

## Correlation of Age, PSA Value, Gleason Score, and Staging with Metastasis in Prostate Cancer

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### Abstract

Prostate cancer is the fifth most common cancer among men in Indonesia and carries a substantial risk of metastasis. However, data on prognostic factors such as age, prostate-specific antigen (PSA) value, Gleason score, and local stage among Indonesian patients are still limited. This retrospective cross-sectional study analyzed medical records of prostate cancer patients treated at Dr. Hasan Sadikin General Hospital, Bandung, between 2019–2022. Independent variables were age, PSA value, Gleason score, and local stage; the dependent variable was metastatic status. Data were analyzed using chi-square and multivariate logistic regression tests. A total of 81 patients were included, of whom 44 (54.3%) had metastases. Bivariate analysis showed significant associations of PSA value, Gleason score, and local stage with metastasis ( $p < 0.05$ ). In multivariate analysis, only Gleason score and local stage remained significant independent predictors ( $p < 0.05$ ). The findings indicate that Gleason score and local tumor stage are reliable predictors of metastasis in prostate cancer, while age and PSA are not independent predictors in this cohort. Gleason score and local stage should be prioritized for risk assessment in prostate cancer management in Indonesian hospitals.

**Keywords:** Neoplasm metastasis, prostatic neoplasms, risk factors

### Introduction

Cancer is characterised by uncontrolled cell division and the gradual appearance of symptoms.<sup>1</sup> Depending on the cell type, location, growth pattern, degree of malignancy, and metastatic potential, each malignancy exhibits unique characteristics.

Prostate cancer is the most commonly diagnosed cancer in 112 countries<sup>2</sup> and ranks fifth among Indonesian men, with 13,563 new cases and 4,863 deaths reported in 2020.<sup>3</sup> A local study at Dr. Hasan Sadikin Hospital in Bandung conducted in 2021 found that the majority of prostate cancer patients were aged between 60 and 69 years. Furthermore, most patients presented with prostate-specific antigen (PSA) levels exceeding 20 ng/mL. Of the 38 patients included in that study, the majority had a Gleason score of 8 ((4+4), (3+5), or (5+3)) and 52.2% presented at stage IV, indicating late

presentation and limited screening awareness. Despite limitations in facilities and urologists availability in Indonesia, such data contribute to improved diagnosis and treatment efforts.<sup>4</sup>

Metastatic prostate cancer refers to malignancy that has spread beyond the prostate gland to other areas of the body surrounding tissues or distant organs.<sup>5,6</sup> Internationally, advanced age, elevated PSA levels, high Gleason scores, and advanced local stages are identified as predictors of metastasis. Research by Peng et al. indicates that elderly patients, with an average age of 75.45 years, are more likely to develop metastases.<sup>7</sup> Higher PSA levels are generally associated with more aggressive prostate cancer.<sup>8</sup> Thomsen et al. reported that 64.9% of patients with PSA values of 400 ng/mL or higher had metastases.<sup>9</sup> The European Association of Urology (EAU) recommends evaluating patients with Gleason scores greater than 7 for metastases.<sup>7</sup> Clinically, local expansion is classified into four groups (T1 to T4). According to the study of Cosma et al., a large number of prostate cancer patients show metastases at stages T3a, T3b, and T4.<sup>10</sup>

However, patient characteristics and healthcare access in Indonesia differ markedly from those in Western populations, where

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most cases are detected in early stages. These differences highlight the importance of local studies to determine which clinical factors best predict metastasis in Indonesian patients.<sup>11</sup> Due to the limited number of studies on this topic, information about the variables influencing prostate cancer metastasis in Indonesia remains scarce. Understanding these risks patients face can aid in identifying solutions to prevent health complications and assist both patients and physicians in implementing early interventions. Dr. Hasan Sadikin Hospital serve as a tertiary hospital in most populous province of Indonesia, making it a critical site for studying prostate cancer trends and outcomes.<sup>12</sup>

This study aims to identify and analyse the factors influencing prostate cancer metastasis among patients at Dr. Hasan Sadikin Hospital. The novelty of this study lies in its focus on Indonesian patient characteristics, providing insight specific to local conditions and healthcare challenges.

## Methods

This observational analytical utilized a cross-sectional method to examine the relationship between age, PSA value, Gleason score, and local stage with metastatic status. The research was conducted at Dr. Hasan Sadikin Hospital, Bandung, from October 2023 to December 2023. The subject of the study were prostate cancer patients treated at Dr. Hasan Sadikin Hospital between 2019 and 2022. Samples were determined using the consecutive sampling method. Data collection relied on secondary data from the medical records of prostate cancer patients in the Urology Department.

Inclusion criteria consisted of prostate cancer patients with complete medical records and no history of other malignancies. Exclusion criteria included patients whose medical records lacked information on age at diagnosis, total PSA levels, local staging based on digital rectal examination, or metastasis status (M1a, M1b, and/or M1c) as determined by bone scans, CT scans, or MRI. Of the 147 medical records reviewed, 81 patients met the inclusion criteria. The dependent variable was prostate cancer metastasis, while the independent variables were age, PSA value, Gleason score, and local stage.

Age was dichotomized (< 75 and ≥ 75 years) based on established thresholds associated with higher metastasis risk.<sup>7</sup> PSA was grouped (<100 and ≥100 ng/mL) to facilitate clinical

interpretation and comparison with prior research.<sup>9</sup> The Gleason score was categorized into three groups: 6, 7, and ≥8. Local stage was classified into two categories: organ-confined (T1 and T2) and locally advanced/advanced (T3 and T4). Dichotomization was chosen to enhance interpretability in clinical settings.

Data collection involved extracting secondary data from medical records, including age at diagnosis, total PSA value, Gleason score, local stage (based on digital rectal examination), and metastatic status (M1a, M1b, or M1c, as determined by bone scans, CT scans, or MRI). Data analysis was performed using the Statistical Program for Social Sciences (SPSS) version 25.

A homogeneity test was conducted using Levene's test; homogeneity was assumed if the significance value (p) was ≥0.05. Univariate analysis summarized frequency and percentage for the dependent variable, alongside median, standard deviation, and range for independent variables. Bivariate analysis employed the chi-square test to evaluate relationships between clinical factors and metastatic status.

Significant results were further analyzed using multivariate predictive logistic regression to identify independent predictors of metastasis. Ethical approval was obtained from the Health Research Ethics Committee, Faculty of Medicine, Universitas Padjadjaran (1318/UN6.KEP/EC/2023).

## Results

Clinical characterization of patients with metastatic prostate cancer treated at Dr. Hasan Sadikin Hospital between 2019 and 2022 is presented in Table 1. This study analyzed data from 81 prostate cancer patients, including 44 cases (54.3%) with metastasis and 37 cases (45.7%) without metastasis. The mean age was 71.2 ± 8.5 years, and the median PSA value was 98.4 ng/mL [IQR 35.8–192.5]. The proportion of patients aged <75 years was higher than those aged ≥75 years among all prostate cancer cases, with 47 cases (58%) and 34 cases (42%), respectively. Additionally, 50 cases (61.7%) had PSA values <100 ng/mL, which was higher than the 31 cases (38.3%) with PSA values ≥100 ng/mL.

Gleason scores were divided into three categories: 6 (7 cases, 8.6%), 7 (26 cases, 32.1%), and 8–10 (48 cases, 59.3%). Notably, Gleason scores of 8–10 were more prevalent than scores of 7 or 6. Organ-confined stages (T1/T2) were

**Table 1 Clinical Characteristics of Patients with Prostate Cancer**

Characteristic	Non-Metastatic (n=37) (%)	Metastatic (n=44) (%)
Age (years), mean±SD	75.4±8.1	74.4±9.3
<75	21 (25.9)	26 (32.1)
≥75	16 (19.8)	18 (22.2)
PSA Level (ng/mL) mean±SD	39.9±26.4	494.9±682.4
<100	37 (45.7)	13 (16)
≥100	0 (0)	31 (38.3)
Gleason Score		
6	7 (7.6)	0 (0)
7	15 (18.5)	11 (13.6)
8-10	15 (18.5)	33 (40.7)
Local Stage		
Organ confined (T1 and T2)	34 (42)	28 (34.6)
Locally advanced (T3 and T4)	3 (3.7)	16 (19.8)

observed in 62 cases (76.5%), a higher proportion than locally advanced/advanced stages (T3/T4), which accounted for 19 cases (23.5%). Among the metastatic group, 26 cases (32.1%) involved patients aged <75 years, while 18 cases (22.2%) were aged ≥75 years. PSA values <100 ng/mL were more frequent in the non-metastatic group (37 cases, 45.7%), whereas PSA values ≥100 ng/mL were exclusively observed in the metastatic

group (31 cases, 38.3%).

Gleason score 6 cases were only observed in the non-metastatic group (7 cases, 7.6%). The non-metastatic group had more cases with a Gleason score of 7 (15 cases, 18.5%) than the metastatic group (11 cases, 13.6%). In contrast, the metastatic group had a higher proportion of Gleason scores of 8-10 (33 cases, 40.7%) compared to the non-metastatic group

**Table 2 Bivariate Analysis of Clinical Characteristics and Metastasis**

Characteristic	Non-Metastatic (n) (%)	Metastatic (n) (%)	p-value*
Age			
<75	21 (25.9)	26 (32.1)	0.832
≥75	16 (19.8)	18 (22.2)	
PSA Level (ng/mL)			
<100	37 (45.7)	13 (16)	0.000
≥100	0 (0)	31 (38.3)	
Gleason Score			
6	7 (7.6)	0 (0)	0.001
7	15 (18.5)	11 (13.6)	
8-10	15 (18.5)	33 (40.7)	
Local Stage			
Organ confined (T1 and T2)	34 (42)	28 (34.6)	0.003
Locally advanced (T3 and T4)	3 (3.7)	16 (19.8)	

\*Chi-Square test

**Table 3 Relationship of Clinical Characteristics of Patients with Metastatic Prostate Cancer with Predictive Logistic Regression Test**

Characteristic	Non-Metastatic (n) (%)	Metastatic (n) (%)	p-value
Age			
<75	21 (25.9)	26 (32.1)	0.997
≥75	16 (19.8)	18 (22.2)	
PSA Value (ng/mL)			
<100	37 (45.7)	13 (16)	0.996
≥100	0 (0)	31 (38.3)	
Gleason Score			
6	7 (7.6)	0 (0)	0.043
7	15 (18.5)	11 (13.6)	
8-10	15 (18.5)	33 (40.7)	
Local Stage			
Organ confined (T1 and T2)	34 (42)	28 (34.6)	0.021
Locally advanced/advanced (T3 and T4)	3 (3.7)	16 (19.8)	

(15 cases, 18.5%). Regarding local stage, the confined organ stage (T1/T2) was less prevalent in the metastatic group (28 cases, 34.6%) than in the non-metastatic group (34 cases, 42.0%). Conversely, the locally advanced/advanced stage (T3/T4) was more common in the metastatic group (16 cases, 19.8%) compared to the non-metastatic group (3 cases, 3.7%).

Bivariate analysis using the chi-square test (Table 2) indicated that PSA value, Gleason score, and local stage were significantly associated with prostate cancer metastasis ( $p < 0.05$ ).

Subsequent multivariate analysis with logistic regression (Table 3) revealed that among the four factors, local stage was the most influential predictor of metastasis, followed by Gleason score. PSA value and age were not statistically significant independent predictors.

## Discussion

This observational analytical study evaluated the factors influencing prostate cancer metastasis, specially age, PSA value, Gleason score, and local stage. Patients with metastatic prostate cancer generally have a markedly reduced five-year survival rate; thus, identifying risk factors at the time of diagnosis is crucial for preventing disease progression and guiding appropriate management.

Age is a well-recognized risk factor for prostate cancer morbidity and mortality. However, previous research have reports contradictory findings regarding its relationship with metastatic status.<sup>14,15</sup> Some studies, have suggested that age is not associated with the risk of metastasis, whereas others report a significant relationship. For example, Kim et al.<sup>16</sup> reported findings that contradict those of Shih et al.'s<sup>17</sup> who suggested that age is not a risk factor for prostate cancer metastasis. In this present study, no significant association was found between age and metastatic status, as indicated by a p-value of 0.832 ( $>0.05$ ). These findings suggest that age alone may not significantly influence the likelihood of, prostate cancer metastasis in this population.<sup>7</sup>

The PSA level remains one of the most important markers for detecting and diagnosing prostate cancer. Previous research has shown that the risk of metastasis ranges from 41.4% to 79.9% when the PSA level exceeds 100 ng/mL, whereas, the risk decreases substantially when PSA levels are below 20 ng/mL.<sup>7</sup> Several studies have identified PSA level as an independent risk factor for prostate cancer metastasis.<sup>16, 17</sup> In this study, higher PSA levels were associated with metastatic prostate cancer groups, as evidenced by a significance value of  $p=0.000$ , ( $<0.05$ ). However, logistic regression analysis showed that PSA was not an independent predictor

of metastasis ( $p=0.997$ ,  $>0.05$ ). The lack of a significant independent relationship between PSA and metastasis in multivariate analysis may be due to collinearity with Gleason score and local stage, as high PSA values often accompany advanced histologic grade and tumor stage. Similar findings were reported by Liu et al. in a SEER-China study. Therefore, while PSA remains a valuable marker, caution is advised for patients with low PSA levels.<sup>18</sup>

The Gleason score is a widely utilized method for determining metastatic risk.<sup>19</sup> The American Urological Association (AUA) notes that individuals with a Gleason score of  $\geq 8$  are at a higher risk for metastatic disease.<sup>20</sup> This study corroborates these findings, as the Gleason score and metastasis group had a significant correlation ( $p=0.001$ ,  $<0.05$ ). Logistic regression analysis also confirmed the significant influence of Gleason scores on prostate cancer metastasis.

The Batson venous plexus, which connects the prostate with the pelvic and spinal venous systems, plays an important role in the pathophysiology of prostate cancer metastasis by facilitating the spread of tumor cells to the spine, particularly the lumbar and pelvic regions.<sup>4</sup> Staging is critical for determining prognosis, and this study found that the likelihood of metastasis increases with higher local stages  $p = 0.003$ ,  $<0.05$ . Multivariate analysis supported local stage as a strong predictor. These results align with models such as those developed by the SEER program and Memorial Sloan Kettering Cancer Center (MSKCC), where tumor stage consistently serves as a primary predictor of metastatic risk.<sup>9</sup>

This study represents one of the first analyses examining the relationship between age, PSA value, Gleason score, and local stage with metastatic status among prostate cancer patients in this setting. The predominance of advanced stage and high Gleason scores in this cohort may reflect late presentation, limited screening, and diagnostic challenges in Indonesia, where most patients are referred to tertiary hospitals at advanced disease stages. These contextual factors may explain differences between our findings and studies conducted in high-income countries. The results emphasize the importance of strengthening early detection, diagnostic evaluation, and staging strategies to identify patients at risk of metastasis before progression.

Several limitations of this study should be acknowledged. First, the retrospective, single-centre design relied on secondary data from the medical records of Dr. Hasan Sadikin Hospital

Bandung between 2019 to 2022. Second, variations in sample size, ethnicity, and regional factors may contribute to inconsistent results. Future research should consider multicentre designs to obtain more representative data and better reflect broader clinical conditions.

In conclusion, Gleason score and local stage were significantly associated with prostate cancer metastasis at Dr. Hasan Sadikin Hospital Bandung between 2019 and 2022, whereas age and PSA level were not significantly associated with metastatic status.

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