma patients with obesity.⁴ Obesity can be

measured using the Body Mass Index (BMI) calculation. According to WHO, an individual is classified as overweight if the BMI is ≥ 25 and classified as obese if the BMI is ≥ 30 .⁵

The prevalence of smoking in Indonesia has been increasing each year. Approximately 225,700 people in Indonesia die due to smoking or other tobacco-related diseases.⁶ Cigarette smoke contains more than 70 carcinogens, as evaluated by the International Agency for Research on Cancer (IARC). Smokers have a higher risk of recurrence and mortality from prostate adenocarcinoma compared to non-smokers.²

The examinations used to diagnose prostate adenocarcinoma include digital rectal examination (DRE), PSA levels, and prostate biopsy. PSA levels are the most significant variable compared to DRE. PSA is a serine-calcine protease produced by prostate epithelial cells. Elevated PSA levels are also used as a marker in several prostate diseases, such as prostatitis, BPH, and prostate adenocarcinoma. The current standard value of

PSA in Indonesia is 4 ng/ml. If there is an increase in PSA level, the next step can be prostate biopsy with guided Transrectal Ultrasonography (TRUS). The histopathological examination of biopsy specimens is evaluated using the Gleason score. This score can be used to determine the level of tumor differentiation and determine the prognosis in patients with prostate adenocarcinoma.²

According to research conducted by Nwadi et al. showed that there was a significant correlation between BMI and Gleason score.⁸ The same results were also obtained from research conducted by Zhou et al.¹⁰ However, in Indonesia, the relationship between BMI and Gleason score remains unclear. Studies by Abdurrahman et al. and Homalessy et al. found no correlation between BMI values in Indonesia with an increase in Gleason score.^{11 12} Conversely, research by Pouresmaeili et al. on the Iranian population indicated a relationship between smoking with the incidence of prostate cancer.¹³

Based on previous research in Indonesia has shown a gap in the relationship between increased BMI and Gleason score, and there is limited research on the relationship between smoking and Gleason score in Indonesia. The results of the study found that 70% of patients presenting at Gatot Soebroto Army Central Hospital are already diagnosed with advanced-stage cancer. Based on this background, the researchers are interested in conducting research at Gatot Soebroto Army Central Hospital related to the correlation between BMI and smoking as risk factors with Gleason score in prostate adenocarcinoma. The results obtained later are expected to aid in early detection and prognosis determination for prostate adenocarcinoma patients and to raise awareness about the dangers of obesity and smoking.

MATERIALS AND METHODS

This study uses an observational analytic design that aims to determine the relationship between variables by testing hypotheses. This study used a cross-sectional approach, namely data taken and processed at the same time to analyze the relationship between independent and dependent variables. The population of this study were all patients diagnosed with prostate adenocarcinoma at Gatot Soebroto Army Hospital during the period January 2020 - October 2023. The study sample consisted of 66 patients diagnosed with prostate adenocarcinoma and met the inclusion and exclusion criteria. All samples had a history of smoking, anthropometric examination including weight and height, and prostate biopsy and histopathological examination using the Gleason score for the period January 2020 - October 2023.

The technique used for sampling in this study was a non-probability sampling technique, namely total sampling. In total sampling, the entire population of patients who meet the research criteria are used as samples. In this study, the independent variables consisted of BMI and smoking, while the dependent variable was Gleason score in prostate adenocarcinoma.

The research instrument used was secondary data collected by recording patient medical records at Gatot Soebroto Army Hospital. Body mass index (BMI) according to WHO criteria is

divided into underweight, normal, overweight, and obese categories.⁵ Smoking was classified on a nominal scale. Meanwhile, Gleason score was categorized as Gleason score ≤ 6 (Well differentiated), Gleason score 7 (Moderately differentiated), and Gleason score 8-10 (Poorly differentiated).⁷

The collected data will be tested and analyzed univariately and bivariately. Univariate analysis is used to describe the characteristics of each variable studied. Furthermore, bivariate analysis was carried out to determine whether there was a significant relationship between two variables, namely the relationship between BMI and smoking with Gleason score in prostate adenocarcinoma. In this study, the Spearman correlation test was used to test two variables with ordinal data or one variable with ordinal data and the other with nominal data.

RESULTS

Table 1. Distribution of sample characteristics

No	Karakteristik	Frekuensi (n)	Presentase (%)
1	Age		
	50-59 years old	4	6,1%
	60-69 years old	20	30,3%
	70-79 years old	32	45,5%
	90-89 years old	12	18,2%
	Total	66	100%
2	Body Mass Index (BMI)		
	<i>Underweight</i>	3	4,5%
	Normal	29	43,9%
	<i>Overweight</i>	31	47,0%
	Obesity	3	4,5%
	Total	66	100%
3	Smoking history		
	No	22	33,3%
	Yes	44	66,7%
4	Gleason Score		
	≤ 6 (<i>Well differentiated</i>)	0	0%
	7 (<i>Moderately differentiated</i>)	17	25,8%
	8-10 (<i>Poorly differentiated</i>)	49	74,2%
	Total	66	100%

From the data presented in Table 1 above, it can be concluded that the majority of prostate adenocarcinoma patients at Gatot Soebroto Army Central Hospital during the period from January 2020 to October 2023 were in the 70-79 year age group, comprising 30 patients (45.5%), while the smallest number of patients were in the 50-59 year age group, with only 4 patients (6.1%).

The majority of patients had an overweight Body Mass Index (BMI), totaling 31 patients (47.0%), followed by the normal BMI group with 29 patients (43.9%), and the underweight and obese BMI groups, each comprising 3 patients (4.5%).

Furthermore, Table 1 shows that 44 patients (66.7%) had a history of smoking, while 22 patients (33.3%) did not have a smoking history. The majority of prostate adenocarcinoma patients had a Gleason score of 8-10 (poorly differentiated), totaling 49 patients (74.2%), while patients with a Gleason score of 7 (moderately differentiated) numbered 17 (25.8%). No patients had a Gleason score of ≤ 6 (0%). The average Gleason score of 8.48 indicates a higher level of malignancy and a poor prognosis.

Table 2. Cross tabulation and bivariate test results of BMI with gleason score in prostate adenocarcinoma

Variable	Gleason Score				P value	r				
	≤ 6		7				8-10		Total	
	n	%	n	%			n	%	n	%
BMI	1									
Underweigh	0	0	2	33,3	3	100				
t	0	0	66,7	19	29	100				
Normal	0	0	10	65,5	31	100				
Overweight	0	0	34,5	26	3	100	0,017	0,294		
Obesity			5	83,9						
			16,1	3						
			0	0	100					
Total	0	17	49	66						

Table 2 shows that prostate adenocarcinoma patients with above-normal BMI status such as overweight and obesity tend to have high Gleason scores (8-10), namely 26 patients (83.9%) and 3 patients (100%). On the other hand, prostate adenocarcinoma patients with underweight BMI status tended to have a low Gleason score (7) as many as 2 patients (66.7%).

Analysis using spearman test and cross tabulation test between BMI and Gleason score. Based on Table 2 above, the significance value <0.05 (0.017) was obtained. It can be concluded that there is a significant relationship between BMI and Gleason score in prostate adenocarcinoma patients. Furthermore, with a positive correlation coefficient (r) value of 0.294 which is in the interval 0.20-0.399, it can be concluded that there is a positive relationship with weak strength. Thus, the higher the BMI value, the higher the Gleason score in prostate adenocarcinoma. Therefore, the relationship between BMI and Gleason score has a weak, significant, and unidirectional relationship.

Table 3. Cross tabulation and bivariate test results of smoking with gleason score in prostate adenocarcinoma

Variable	Gleason Score				P value	r				
	≤ 6		7				8-10		Total	
	n	%	n	%			n	%	n	%
Smoking										
No	0	0	12	54,5	10	45,5	22	100	0,00	0,46
Yes	0	0	5	11,4	39	88,6	44	100	0	5
Total	0	17	49	66						

Table 3 shows that prostate adenocarcinoma patients who have a history of smoking tend to have a high Gleason score (8-10), as many as 39 patients (88.6%). Furthermore, in prostate adenocarcinoma patients who did not have a history of smoking, there was a tendency to have a low Gleason score (7) as many as 12 patients (54.5%).

Spearman test and cross tabulation test between smoking history and Gleason score were analyzed. Based on Table 3 above, the significance value <0.05 (0.000) was obtained. It can be concluded that there is a significant relationship between smoking and Gleason score in prostate adenocarcinoma patients. Furthermore, with a positive correlation coefficient (r) value of 0.465 which is in the interval 0.40-0.599, it can be concluded that there is a positive relationship with moderate strength between the two variables. Thus, a history of smoking leads to a higher Gleason score in prostate adenocarcinoma. Therefore, the relationship between smoking and Gleason score has a moderate, significant, and unidirectional relationship.

1. DISCUSSION

The results of this study showed a relationship between BMI and Gleason score in prostate adenocarcinoma patients (0.017). This finding is in line with research conducted by Nwadi et al. where the results showed a correlation between BMI and Gleason score and had a significance value of 0.0003.⁸ Other studies such as Kryvenko et al. and Zhou et al. also found that men who have an increased BMI (overweight or obese) are more likely to have higher and more aggressive Gleason scores.^{9 10} Another study by Tzenios et al. showed that 54% of obese patients had a higher risk of prostate adenocarcinoma progression compared to normal weight and that increased BMI was associated with a higher risk of death.¹⁴

This study supports the theory that increased BMI is associated with increased body fat or adipose tissue which can result in the release of pro-inflammatory mediators. These mediators can trigger an increase in prostate cell proliferation through a disrupted wnt signal pathway.^{15 16 17}

The results also showed an association between smoking and Gleason score in prostate adenocarcinoma patients (0.000). This finding is in line with research conducted by Larissa, where the results showed an association between smoking and Gleason score and had a significance value of 0.012.¹⁸ Another study conducted by Kenfield et al. reported that 14.7% of smokers had a higher stage compared to 8.3% of those who never smoked.¹⁹ Active and former smokers who initially have low smoking intensity, but then increase, have a higher risk of progression or aggressiveness of prostate adenocarcinoma.²⁰

Several mechanisms may explain the association between smoking and the development of prostate adenocarcinoma risk. This is attributed to the content of cigarettes that are known to contain carcinogens, including nitrosamine compounds that can cause mutations of the p53 tumor suppressor gene. The association with smoking is also influenced by hormonal factors, men who smoke tend to have elevated testosterone levels which may increase the risk or contribute to the development of prostate adenocarcinoma.²¹ Prolonged inflammatory processes due to exposure to cigarette content such as cadmium, benzopyrene, and polycyclic aromatic hydrocarbons can cause tissue damage and the wnt signal pathway is disrupted, triggering excessive prostate cell growth.^{15 22}

In the implementation of this study, several limitations may affect the perfection of the writing. The data used in this study were obtained from conventional medical records, so data collection requires higher accuracy. Some data on body weight and height are different, so researchers set data collection at the time of the first treatment, there is still a lack of information about smoking history such as smoking intensity, and only know the relationship between variables not causal relationships.

2. CONCLUSIONS AND SUGGESTIONS

From the results of the analysis and discussion of research on prostate adenocarcinoma patients at RSPAD Gatot Soebroto, it can be concluded that most patients have a poor prognosis seen from the average Gleason score of 8.48. In addition, there is a significant relationship between BMI and Gleason score in prostate adenocarcinoma patients at Gatot Soerbroto Army Hospital in the period January 2020 - October 2023 (p-value = 0.017).

Furthermore, there is also a significant relationship between smoking and Gleason score in prostate adenocarcinoma patients at Gatot Soerbroto Army Hospital in the period January 2020 - October 2023 (p-value = 0.000).

Further research is needed with different methods, for example a retrospective cohort study, so that researchers can identify other factors that can affect the increase in Gleason score in prostate adenocarcinoma patients, such as prostate volume, PSA (Prostate Specific Antigen) density, PSA mass and prostate gland density. In addition, it is necessary to collect data on the amount of smoking and details of smoking cessation. Smokers

who have increased BMI need further research to clarify the main cause and potential prevention of prostate adenocarcinoma mortality.

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