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CLINICOPATHOLOGICAL CHARACTERISTICS OF PROSTATE CANCER AT THE ANATOMICAL PATHOLOGY LABORATORY OF RSUP DR. M. DJAMIL PADANG 2018–2022

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ABSTRACT

Prostate cancer is one of the most common and deadliest cancers among men, both worldwide and in Indonesia. Prostate cancer is a malignant disease characterized by abnormal cellular proliferation within the prostate tissue. Age is the most common risk factor for prostate cancer, with the risk increasing markedly in men aged 50 years and older. The most frequently identified subtype of prostate cancer is adenocarcinoma. This study was a descriptive observational study using medical record data of patients diagnosed with prostate cancer based on histopathological findings at the Anatomical Pathology Laboratory of Dr. M. Djamil General Hospital, Padang, during the period 2018–2022. Total sampling was employed. The variables analyzed included age, clinical manifestations, prostate-specific antigen (PSA) levels, histopathological cell type, and the degree of cellular differentiation of prostate cancer. The results showed that a total of 41 prostate cancer patients met the inclusion criteria. The most common age group was 55–70 years (63.4%). Local clinical manifestations were observed in 92.7% of patients, serum PSA

levels >20 ng/mL in 82.9%, adenocarcinoma as the histopathological type in 100%, and poorly differentiated tumors in 82.9% of cases. The predominant histopathological type of prostate cancer was adenocarcinoma. Most patients were aged 55–70 years, commonly presented with local clinical symptoms, had serum PSA levels >20 ng/mL, and most frequently exhibited a poorly differentiated degree of tumor differentiation.

ABSTRAK

Kanker prostat merupakan salah satu kanker yang paling umum dan mematikan pada laki-laki, baik secara global maupun di Indonesia. Kanker prostat adalah penyakit ganas yang ditandai oleh proliferasi sel abnormal pada jaringan prostat. Usia merupakan faktor risiko paling umum, dengan peningkatan risiko yang signifikan pada laki-laki berusia 50 tahun ke atas. Subtipe kanker prostat yang paling sering ditemukan adalah adenokarsinoma. Penelitian ini merupakan studi observasional deskriptif menggunakan data rekam medis pasien yang didiagnosis kanker prostat berdasarkan temuan histopatologis di Laboratorium Patologi Anatomi RSUP Dr. M. Djamil Padang selama periode 2018–2022. Teknik total sampling digunakan. Variabel yang dianalisis meliputi usia, manifestasi klinis, kadar prostate-specific antigen (PSA), tipe histopatologi sel, serta derajat diferensiasi sel kanker prostat. Penelitian menunjukkan bahwa sebanyak 41 pasien kanker prostat memenuhi kriteria inklusi. Kelompok usia terbanyak adalah 55–70 tahun (63,4%). Manifestasi klinis lokal ditemukan pada 92,7% pasien, kadar PSA serum >20 ng/mL pada 82,9%, tipe histopatologi adenokarsinoma pada 100% kasus, serta derajat diferensiasi buruk pada 82,9% pasien. Tipe histopatologi kanker prostat yang dominan adalah adenokarsinoma. Sebagian besar pasien berusia 55–70 tahun, umumnya datang dengan gejala klinis lokal, memiliki kadar PSA serum >20 ng/mL, dan paling sering menunjukkan derajat diferensiasi tumor yang buruk.

INTRODUCTION

Prostate cancer is one of the most common malignancies and a leading cause of cancer-related mortality among men worldwide and in Indonesia. Data from the Global Cancer Observatory (GCO) in 2020 indicate that prostate cancer ranks first in cancer incidence among men, with 1,414,259 new cases, and second as a cause of cancer-related death, with 375,304 deaths annually worldwide. (Globocan, 2020) In Indonesia, prostate cancer ranks fifth in incidence, with 13,563 new cases and 4,863 deaths reported in 2020. (WHO, 2020) A previous study conducted at Dr. M. Djamil General Hospital, Padang,

reported approximately 100 prostate cancer cases during the period 2014–2018. (Diyanah, 2019)

Prostate cancer is a malignant disease characterized by abnormal cellular proliferation within the prostate tissue, with age being the most important risk factor. The risk increases significantly in men aged ≥50 years, and approximately 60% of cases occur in men older than 65 years. (Society, 2021) (NCBI, 2015) A study by Andreas et al. at Dr. M. Djamil General Hospital, Padang, demonstrated that the highest number of cases was found in the 70–79-year age group. (Andreas MI, 2017)

In the early stages, prostate cancer is generally asymptomatic, and most cases are diagnosed when patients have already developed symptoms. Men older than 50 years presenting with lower urinary tract symptoms (LUTS), hematuria, or erectile dysfunction should be suspected of having prostate cancer. (Osteroi Jakupsstovu J, 2018) However, LUTS are also commonly observed in benign conditions such as benign prostatic hyperplasia (BPH) and prostatitis and are not strongly correlated with the likelihood of prostate cancer or disease stage at diagnosis, thereby complicating early detection. (Jones D, 2018)

Prostate-specific antigen (PSA) testing and digital rectal examination are commonly used as adjunctive tools in prostate cancer detection; however, both modalities have limitations due to their low specificity and positive predictive value. (Kirby, 2016) (Streicher J, 2019) Prostate biopsy remains the gold standard for the diagnosis of prostate cancer and allows for histopathological classification, with adenocarcinoma being the most frequently identified subtype. (PA, 2017)

The Gleason score is the principal histopathological grading system used to assess prostate cancer and has significant prognostic value. It is classified into well differentiated (≤6), moderately differentiated (7), and poorly differentiated (8–10) categories. (Nagpal K, 2019) (Louisa J, I Wayan Juli Sumadi, Herman Saputra, Ni Putu Ekawati, 2023) Nevertheless, Gleason scoring is subjective and may vary depending on the interpretation of individual pathologists. A previous study at Dr. M. Djamil General Hospital, Padang, reported that the most common Gleason score category was moderately differentiated. (Andreas MI, 2017)

To date, no study has specifically described the clinicopathological characteristics of prostate cancer at the Anatomical Pathology Laboratory of Dr. M. Djamil General Hospital, Padang. Therefore, this study aims to describe the clinicopathological characteristics of prostate cancer during the 2018–2022 period, providing a basis for evaluation and supporting diagnostic decision-making for clinicians and anatomical pathologists.

METHODS

This descriptive observational study utilized secondary data obtained from medical records of prostate cancer patients from the Departments of Surgery and Anatomical Pathology at Dr. M. Djamil General Hospital, Padang. The study was

conducted between December 2022 and February 2024 and included patients diagnosed with prostate cancer based on histopathological examination during the period 2018–2022. The study population comprised all histopathologically confirmed prostate cancer patients, and a total sampling technique was applied. Patients were included if their medical records contained at least two of the following variables: age, clinical manifestations, degree of differentiation, and serum prostate-specific antigen (PSA) levels, while those with incomplete medical records were excluded. A total of 34 patients met the eligibility criteria and were included in the analysis. Data were collected using patients' medical records and analyzed using univariate descriptive analysis, with results presented as frequencies and percentages in tables, graphs, and narrative form.

RESULTS AND DISCUSSION

Based on Table 1, it can be concluded that in this study, the majority of prostate cancer patients at RSUP Dr. M. Djamil Padang during the period 2018–2022 were in the 55–70 years age group (63.4%), with the most frequently observed clinical manifestation being local symptoms (92.7%). Most patients had serum PSA levels >20 ng/mL (82.9%). The predominant histopathological characteristic of prostate cancer in the Department of Anatomical Pathology at RSUP Dr. M. Djamil Padang during 2018–2022 was adenocarcinoma (100%), with the most common degree of differentiation being poorly differentiated (82.9%).

The results of this study showed that in the 55–70 years and >70 years age groups, the most common histopathological type of prostate cancer was adenocarcinoma. Meanwhile, non-adenocarcinoma histopathological types were not found in any age group (0%). (Figure 1).

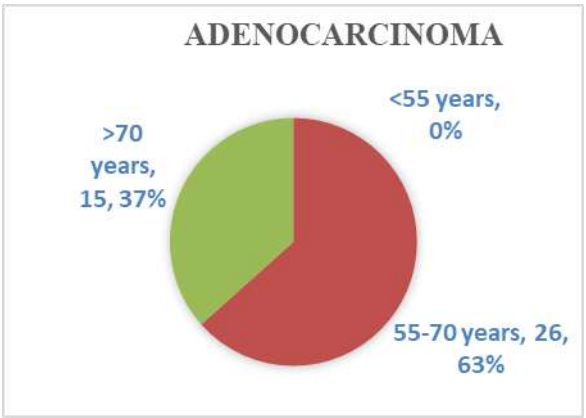

Figure 1. Distribution of Histopathological Types of Prostate Cancer by Age

The results of this study showed that the majority of prostate cancer patients had PSA levels >20 ng/mL with an adenocarcinoma histopathological type, which was found in 34 patients (100%). However, non-adenocarcinoma histopathological types were not identified across all PSA level groups (0%). (Figure 2)

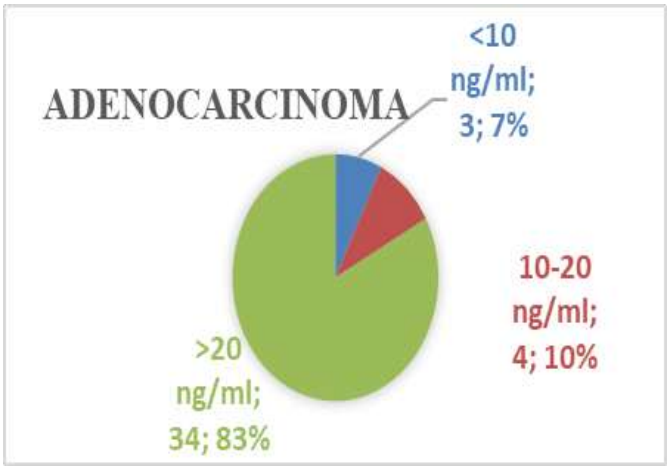

Figure 2. Distribution of Histopathological Types of Prostate Cancer by PSA Levels

The results of this study showed that the histopathological type of prostate cancer based on the degree of differentiation was predominantly adenocarcinoma with a poorly differentiated grade, which was identified in 34 patients (100%). No non-adenocarcinoma histopathological types were found across all differentiation grade categories (0%). (Figure 3)

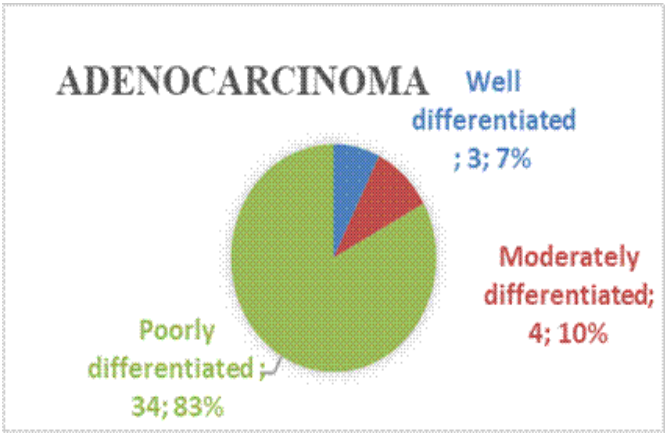

Figure 3. Distribution of Histopathological Types of Prostate Cancer by Degree of Differentiation

The results of this study showed that, based on PSA levels, the majority of prostate cancer patients had a poorly differentiated grade with PSA levels >20 ng/mL, accounting for 31 patients (91.2%), while PSA levels of 10–20 ng/mL were observed in 3 patients (75%). No patients with PSA levels <10 ng/mL were found in the poorly differentiated group (0%). (Table 2).

Table 1. Distribution of Clinicopathological Characteristics of Prostate Cancer Based on Age, Clinical Manifestations, PSA Levels, Histopathological Type, and Degree of Differentiation

Patient Characteristics	Frequency (f)	Percentage (%)
Age (year)		
< 55	0	0
55-70	26	63,4
> 70	15	36,6
Clinical Manifestation (Symptoms)		
Locally	38	92,7
Metastatic	1	2,4
Mix	2	4,9
Histopatology Tipe		
Adenocarcinoma	41	100
Non-Adenocarcinoma	0	0
Differentiate Type		
Well differentiated (score ≤ 6)	3	7,3
Moderately differentiated (score 7)	4	9,8
Poorly differentiated (score 8-10)	34	82,9
Total	41	100

Table 2. Distribution of Degree of Differentiation of Prostate Cancer Patients by PSA Levels

Skor *Gleason (Diff Type)*	PSA Levels		
	Low (<10 ng/ml)	Middle (10-20 ng/ml)	High (>20 ng/ml)
	f (%)		
Well	2 (66,7)	0 (0)	1 (2,9)
Moderately	1 (33,3)	1 (25)	2 (5,9)
Poorly	0 (0)	3 (75)	31 (91,2)
Total	3	4	34

The results of this study showed that among patients presenting with local symptoms, metastatic symptoms, and mixed symptoms, the most common histopathological type of prostate cancer was adenocarcinoma. Patients with local symptoms more frequently had adenocarcinoma, accounting for 38 patients (100%), compared with those presenting with metastatic symptoms, in whom only 1 patient (100%) was identified, and those with mixed symptoms, comprising 2 patients (100%). However, no non-adenocarcinoma histopathological types were found in patients with local, metastatic, or mixed symptoms (0%). (Figure 4)

The most common clinical manifestation was local symptoms. Patients with poorly differentiated tumors most frequently presented with local symptoms, accounting for 31 patients (91.2%), compared with those with moderately differentiated tumors (4 patients; 100%) and well-differentiated tumors (3 patients; 100%). In the poorly differentiated group, 1 patient (2.9%) presented with metastatic symptoms and 2 patients (5.9%) presented with mixed symptoms. (Figure 5)

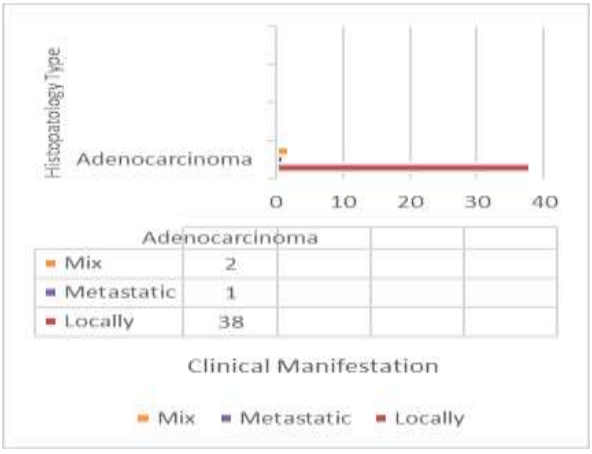

Figure 4. Distribution of Clinical Manifestations of Prostate Cancer Patients by Histopathological Type

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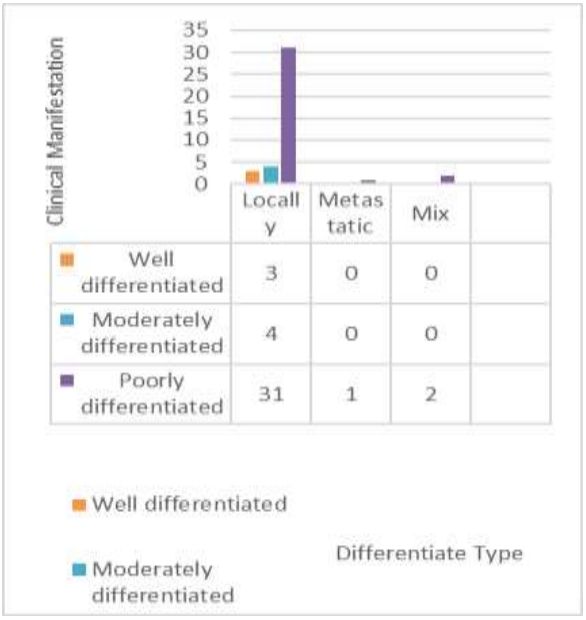

Figure 5. Frequency Distribution of Clinical Manifestations of Prostate Cancer Patients by Degree of Differentiation

Based on data from 41 patients diagnosed with prostate cancer in this study, the majority of patients were within the age range of 55–70 years, accounting for 26 cases (63.4%), while 15 cases (36.6%) were aged >70 years. This finding is consistent with the literature stating that the risk of prostate cancer increases rapidly in men aged over 50 years. (NCBI, 2015) According to theory, in Asian men, there is a significant increase in the risk of prostate cancer after the age of 65 years. (Louisa J, I Wayan Juli Sumadi, Herman Saputra, Ni Putu Ekawati, 2023) Similarly, a study reported by the American Cancer Society (2016) showed that approximately 6 out of 10 prostate cancer cases occur in men aged over 65 years. (Society, 2021)

These findings are consistent with a previous study conducted by Jennifer et al. at RSUP Prof. Dr. I.G.N.G. Ngoerah Denpasar, which reported that the majority of prostate cancer cases occurred in men aged ≥50 years. (Society, 2021) Similar results were reported by Putriyuni and Hilbertina (2015), who found that the highest number of cases occurred in the 61–70-year age group, accounting for 63 cases (38.65%), while only 3 cases were found in patients aged <50 years.[15] A study by Junaidi (2012) at RS Adam Malik Hospital Medan during the period July 2010–June 2012 reported a mean patient age of 65.3 years, with the most common age group being 56–60 years among 33 examined cases of prostate adenocarcinoma. (Diyanah, 2019) In addition, the results of this study are comparable to those reported by Andreas et al. during the period 2010–2013 at RSUP M. Djamil Padang, which showed that prostate cancer cases were most frequently found in the 70–79-year age group, totaling 20 cases, with no cases identified in patients aged ≤49 years or ≥90 years. (Andreas MI, 2017)

In countries such as the United States, Australia, Sweden, the United Kingdom, Italy, Japan, Hong Kong, and China, the incidence of prostate cancer increases exponentially with age. This finding is consistent with the study conducted by Fradet et al., which reported that the incidence of prostate cancer in Canada was approximately 100 per 100,000 men aged 50–54 years, 500 per 100,000 men aged 60–64 years, and more than 700 per 100,000 men aged ≥80 years. The incidence begins to increase in the 45–49-year age group and rises sharply until the 65–69-year age group. (Sharma M, Lawson J, Karunanayake C, Ja D, Punam P, 2016;1)

Advancing age represents a significant challenge associated with an increased burden of medical problems. As life expectancy increases, the number of elderly patients with prostate carcinoma is expected to rise. According to the study by Catherine et al. (2004), prostate malignancy predominantly occurs in men aged ≥70 years. (PN., 2023) The increasing incidence of prostate cancer in older individuals is associated with prostatic degeneration, rendering prostate cells more susceptible to mutations and malignant transformation. Consistent with this, Solang et al. (2016) reported an annual increase in prostate cancer cases from 2013 to 2015, namely 25.9%, 35.2%, and 38.9%, respectively, with advanced age identified as a significant risk factor for prostate cancer. (Fajarudin L, Siti Sundari A, Wahyu Indriati D, 2020)

The results of this study showed that the most common clinical manifestation of prostate cancer was local symptoms, observed in 38 cases (92.7%), followed by mixed symptoms in 2 cases (4.9%) and metastatic symptoms in only 1 case (2.4%). In this study, local symptoms mainly included lower urinary tract symptoms (LUTS), such as urinary retention, weak urinary stream, incomplete bladder emptying, and nocturia, followed by hematuria, penile pain, and erectile dysfunction. Meanwhile, metastatic symptoms observed in this study included bone metastasis accompanied by paraplegia.

According to the literature, most prostate cancer cases in developing countries are usually diagnosed at an advanced stage. Prostate cancer is often asymptomatic in its early stages; however, as the disease progresses, metastatic symptoms may develop.[19] This finding is consistent with the study conducted by Solang et al. (2016) at RSUP Prof. Dr. R. D. Kandou Manado, which reported that among 54 prostate cancer patients, the most frequently observed manifestations were various local symptoms, with some patients presenting more than one symptom. These symptoms included difficulty urinating in 24 patients (44.4%), hematuria in 22 patients (40.7%), flank pain in 3 patients (5.5%), dysuria in 5 patients (9.2%), frequent urination in 3 patients (5.5%), generalized weakness in 5 patients (9.2%), abdominal pain in 6 patients (11.1%), bone pain in 3 patients (5.5%), constipation in 2 patients (3.7%), and decreased consciousness, leg pain, leg edema, fractures, dyspnea, and dizziness in 1 patient each (1.8%). (Solang VR, Monoarfa A, Tjandra F, 2016)

In contrast, the study conducted by Catherine et al. (2004) involving 60 patients with prostate carcinoma with a mean age of 78 years (range 68–92 years) reported that 46

patients had metastatic prostate carcinoma and 5 patients had progressive locally advanced disease without evidence of metastasis. (PN., 2023)

Prostate cancer metastasis can be divided into four stages. First, cancer cells grow within the prostate gland, then invade surrounding tissues, followed by intravasation into the bloodstream. Second, cancer cells migrate through the bloodstream and reach the bone. Third, cancer cells infiltrate the bone marrow. Fourth, cancer cells form colonies and interact with osteoclasts and osteoblasts. The pathogenesis of bone metastasis in prostate cancer is associated with the presence of a venous plexus (Batson's plexus). Venous blood flow from the prostate passes through Batson's plexus to the vertebral column and pelvis, explaining why prostate cancer metastases are commonly found in the spine, particularly the lumbar vertebrae and pelvis. (C, 2012) (Lubis AS, 2018)

Serum PSA level is a diagnostic and prognostic parameter in prostate cancer. The higher the serum PSA level, the greater the suspicion of prostate cancer. The PSA reference value currently used in Indonesia is 4 ng/mL. (Safriadi F, Umbas R, Danarto, Hakim L, Warli SM, Hamid AR, Hudaya S, Ismy J, Soerohardjo I, Widjanarko S, Yudiana W, Shidqy EM , 2022) PSA testing is sensitive for detecting prostatic lesions but is not specific for prostate adenocarcinoma. However, increasing serum PSA levels are associated with a higher likelihood of prostate cancer. PSA exhibits absolute tissue specificity for prostatic epithelium and is expressed in most prostate cancers. Only a small proportion of prostate cancers show low or undetectable PSA levels, which occurs almost exclusively in poorly differentiated tumors. (L, 2012)

In this study, the majority of prostate cancer patients had PSA levels >20 ng/mL, accounting for 34 patients (82.9%), followed by PSA levels of 10–20 ng/mL in 4 patients (9.8%) and PSA levels <10 ng/mL in 3 patients (7.3%). These findings are consistent with a study conducted at Sardjito Hospital, Yogyakarta, in 2014, which reported that most patients had PSA levels >20 ng/mL, totaling 56 patients (67.47%), followed by PSA levels of 10–20 ng/mL in 17 patients (20.48%), PSA levels of 4–10 ng/mL in 6 patients, and PSA levels <4 ng/mL in 4 patients. (Lubis AS, Batasan Prostate Specific Antigen (PSA) pada Pasien Kanker Prostat untuk Memprediksi Metastasis ke Tulang di Rumah Sakit Sardjito, Yogyakarta., 2014) Similar findings were reported by Putriyuni and Hilbertina (2015), which showed that the majority of serum PSA levels were >20 ng/mL. (Putriyuni A, Hilbertina N., 2015)

Regarding histopathological type, all 41 patients (100%) in this study exhibited adenocarcinoma. Similar findings were reported by Solang et al., who found that among 54 prostate cancer patients, only 23 had available histopathological results, all of which demonstrated adenocarcinoma (100.0%). (Solang VR, Monoarfa A, Tjandra F, 2016)These results are also supported by a study conducted by Jennifer et al. (2023), which reported that nearly all samples exhibited prostate adenocarcinoma, totaling 78 patients. (Louisa J, I Wayan Juli Sumadi, Herman Saputra, Ni Putu Ekawati, 2023)

According to the literature, the most common type of prostate cancer is adenocarcinoma, followed by urothelial carcinoma. Five different types of prostate

cancer have been identified, namely granular neoplasms, urothelial carcinoma, squamous cell carcinoma, basal cell carcinoma, and neuroendocrine tumors. Prostate adenocarcinoma is the most common type (granular subtype, 95%), while other types include interstitial cell carcinoma, neuroendocrine carcinoma, or sarcoma. (Fajarudin L, Siti Sundari A, Wahyu Indriati D, 2020)

In this study, the majority of prostate cancer patients exhibited poor differentiation, with 34 patients (82.9%), followed by moderate differentiation in 4 patients (9.8%) and well differentiation in 3 patients (7.3%). These findings are consistent with the study conducted by Solang et al. (2016), which reported that most prostate cancer patients had Gleason scores of 8–10 (poorly differentiated), accounting for 7 patients (46.7%), while Gleason scores of 2–4 (well differentiated) and 5–7 (moderately differentiated) were each found in 4 patients (26.7%). (Solang VR, Monoarfa A, Tjandra F, 2016) Similar results were reported by Putriyuni and Hilbertina (2015), who found that the most common histopathological grade was poorly differentiated, accounting for 76 cases (46.63%), followed by moderately differentiated tumors in 46 cases (28.22%) and well differentiated tumors in 41 cases (25.15%). (Putriyuni A, Hilbertina N., 2015) In contrast, a study conducted by Andreas et al. (2014) reported that among 51 cases, 48 cases had documented Gleason scores, with the most common score being 5–7 (moderately differentiated), accounting for 23 cases (45.10%). (Andreas MI, 2017)

In determining the degree of cellular differentiation in prostate cancer, the Gleason scoring system is commonly used. The Gleason score is one of the strongest prognostic indicators for assessing the grade of prostate adenocarcinoma. However, variations in the application of the Gleason scoring system are still frequently encountered. (PB, 2021) These differences may be attributed to the use of different Gleason scoring systems. This study referred to the WHO 2016 classification, whereas the study by Putriyuni et al. (2015) used the revised ISUP (International Society of Urological Pathology) 2005 Gleason system, and the study by Andreas et al. (2014) referred to the WHO 2004 classification. (K, 2018)

CONCLUSION

In conclusion, the majority of prostate cancer patients treated at RSUP Dr. M. Djamil Padang during the period 2018–2022 were aged 55–70 years and predominantly presented with local symptoms. Most patients had serum PSA levels >20 ng/mL, poorly differentiated tumors, and an adenocarcinoma histopathological type. Adenocarcinoma was the most frequent histopathological type across age groups, particularly among patients aged 55–70 years, as well as across PSA categories, with the highest proportion observed in patients with PSA levels >20 ng/mL. Based on tumor differentiation, adenocarcinoma with poor differentiation was the most common finding. Furthermore, the highest proportion of differentiation grade based on PSA levels was poorly differentiated tumors in patients with PSA levels >20 ng/mL. Local symptoms were the most frequent clinical manifestation of prostate cancer when analyzed by

histopathological type, particularly in patients with adenocarcinoma, and also when analyzed by differentiation grade, with local symptoms predominating in poorly differentiated tumors

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