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Risk Factors Affecting the Recurrence of Phyllodes Tumor at Dr. Soetomo General Hospital in 2019–2024

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ABSTRACT

This study aimed to identify the risk factors influencing recurrence among patients treated surgically at Dr. Soetomo General Hospital from 2019 to 2024. This was a descriptive observational study with a cross-sectional design. Medical records of patients diagnosed with phyllodes tumors and surgically treated at Dr. Soetomo General Hospital between 2019 and 2024 were reviewed. A total of 70 patients who met the inclusion criteria were included. Variables analyzed included age, family history, tumor grade, tumor size, type of surgery, adjuvant radiotherapy, surgical margin status, stromal cellularity, stromal atypia, mitotic rate, and Ki-67 index. Most patients were younger than 65 years (65.7%), presented with benign– borderline tumors, had tumors smaller than 5 cm (68.6%), and underwent wide excision without radiotherapy (92.9%). Recurrence occurred in 10 patients (14.3%), with an average disease-free interval of 23 months. The most significant risk factor for recurrence was inadequate surgical margins (<1–2 cm). Other contributing factors included age, type of surgery, high mitotic activity, and excessive stromal overgrowth. The recurrence rate of phyllodes tumors at Dr. Soetomo General Hospital was relatively low. However, inadequate or positive surgical margins remain the primary risk factor for recurrence. Appropriate surgical techniques ensuring adequate margins and a follow-up period of at least 2–3 years are crucial for early detection and management of recurrence.

KEYWORDS: Phyllodes Tumor, Risk Factors, Recurrence, Surgical Margin, Breast

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INTRODUCTION

Phyllodes tumor is a fibroepithelial lesion that presents as a breast mass in women. The epidemiology of this tumor varies globally, with an incidence of 2.1 cases per one million women, peaking at the age of 45–49 years [1,2]. Notably, the incidence is higher among Asian women, reaching 3.83%, with a younger peak age of occurrence at 25–30 years compared to Western women [3]. Clinically and radiologically, phyllodes tumor share striking similarities with fibroadenomas, and imaging modalities such as ultrasound (USG) and mammography generally cannot reliably distinguish between the two [4–6]. Definitive diagnosis requires histopathological evaluation following excisional biopsy [4,7]. The mainstay of treatment is wide surgical excision with a surgical margin of at least 1 cm, in accordance with the recommendations of the National Comprehensive Cancer Network (NCCN) [4,8].

Historically, phyllodes tumors have been associated with a risk of recurrence, both local and metastatic. The World Health Organization (WHO) classifies phyllodes tumors into three categories of malignancy: benign, borderline, and malignant. Importantly, recurrence and metastasis are not confined to malignant tumors but are also observed in benign and borderline types. The incidence of recurrence ranges between 10–40% of cases, with most occurring within the first two years after initial treatment [4,9,10]. Recurrence is linked to poor prognosis, as multiple studies have demonstrated significantly reduced survival among patients experiencing local recurrence or metastasis [11,12].

Given this clinical challenge, identifying patients at higher risk of recurrence is crucial for early detection and timely management to improve outcomes. However, risk factors for recurrence remain controversial, with studies reporting inconsistent findings. A factor identified as significant in one study may not be validated in another [13,14]. Furthermore, research on the risk factors for recurrence of phyllodes tumors is scarce in the Indonesian population and has not been conducted at Dr. Soetomo General Hospital. Therefore, this study aims to identify risk factors associated with increased recurrence rates in patients with phyllodes tumors who have undergone surgical management at Dr. Soetomo General Hospital.

RESEARCH METHOD

This observational study used a cross-sectional approach based on medical records of patients diagnosed with phyllodes tumors who underwent surgical management at Dr. Soetomo General Hospital between 2019 and 2024. The unit of analysis was individual patients treated surgically at this hospital.

Adult patients were eligible if they had a histopathologically confirmed phyllodes tumor; received surgical treatment with either mastectomy or breast-conserving surgery; were classified as benign, borderline, or malignant; and had recurrence events which defined as ipsilateral local recurrence or distant metastasis confirmed to originate from a phyllodes tumor by histopathology. Patients also had to be registered in the hospital medical record system with complete baseline and follow-up data for all study variables. Exclusion criteria comprised a prior malignancy other than phyllodes tumor, metastatic disease at first presentation, and a follow-up duration of less than five months. The minimum sample size was determined using Slovin's formula for a known population, with N = 70 phyllodes-tumor patients during the study period, a 95% confidence level, and a 5% margin of error, yielding a required minimum of 60 patients. Sampling was retrospective: records from January 2019 to December 2024 were screened against the criteria, and incomplete records were excluded; follow-up was traced retrospectively to ascertain recurrence and survival outcomes. The dependent variable was phyllodes-tumor recurrence (local or distant). Independent variables included age, family history of breast malignancy, histological grade, primary tumor size, type of surgery, receipt of adjuvant radiotherapy, resection-margin status, stromal hypercellularity, stromal nuclear atypia, mitotic count, and Ki-67 index. Operational definitions followed the literature and were measured from medical records and histopathology reports, with variables captured on categorical, ordinal, or numerical scales as appropriate.

Data collection proceeded by identifying eligible patients within the specified years, screening records to apply inclusion and exclusion criteria, extracting baseline demographic, clinical, and histopathological information at the time of primary surgery, and reviewing subsequent entries to document recurrence or metastasis. All analyses were performed in IBM SPSS Statistics version 25, using descriptive statistics to summarize frequencies and percentages for categorical variables and means or medians for numerical variables according to distribution, with results presented as proportions and descriptive summaries.

RESULTS

A total of 70 patients diagnosed with phyllodes tumors and fulfilling the inclusion criteria were analyzed in this study. Most patients were younger than 65 years old (n = 46, 65.7%), while 24 patients (34.3%) were aged 65 years or older. With respect to histological classification, benign phyllodes tumors represented the largest subgroup (n = 30, 42.9%), followed by borderline (n = 28, 40.0%) and malignant tumors (n = 12, 17.1%).

Table 1: Characteristics of Phyllodes Tumor Patients

Variable	Category	Frequency (n)	Percentage (%)
Age	<65 years	46	65.7
	≥65 years	24	34.3
Histological grade	Benign	30	42.9
	Borderline	28	40.0
	Malignant	12	17.1
Tumor size	<5 cm	48	68.6
	>5 cm	22	31.4
Surgical procedure	Wide excision	41	58.6
	Mastectomy	29	41.4
Adjuvant radiotherapy	Yes	5	7.1
	No	65	92.9
Resection margin	Negative	50	71.4
	Positive	20	28.6
Stromal hypercellularity	Mild–moderate	45	64.3
	Severe	25	35.7
Stromal nuclear atypia	Mild–moderate	47	67.1
	Severe	23	32.9
Mitosis count	≤5 mitoses/HPF	41	58.6
	>5 mitoses/HPF	29	41.4
Phyllodes tumor recurrence	No	60	85.7
	Yes	10	14.3
Disease-free survival (months, recurrent cases only)	14	1	1.4

	16	1	1.4
	17	2	2.9
	18	1	1.4
	19	1	1.4
	21	1	1.4
	24	1	1.4
	25	1	1.4
	27	1	1.4
Summary statistics (DFS)	Minimum	14 months	–
	Maximum	27 months	–
	Mean	23.02 months	–
	Standard deviation	3.22 months	–

In terms of tumor size, the majority of tumors measured less than 5 cm (n = 48, 68.6%), while tumors larger than 5 cm were observed in 22 patients (31.4%). Regarding surgical management, wide excision was the most frequently performed procedure (n = 41, 58.6%), compared with mastectomy (n = 29, 41.4%). Only a small proportion of patients received adjuvant radiotherapy (n = 5, 7.1%), while most did not (n = 65, 92.9%).

Histopathological examination revealed that negative resection margins were achieved in 50 patients (71.4%), whereas positive margins were found in 20 patients (28.6%). Stromal hypercellularity was predominantly mild to moderate (n = 45, 64.3%), with 25 patients (35.7%) showing marked hypercellularity. Similarly, nuclear atypia of the stroma was mild to moderate in 47 patients (67.1%) and severe in 23 patients (32.9%). Mitosis counts demonstrated that 41 patients (58.6%) had ≤5 mitoses per high-power field (HPF), while 29 patients (41.4%) had >5 mitoses/HPF.

Overall, recurrence of phyllodes tumor was identified in 10 patients (14.3%), while the majority of patients (n = 60, 85.7%) remained recurrence-free during the observation period. The mean disease-free survival (DFS) among patients with recurrence was 23.02 months, with a standard deviation of 3.22 months, ranging from a minimum of 14 months to a maximum of 27 months. Specifically, one patient experienced recurrence at 14 months, one at 16 months, two at 17 months, one at 18 months, one at 19 months, one at 21 months, one at 24 months, one at 25 months, and one at 27 months.

These findings suggest that while the recurrence rate in this study population was relatively low, recurrence events occurred within a wide time frame, beginning as early as 14 months and extending beyond 2 years after initial treatment. This highlights the importance of long-term follow-up, as the risk of recurrence persists beyond the early postoperative period. The results also reinforce that most patients with benign or borderline tumors, smaller tumor size, negative margins, and lower mitotic activity experienced favorable outcomes with low recurrence rates.

DISCUSSION

In this study, the majority of patients with phyllodes tumors were younger than 65 years old (65.7%), confirming that age is an important risk factor for the development of this tumor [1]. Phyllodes tumors are most frequently observed in middle-aged women, particularly those in their forties and fifties, and are more often diagnosed in premenopausal women [3]. This finding is consistent with prior studies reporting that younger age groups, especially Asian women, show a higher incidence compared to Western populations [3,4].

According to histological grade, benign phyllodes tumors were the most frequent (42.9%), followed by borderline (40.0%) and malignant types (17.1%). This distribution aligns with the general consensus that most phyllodes tumors are benign, though borderline and malignant types also contribute significantly to the overall disease burden [4]. Benign tumors tend to grow slowly and carry a lower risk of recurrence once excised, while borderline tumors grow more rapidly and require stricter follow-up due to their higher recurrence risk [7]. Malignant phyllodes tumors, although less common, are clinically aggressive and often necessitate wide excision or mastectomy, sometimes followed by adjuvant radiotherapy or chemotherapy to reduce the risk of metastasis [9].

Tumor size also appeared to play a role, as most tumors in this cohort were smaller than 5 cm (68.6%), with larger tumors (>5 cm) found in 31.4% of patients. Although size itself is not a direct etiological factor, it has significant implications for treatment strategy and recurrence risk. Previous studies have identified large tumor size (>5–10 cm) as an independent predictor of local recurrence and distant metastasis [13,15]. Hormonal imbalance, pregnancy, breastfeeding, breast trauma, and genetic predisposition, such as Li-Fraumeni syndrome, have been implicated as possible drivers of tumor growth [16,17].

In terms of treatment, wide excision was the most common surgical procedure (58.6%), followed by mastectomy (41.4%). The primary principle of surgical management is to achieve adequate margins of at least 1 cm, particularly for borderline and malignant tumors [4]. When margins are positive or close (<1 cm), the risk of local recurrence significantly increases [18]. In this study, negative margins were achieved in 71.4% of patients, while 28.6% had positive margins, a distribution that highlights the challenges in achieving wide margins, especially in large tumors or those located unfavorably within the breast.

The use of adjuvant radiotherapy was rare in this cohort, with only 7.1% of patients receiving it. Although its role in phyllodes

tumors remains controversial, several studies have suggested that radiotherapy may be beneficial in reducing local recurrence in high-risk patients, particularly those with large tumors, positive or close margins, and high stromal cellularity [9,19,20]. Current NCCN guidelines recommend radiotherapy selectively, with emphasis on malignant tumors or cases where re-excision is not feasible [4].

Histopathological factors such as stromal hypercellularity, nuclear atypia, and mitotic activity are crucial in determining tumor behavior [21]. In this study, most patients had mild-to-moderate stromal hypercellularity (64.3%) and atypia (67.1%), with severe changes observed in about one-third of cases. A higher degree of stromal cellularity and nuclear atypia has been associated with more aggressive tumor biology and higher recurrence rates [7]. Mitosis count further supported this, as 41.4% of patients had >5 mitoses/HPF, a marker strongly associated with borderline and malignant tumors [13].

Overall, recurrence occurred in 14.3% of patients, which is relatively low compared to the 10–40% recurrence rate reported in the literature [4,9]. Disease-free survival among recurrent cases ranged from 14 to 27 months, with a mean of 23 months, which is consistent with studies indicating that most recurrences occur within the first two years after treatment [11]. Key factors contributing to recurrence in prior studies include positive or narrow margins, large tumor size, high mitotic activity, and marked stromal overgrowth [13,14].

These findings highlight two important clinical implications. First, the overall recurrence rate in this population was low, suggesting that surgical management at Dr. Soetomo General Hospital has been largely effective. Second, the variability in recurrence-free survival underscores the need for individualized follow-up protocols. Even though most patients remained recurrence-free, recurrences occurred across a wide time frame, from just over one year to more than two years postoperatively. This emphasizes the importance of long-term monitoring, ideally for at least 2–3 years, to enable early detection and management of recurrence [12].

CONCLUSION

This study demonstrated that the majority of patients with phyllodes tumors were younger than 65 years, with most tumors classified as benign or borderline, measuring less than 5 cm in size, and predominantly managed with wide excision without adjuvant radiotherapy. The average disease-free survival was approximately 23 months, indicating that most patients had a favorable prognosis, although a small proportion experienced recurrence during the follow-up period. Descriptive analysis further revealed that 85.7% of patients did not experience recurrence, while 14.3% developed recurrent phyllodes tumors, a figure consistent with previous studies reporting recurrence rates of 10–40%. The most influential factor for recurrence was a resection margin of less than 1–2 cm, with other contributing factors including patient age, type of surgery, mitotic activity, and stromal overgrowth.

These findings provide clinically relevant insights for identifying patients at higher risk of recurrence, emphasizing the role of histopathological features and surgical margins in prognosis. The results of this study may serve as a useful reference for clinicians in optimizing the management of phyllodes tumors. However, further research with more complex, comprehensive, and prospective study designs is required to validate these results, ideally incorporating additional variables and randomized controlled settings to provide more representative evidence in the clinical management of phyllodes tumors.

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