


Prevalence and Characteristics of Penile Cancer in Karangasem Regency, Indonesia, 2020-2022

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ABSTRACT

Background: Indonesia reported 1,143 penile carcinoma cases from 2004 to 2013. Bali reported the highest age-standardized incidence rate (ASR) in 2004-2013. **Method**: A quantitative descriptive retrospective study was conducted at Karangasem General Hospital and Balimed Karangasem Hospital. **Results**: This study involved 29 patients diagnosed with penile cancer in 2020-2022. The highest number of cases was found in 2020. Most cases were in the 60-69 year age-group (34.5%), with a low educational level (75.9%), a smoking habit (75.9%), no history of circumcision (100%), and squamous cell carcinoma (86.2%). The treatment was mainly partial penectomy (41.3%). **Conclusion**: The study found that the highest prevalence of penile cancer was 6.02 per 100,000 people in 2020.

Keywords: Characteristics, penile cancer, prevalence, squamous cell carcinoma.

ABSTRAK

Latar belakang: Indonesia melaporkan 1.143 kasus karsinoma penis dari tahun 2004 hingga 2013. Angka kejadian terstandarisasi berdasarkan usia (ASR) tertinggi pada tahun 2004-2013 dilaporkan di Bali. **Metode**: Studi retrospektif deskriptif kuantitatif di Rumah Sakit Umum Daerah Karangasem dan Rumah Sakit Balimed Karangasem periode 2020-2022. **Hasil**: Penelitian ini melibatkan 29 pasien yang didiagnosis kanker penis. Jumlah kasus kanker penis tertinggi pada tahun 2020. Sebagian besar kasus di kelompok usia 60-69 tahun (34,5%), dengan tingkat pendidikan rendah (75,9%), kebiasaan merokok (75,9%), tidak ada riwayat sunat (100%), dan jenis karsinoma sel skuamosa (86,2%). Sebagian besar pengobatan adalah penektomi parsial (41,3%). **Simpulan**: Dari penelitian ini didapatkan angka prevalensi kanker penis tertinggi adalah 6,02 per 100.000 orang pada tahun 2020. **Suyadnya IM, Adi Kurniawan IP. Prevalensi dan Karakteristik Kanker Penis di Karangasem, Indonesia, 2020-2022.**

Kata Kunci: Karakteristik, kanker penis, prevalensi, karsinoma sel skuamosa.

INTRODUCTION

Carcinoma of the penis is a rare neoplasm. Cases of penile carcinoma accounted for <1% of all malignancies in men in the United States in 2018, with approximately 2,100 new cases and a total of approximately 400 deaths each year.[1] Data from the International Agency for Research on Cancer in 2020 reported 36,068 new cases of penile cancer, of which >95% were squamous cell carcinoma (SCC).[2] There were 13,211 cases of death due to penile cancer in that year, ranked as the 31st cause of death due to cancer.[2] Asia reported 0.74 cases of penile carcinoma per 10,000 men, with a total of 20,315 cases in 2020.[2] In 2021, the United States reported around 2.070 new cases, totaling 470 deaths per year.[3] Brazil is the country with the most reported new cases of penile carcinoma. In America, it is the fourth most common tumor found in Brazilian men. There are around 2.8-6.8 cases of penile carcinoma per 100,000 men in Brazil.[4] Indonesia reported 1,143 cases of penile carcinoma from 2004 to 2013. Bali reported 2.1 cases per 100,000 men in 2004-2013, the highest age-standardized incidence rate (ASR), while other provinces in Indonesia only reported <1 per 100,000 men. The incidence of penile cancer is highest in the elderly group, with the highest age-specific incident rate (AR) found in Bali, South Sumatra, and South Sulawesi in the age group of 65-76 years.[5] Penile carcinoma is found most frequently in men aged 50-70, at an early stage, and is generally treatable. Penile cancer mostly occurs in the glans penis (48% cases), followed by in the foreskin (21%), glans penis and foreskin (9%), coronal sulcus (6%), and most rarely in the penile shaft (<2%).[4]

The etiology of penile carcinoma is multifactorial. The most frequent risk factors are HPV infection, phimosis, poor hygiene, not being circumcised, lichen sclerosis, inflammatory conditions such as balanitis xerotica obliterans, compromised immune systems, exposure to UVA, for example in phototherapy, smoking, obesity, frequent multiple sexual partners, and old age.[4] The most common HPV serotypes associated with penile cancer are types 16 and 18, with a

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predominance of type 16.[4]

The pathogenesis of penile carcinoma is still not fully understood due to rare findings and the small amount of tissue available for molecular studies.[6] In HPV-associated penile carcinoma, the HPV virions have access to the basal cells of the epithelial mucosa via microabrasions and specific receptors. Persistent HPV infection in the epithelium and integration of HPV DNA into the host cell genome result in a malignant phenotypic transformation.[6] This results in the overexpression of viral proteins that affect the control of cell cycle dysregulation, which regulates the cancer phenotype.[6] Viral proteins can also target the host's tumor suppressor proteins, inhibiting DNA repair, growth arrest, and apoptosis.[7] The accumulation of infected cells will result in secondary genetic events, such as mutations that can lead to cancer.[6] Penile SCC only causes local destruction, rarely metastasizes, and has lower mortality.[7]

Circumcision was an uncommon procedure in Bali, which may be a risk factor for penile cancer.[5] This study focused on the prevalence and characteristics of penile carcinoma patients in Karangasem Regency, Bali, in 2020-2022.

METHOD

This research is a quantitative descriptive retrospective study, conducted at Karangasem General Hospital and Balimed Karangasem Hospital from 2020 to 2022. This study includes all patients diagnosed with penile carcinoma at Karangasem General Hospital and Balimed Karangasem Hospital from 2020 to 2022. Data were obtained from medical records. A descriptive analysis was carried out to describe the patient's characteristics, including age, education, smoking habit, history of circumcision, disease stage, previous history of penile carcinoma, and therapy. The analysis was performed using SPSS software.

RESULTS

This study included all 29 patients diagnosed with penile carcinoma at Karangasem General Hospital and Balimed Karangasem Hospital in the 2020-2022 period. Data was obtained from the patient's medical record.

The distribution of penile carcinoma patients in Karangasem Regency in the 2020-2022 period is shown in **Table 1**. The highest incidence of penile carcinoma was found in 2020 (15 cases; 51.7%). Cases decreased in 2021 compared to 2020 and continued to decrease in 2022. Based on the total population in Karangasem Regency, the prevalence of penile cancer was 6.02 per 100,000 people in 2020, 2.36 per 100,000 in 2021, and 1.93 per 100.000 in 2022.

Table 2 shows the characteristics of penile cancer patients. Cases in this study were found starting at the age of 40 years, mostly in the age group of 60-69 years (10 cases; 34.5%), while the fewest cases were found in the age group > 80 years (2 cases; 6.9%). Most cases had low levels of education; 22 cases (75.9%) had elementary school education, and only 7 cases (24.1%) received high school education. Most cases (22%-75.9%) had smoking habits. All cases in this study were not circumcised (29%-100%).

Table 3 shows the TNM staging of penile cancer. Based on the tumor category (T), tumors that invaded the corpus cavernosum with or without urethral involvement (T3) were found in 14 cases (48.3%), followed by T1 in 10 cases (34.5%); no T0 or T2 cases were recorded. The nodule category (N) indicated cases with lymph node involvement (Nx), found in 10 cases (34.5%), and no lymph node metastases (N0) in 9 cases (31.1%). Most cases (16%-55.2%) were without metastases (M0).

The most common histological type was squamous cell carcinoma (SCC) in 25 cases (86.2%), while other histological types were only found in 4 cases (13.8%) **(Table 4).**

The most common treatment given was partial penectomy, with 12 cases (41.3%), followed by total penectomy, with 9 cases (31.1%). The last therapy was chemotherapy in 1 case (3.4%). **(Table 5)**

DISCUSSION

Penile cancer is a malignancy whose predominant histological type is squamous cell carcinoma (SCC).[10] According to the International Society of Urological Pathology (ISUP), penile cancer can be classified based on its relationship with human papillomavirus (HPV) infection.[10] Penile cancer subtypes related to HPV were divided into warty and basaloid types, while penile cancer subtypes not related to HPV were divided into usual, verrucous, papillary not otherwise specified (NOS), and sarcomatoid types. Although verrucous and papillary types are said to be unrelated to HPV, these types are still found in tumors associated with HPV.[8]

Table 1. Distribution of penile cancer patients in Karangasem, 2020-2022.

Year	Patients (%)
2020	15 (51.7)
2021	9 (31.1)
2022	5 (17.2)
Total	29 (100)

Table 2. Characteristics of penile cancer patients in Karangasem from 2020-2022.

Characteristics	n (%)
Age	
40-49	3 (10.3)
50-59	5 (17.2)
60-69	10 (34.5)
70-79	9 (31.1)
Education	
Elementary	22 (75.9)
Senior High School	7 (24.1)
Smoking Habit	
Yes	22 (75.9)
No	7 (24.1)
Circumcision	
No	29 (100)


This study found that the incidence of penile cancer in 2020 was 15 cases per year, the highest incident in the 2020-2022 period with a prevalence of 6.02 per 100,000 people; it then decreased to 9 cases and 5 cases in 2021 and 2022, respectively. Another region of Indonesia has a different incidence of penile cancer. A 10-year period (1976-1985) study in the Urology division of Hasan Sadikin Hospital, Bandung, found that 6% of inpatient cancer patients were diagnosed with penile cancer.[14] A 5-year period (1988-1993) study in Cipto Mangunkusumo Hospital, Jakarta, found 3.6 cases of penile cancer per year, which increased to 6.3 cases per year based on an 11-year study in 1994-2005.[30] A study from 2010-2014 at Sanglah General Hospital shows 11.4 cases of penile cancer per year.[9] Lestari, *et al*, state that the total number of cases of penile cancer in Indonesia from 2004 to 2013 was 1,143 with the highest number of cases found in 2007. That study also reported that Bali was the province with the highest penile cancer incidence in Indonesia, with 449 cases in the period, followed by 155 cases in Jakarta, 90 cases in North Sumatra, 85 cases in Yogyakarta, and the lowest in West Java, with 13 cases.[5]

Penile cancer incidence increased among older men, with an average diagnosis at age 60 and a peak incidence at age 70. There is no consensus on the age distribution of penile cancer cases.[10] Tanaka, *et al,* stated that the distribution of penile cancer by age in Japan was >60 years of age, with the highest in the 70-79 age group (36.3%), followed by the 60-69 age group (21.9%).[11] Similar results were also found by Zhan, *et al*; 26.3% of penile cancer was found in people aged 70-80, followed by 23.4% in people aged 60-70.[12] That is in line with this study; most cases were found at the age of >60 years, highest in the 60-69 year age group. The age-related trend in penile cancer cases is not absolute. Other factors, such as HPV infection and neonatal circumcision, can also influence cases of penile cancer.[12] Alfonso, *et al*, stated that the average age at penile cancer diagnosis was 58 years (26-92 years), with 64.8% of cases having positive HPV results.[13] Zamzami in Pekanbaru also found that 62.5% of cases of penile cancer were in the 46-55-year-old group.[7] Kusumajaya and Safriadi found that 53.8% of penile cancer cases were in the 50-60 years group.[14]

Low education level is associated with an increased incidence of penile cancer, as it may cause people to be less aware of various disease symptoms, lack initiative to seek health facilities, and when combined with long distances to health facilities, contribute to its incidence.[15] Vieira, *et al*, stated that 90% of penile cancer cases occur in patients with a low level of education or who do not attend school.[16] In this study, 75.9% of cases had an elementary education level. But Firmansyah, *et al*, in Medan and Junior, *et al*, in Bali, found that penile cancer cases were mostly at the senior high school education level, 66.7% and 45%, respectively.[17,18]

The smoking habit was found in 75.9% of cases in this study. These results are in line with the study by Martins, *et al*, which found that 60% of a total of 47 cases of penile cancer were smokers or had a history of smoking.[19] Kusumajaya and Safriadi also stated that 69.2% of cases of penile cancer in Bandung, Indonesia, were cigarette smokers.[14] The smoking habit significantly affects the prevalence of all types of cancer, including penile cancer. The tobacco contained in cigarettes is an important risk factor for the development of penile cancer and other neoplasms.[15]

Non-circumcision is one of the contributing factors to the occurrence of penile cancer.[20] Circumcision is a protective factor against penile cancer.[16] Neonatal circumcision can reduce the incidence of penile cancer but does not reduce the risk of penile intra-epithelial neoplasm (PeIN)[2] while circumcision performed before puberty provides close to 100% protection from penile cancer.[21] Firmansyah, *et al*, found 55.6% of penile cancer cases in Haji Adam Malik General Hospital, Medan were not circumcised.[17] This study also found that all cases were not circumcised.

Table 3. Stage of penile cancer in Karangasem from 2020-2022 (n=29).

Variables	n (%)
Tumor Tx	2 (6.9)
T0	0 (0)
T1	10 (34.5)
T2	0 (0)
T3	14 (48.3)
T4	3 (10.3)
Nodule Nx	10 (34.5)
N0	9 (31.1)
N1	0 (0)
N2	3 (10.3)
N3	7 (24.1)
Metastasis Mx	12 (41.4)
M0	16 (55.2)
M1	1 (3.4)

Table 4. Histology type of penile cancer patients in Karangasem from 2020-2022 (n=29).

Histology Type	Patients (%)
Squamous cell carcinoma	25 (86.2)
Other types	4 (13.8)
Total	29 (100)

Table 5. Treatment of penile cancer patients in Karangasem from 2020-2022.

Treatment	Patients (%)
Total penectomy	9 (31.1)
Partial penectomy	12 (41.3)
Biopsy only	7 (24.1)
Chemotherapy	1 (3.4)
Total	29 (100)

The TNM Staging System, based on the American Joint Committee on Cancer (AJCC) 8th edition for penile cancer, is based on the anatomic route and spread of penile cancer.[22] There is a sequential pattern of local, regional, and systemic spread of penile cancer. Local spread occurs centrifugally from the glans to the sulcus and foreskin, and vice versa.[22] A study by Zamzami in Pekanbaru, Indonesia, states that penile squamous cell carcinoma (PSCC) mostly has the ability to localize destruction and rarely metastasize; its mortality is lower than that of non-squamous cell carcinoma; 34.2% of cases were in the T2 and T3 stages, 51.4% were in the N1 stage, and 77.2% were in the M0 stage.[7] This is consistent with the results of this study, which found that metastases were not found in 55.2% of cases. Inguinal lymph node metastasis is one of the important prognostic factors; involvement of the groin node can drastically reduce the 5-year survival rate from 95.7% to 51.1%.[23]

Penile cancer mostly (95%) has a histological type of squamous cell carcinoma.[2] Another histological type (non-squamous cell carcinoma) can be basal cell carcinoma, melanoma, sarcoma, or lymphoma. Wenzel, *et al*, stated that this type of SCC was found more frequently.[24] A study by Zamzami, *et al*, in Arifin Achmad Regional General Hospital, Pekanbaru, Indonesia, also found that 100% of cases are squamous cell carcinoma.[7] While this study found 86.2% were SCC types. Wenzel, *et al*, also stated that the most common type of non-SCC was melanoma (41%), followed by basal cell carcinoma/BCC (34%). It is possible that certain non-SCC types may have a less promising outcome than SCC types; penile melanoma and genitourinary sarcoma are neoplasms with a poor prognosis and have a high rate of recurrence even after surgery.[24]

Carcinoma of the penis at an early stage is generally easier to treat.[4] Local therapy approaches can include penile-sparing techniques and topical chemotherapy using 5-fluorouracil and imiquimod.[25] Therapy with laser ablation is a therapeutic option in cases of superficial penile carcinoma, which produces good functional outcomes.[26] In patients who have never had a circumcision, local supplementation therapy, such as laser therapy with radial circumcision, is recommended for patients' comfort and hygiene. The treatment of choice in patients with invasive tumors is a glossectomy, which removes the tumor and the involved glans by removing the glans spongiosum. Partial glossectomy may be considered in small invasive tumors.[27]

Rooted surgical therapy for penile cancer involving the corpus cavernosum, a partial or total penectomy may be performed. Radical (total) penectomy with perineal urethrostomy has the effect of not being able to penetrate and cannot have an erection.

Another therapy is a partial penectomy. A partial penectomy is effective and has a low recurrence rate.[28] Kusumajaya and Safriadi found that 61.5% of cases of penile cancer at Hasan Sadikin Hospital, Bandung, were treated with a partial penectomy.[14] This study records 41.3% of cases treated with a partial penectomy. A partial penectomy procedure maintains the penile shaft to preserve the function of the penis, but with side effects on sexual function.[28] Sansalone, *et al*, state that there is a decrease in orgasmic function, sexual arousal, satisfaction, and the presence of dysfunctional effectiveness after partial penectomy.[29]

LIMITATIONS

The weakness of the study was that no further evaluation was carried out regarding the staging of penile cancer, so it's recommended to conduct further studies in the future.

CONCLUSION

The highest prevalence of penile cancer in Karangasem Regency was in 2020 and was most common in the 60-69 year age group. The study found the highest prevalence of penile cancer was 6.01 per 100,000 people in 2020, while the lowest was 1.93 per 100.000 people in 2022.

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