

**Phyllodes Tumors of the Breast: Recurrence and the Importance of Clinical Follow-up****Memenin Filloïd Tümörleri: Nüks ve Klinik Takibin Önemi**Berkay KILIÇ¹, Burak İLHAN²**ABSTRACT**

AIM: Phyllodes tumors, including benign and borderline types, have a substantial potential for recurrence. The objective of this study was to evaluate histologic features that can help predict recurrences and to emphasize the importance of close follow-up in this regard.

MATERIAL AND METHOD: The clinicopathologic characteristics of patients, treatment approaches, and follow-up data of the 64 patients treated between 2006 and 2022 at the Institute of Oncology, Istanbul University, with the diagnosis of phyllodes tumors, were evaluated retrospectively by examining the patient files and pathology records.

RESULTS: The median age was 41 (range: 26–63) years, and the median tumor size was 52 (range: 11–210) mm. The phyllodes tumors were classified as benign (n=36, 56.27%), borderline (n=11, 17.24%), and malignant (n=17, 26.49%). High mitotic number, cellular pleomorphism, stromal overgrowth, tumoral heterogeneity, and tumor margin irregularity were independent prognostic factors in the development of local recurrence. The common feature of tumor recurrence in the process of benign and borderline phyllodes tumors was tumor margin irregularity. The median recurrence time for phyllodes tumors was 29.5 (range: 10–64) months. In the study, seven out of 10 recurrences were when excision was performed with an insufficient surgical margin of closer than 1 cm and in three cases when a clear surgical margin was far more than 1 cm (p=0.045).

CONCLUSION: Phyllodes tumors were benign, borderline, and malignant. A negative surgical margin of ≥ 1 cm plays a major role in the management. The study may emphasize the importance of close follow-up, given that the recurrence period is short, especially if tumor margin irregularity is detected on definitive pathological examination, even if it is benign or borderline.

Keywords: Phyllodes tumor, breast surgery, margin status

ÖZET

AMAÇ: Benign ve borderline tipleri de dahil olmak üzere filloïd tümörlerin önemli bir nüks potansiyeli vardır. Bu çalışmanın amacı nüksleri öngörmeye yardımcı olabilecek histolojik özellikleri değerlendirmek ve bu konuda yakın takibin önemini vurgulamaktır.

GEREÇ VE YÖNTEM: Çalışmada 2006-2022 yılları arasında İstanbul Üniversitesi Onkoloji Enstitüsü'nde filloïd tümör tanısıyla tedavi edilen 64 hastaların klinikopatolojik özellikleri, tedavi yaklaşımları ve takip verileri hasta dosyaları ve patoloji kayıtları üzerinden retrospektif olarak incelenerek değerlendirildi.

BULGULAR: Medyan yaş 41 (aralık: 26–63) yıl ve medyan tümör boyutu 52 (aralık: 11–210) mm idi. Filloïd tümörler şu şekilde sınıflandırıldı: Benign (n=36, %56,27), borderline (n=11, %17,24) ve malign (n= 17, %26,49). Yüksek mitotik sayı, hücresel pleomorfizm, stromal aşırı büyüme, tümöral heterojenite ve tümör sınırı düzensizliğinin lokal nüks gelişiminde bağımsız prognostik faktörler olduğu bulundu. Benign ve borderline filloïd tümörlerde nüksün ortak özelliği tümör sınırı düzensizliği idi. Filloïd tümörlerin tekrarlama süresi medyan 29,5 (aralık: 10–64) ay olarak belirlendi. Çalışmada 1 cm'den daha yakın yetersiz cerrahi sınır ile eksizyon yapıldığında 10 olgudan yedisinde, 1 cm'den uzakta temiz cerrahi sınır elde edilen üç olguda ise nüks gözlemlendi (p=0,045).

SONUÇ: Filloïd tümörler benign, borderline ve malign olarak sınıflandırıldı. Tedavisinde ≥ 1 cm'lik negatif cerrahi sınır önemli bir rol oynar. Çalışmamız, nüks süresinin kısa olması nedeniyle, özellikle benign veya borderline tipte olsa bile, kesin patolojik incelemede tümör sınırında düzensizlik saptanması durumunda yakın takibin önemini vurgulamaktadır.

Anahtar Kelimeler: Filloïd tümör, meme cerrahisi, cerrahi sınır

¹ Istanbul University Oncology Institute, Department of General Surgery, Istanbul, Türkiye,

² Istanbul University, Faculty of Medicine, Department of General Surgery, Istanbul, Türkiye,

Makale geliş tarihi / Submitted: Aralık 2023 / December 2023

Sorumlu Yazar / Corresponding Author:

Berkay KILIÇ
Address: Istanbul University, Oncology Institute, Turgut Özal Millet Cd, 34093, Fatih, Istanbul, Türkiye
Phone: +90 212 414 24 34 / 34153 - 34154
E-mail: berkaykilic28@yahoo.com
Berkay KILIÇ: berkaykilic28@yahoo.com, ORCID: 0000-0002-9050-7571.

Makale kabul tarihi / Accepted: Kasım 2024 / November 2024

Yazar bilgileri:

Burak İLHAN: burakmd@yahoo.com, ORCID: 0000-0002-7538-7399.

INTRODUCTION

The etymology of "Phyllodes" can be traced back to its Latin origin, "Phyllo-dium" where the essence of leaf-like characteristics is unveiled through microscopic observation. In 1838, German physician Johannes Müller first described phyllodes tumor (PT) as cystosarcoma phyllodes despite the uncommon cystic component of these tumors and the rarity of malignancy.^{1,2} The term PT was first reported by the World Health Organization in 1981, with Rosen providing a histological subclassification into benign, borderline, and malignant categories.³ A significant proportion of phyllodes tumors, ranging from 35% to 64%, are classified as benign, while the remainder falls into the borderline and malignant categories.⁴ Local recurrence (LR) rates vary, with benign PT having a recurrence rate of 17% and malignant PT at 27%.⁵ If inadequately managed, malignant PT can demonstrate a tendency for rapid growth and the potential for metastasis.

The histologic grading of PT generally correlates with prognosis; however, histologic features might not always reflect the clinical behavior in individual patients.^{6,7} These lesions diagnosed as malignant or benign with fine needle aspiration remain difficult preoperatively. While the risk of misdiagnosis is very high with fine needle biopsy, both epithelial and stromal elements should be seen and evaluated for diagnosis in core needle biopsy (CNB).⁸ In this way, CNB can provide important information about tumor features. An accurate preoperative pathological diagnosis enables precise surgical planning, optimizing excision margin assessment and reducing the risk of tumor recurrence.⁹⁻¹¹

Surgical excision is the cornerstone of treatment for phyllodes tumors. It is crucial to remove these tumors with a safe surgical margin. If a clear surgical margin is not achieved, a re-excision may be necessary, as LR primarily occurs when adequate margins are not established.^{12,13} Barth Jr RJ reported local recurrence rates following breast-conserving surgery (BCS) at 8% for benign phyllodes tumors and between 21% and 36% for borderline and malignant types.¹⁴

The role of adjuvant radiotherapy (RT) in the management of phyllodes tumors is still a subject of debate. In cases of borderline and malignant tumors, where there may be concerns about achieving clear surgical margins following BCS or mastectomy due to large tumor size, RT is thought to potentially lower the risk of LR. Recent studies indicate that administering RT in these scenarios may effectively mitigate the risk of LR.¹⁵

The role of chemotherapy (CT) in managing these tumors is a topic of debate. Chemotherapy may be suitable for aggressive malignant tumors, but the decision to proceed with CT should involve careful consideration of its potential benefits and drawbacks, discussed with the patient. For hormone-sensitive tumors that contain an epithelial component, adjuvant hormone therapy is a possible treatment option, though its effectiveness has not been established.¹⁶

This study aimed to identify specific tumor characteristics associated with recurrence and to determine key factors to consider for ongoing follow-up.

MATERIAL AND METHOD

Study population

Tumor features and patient-related factors were analyzed to predict tumor progression after surgical treatment of 64 patients diagnosed with PT, treated between May 2006 and December 2022, at the Institute of Oncology, Istanbul University. The exclusion criteria were those who did not receive further treatment at our institution or did not have pathology slides available. Each case of PT was reviewed by a dedicated breast pathologist at our institution to confirm the histological diagnosis. The study was approved by the Ethics Committee of Istanbul University (form number: 2023/402; Date: 17.03.2023). A written informed consent form was obtained from all patients.

Clinical presentation

Patients presenting with a rapidly growing but clinically benign breast lump were assessed for family history and underwent thorough

physical examinations. In some cases, the lesion may have been present for several years before suddenly increasing in size and causing symptoms. The tumors vary in size, ranging from small to very large, and typically exhibit a mobile, multinodular appearance that is not painful. Although rare, ulceration and adherence to the chest wall can occur even in malignant tumors. Clinical adenopathy has been reported in 20% of patients; however, the occurrence of metastatic disease in the axilla is uncommon.

Mammography (MG) and ultrasonography (USG) are standard imaging techniques used for evaluating breast lumps. Mammography typically reveals a well-circumscribed oval or lobulated mass with rounded edges, sometimes accompanied by a radiolucent halo and coarse calcifications around the lesion. Color Doppler ultrasonography generally shows marked hypoechogenicity, posterior acoustic shadowing, and poorly defined tumor margins. Magnetic resonance imaging (MRI) may also be employed. On MRI, a heterogeneous internal structure with non-enhancing septation displays hypointense signals on T1-weighted images and hyper- or isointense signals on T2-weighted images. Benign phyllodes tumors typically exhibit slow initial enhancement with a persistent delayed phase, while malignant tumors show rapid initial enhancement with a wash-out phenomenon. Following clinical evaluation and imaging, core biopsy is primarily used for pathological diagnosis.

Surgical procedure

After the initial diagnosis, lumpectomy was performed aiming for a macroscopic surgical margin of 1 cm. If the surgical margin was found to be close, positive, or unknown, re-excision was conducted. In cases where BCS was deemed unsuitable due to the tumor size-to-breast ratio, mastectomy (with or without reconstruction) was performed. Axillary interventions were carried out in select cases based on the surgeon's discretion.

Pathological examination

Phyllodes tumors are classified based on the grading system established by the World Health Organization in 2012⁵ and revised in 2019.¹⁷ Tumors are classified into three categories: benign, borderline, and malignant, based on specific criteria. Benign tumors are characterized by fewer than 5 mitoses observed per 10x magnification field, low stromal excess, minimal atypia, and low cellularity, with evident growth patterns and intact surgical margins. Borderline tumors show 5 to 9 mitoses per 10x magnification field, exhibit moderate stromal atypia and cellularity, and may have excessive growth, with either intact or infiltrated surgical margins. In contrast, malignant tumors present more than 10 mitoses per 10x magnification field, accompanied by high levels of stromal cellularity, atypia, pleomorphism, and stromal overgrowth, as well as infiltrating surgical margins. The Ki-67 index is also included in the pathological evaluations when applicable.

Table 1. WHO subclassification of phyllodes tumors

| | Benign | Borderline | Malign |
|---|---|---------------|---------|
| Mitosis of Per 10 HPF | <5 | 5-9 | ≥10 |
| Stromal overgrowth | Absent | Absent/focal | Present |
| Stromal atypia | Mild | Mild-Moderate | Marked |
| Stromal cellularity | Mild | Mild-Moderate | Marked |
| Cellular pleomorphism | Mild | Mild-Moderate | Marked |
| Intratumoral heterogeneity | Variability in structure and stromal cellularity or atypia in a single tumor | | |
| Tumor margin | Projections of tumor stroma into the peritumoral stroma or adipose tissue | | |
| Leaflike pattern | Enhanced intracanalicular pattern, characterized by projection of cellular stroma into epithelial-lined clefts of cystic spaces | | |
| HPF: high-power field, WHO: World Health Organization | | | |

The pathologist assesses the surgical margins and potential invasion of the pectoral muscle in each specimen. During the pathological analysis performed intraoperatively, a surgical margin was deemed positive if any tumor margin was in contact with the ink or if the margin was less than 2 mm, necessitating re-excision. A surgical margin of two mm or greater is considered negative.

Statistical analysis

Patient demographics, tumor characteristics, surgical methods, and postoperative tumor progression data were compiled using Microsoft Excel software (Microsoft Luxembourg S.a.r.l., 20 Rue Eugene Ruppert, Luxembourg). For the analyses, Fisher's exact test or the χ^2 test was employed for two-tailed univariate assessments. The independent sample t-test was utilized to compare the mean values between two independent groups. Variables that were available for all cases and were statistically significant in the univariate analyses were incorporated into the multivariate analyses using binary logistic regression. A p-value of less than 0.05 was deemed statistically significant. Statistical analyses were performed using version 21.0 of the Statistical Package for the Social Sciences (IBM Corp.).

Table 2. Differences between benign, borderline and malign phyllodes tumors

| | | Benign & Borderline n=47 | Malign n=17 | p |
|------------------------------------|----------------|-----------------------------|----------------------|--------|
| Age, years, median | | 36 (26–51) | 42 (34–63) | 0.029 |
| Tumor size, mm, median | | 42 (11–85) | 75 (45–210) | 0.006 |
| Tumor grade | 1-2 | 46 (97.92%) | 1 (5.86%) | <0.001 |
| | 3 | 1 (2.08%) | 16 (94.14%) | |
| Mitotic number of Per 10 HPF, mean | | 3.42 (\pm 3.11) | 31.62 (\pm 13.32) | <0.001 |
| Stromal atypia | Mild/ Moderate | 45 (95.69%) | 3 (17.62%) | <0.001 |
| | Marked | 2 (4.31%) | 14 (82.38%) | |
| Cellular pleomorphism | No | 46 (97.89%) | 3 (17.61%) | <0.001 |
| | Yes | 1 (2.11%) | 14 (82.39%) | |
| Stromal overgrowth | No | 45 (95.68%) | 2 (11.82%) | <0.001 |
| | Yes | 2 (4.32%) | 15 (88.18%) | |
| Tumoral heterogeneity | No | 44 (93.59%) | 2 (11.79%) | <0.001 |
| | Yes | 3 (6.41%) | 15 (88.21%) | |
| Tumor margin irregularity | No | 35 (74.51%) | 2 (11.78%) | <0.001 |
| | Yes | 12 (25.49%) | 15 (88.22%) | |
| Ki-67, mean | | 2.43 (\pm 3.63) | 36.21 (\pm 8.52) | <0.001 |
| Initial surgery | BCS | 45 (95.74%) | 11 (64.71%) | 0.003 |
| | Mastectomy | 2 (4.26%) | 6 (35.29%) | |
| Margin positivity | | 4 (8.52%) | 5 (29.41%) | 0.048 |
| Overall surgery | BCS | 42 (89.43%) | 8 (47.18%) | 0.001 |
| | Mastectomy | 5 (10.57%) | 9 (52.82%) | |
| Local recurrence | | 4 (8.52%) | 6 (35.32%) | 0.017 |

HPF: high-power field, BCS: breast-conserving surgery

RESULTS

Patient characteristics

Phyllodes tumors were classified as follows: benign (n=36, 56.27%), borderline (n=11, 17.24%), and malign (n=17, 26.49%). The median age was 41 (range: 26–63) years, and the tumor size was 52 (range: 11–210) mm. Patients with malign PT were older than patients with benign & borderline PT (p=0.029), and tumors of malignant tumors were larger than those tumors of benign & borderline tumors (p=0.006). While the tumor grade of malign tumors was usually three, it was grade one or two for benign & borderline tumors (p<0.001). The mitotic number was significantly higher in malign phyllodes tumors (p<0.001). Marked stromal atypia, cellular pleomorphism, stromal overgrowth, tumoral heterogeneity, and tumor margin irregularity tended significantly more to exist in malign tumors compared with benign & borderline ones. The Ki-67 index of a malign PT was higher than the benign and borderline ones (p<0.001).

Fifty-six patients had BCS, whereas eight patients underwent a mas-

tectomy. Three patients underwent axillary sampling, and no nodal metastases were found. Three patients had re-excisions added to BCS, and six patients underwent mastectomy due to positive margins following BCS. Margin positivity was observed in nine out of 56 (16.14%) breast-conserving surgeries: five were malignant, two were borderline, and two were benign phyllodes tumors. Patients with malignant tumors underwent mastectomy more frequently than breast-conserving surgery (p=0.003). When the cases converted to mastectomy due to margin positivity were added, patients with malign PT still had more mastectomies (p=0.001). The overall mastectomy rate was 14/64 (21.92%). Local recurrence was observed more often in patients with malign PT than in patients with benign & borderline PT during the follow-up period (p=0.017).

Local recurrence

The median follow-up period was 72 (range: 12–124) months. Eight LR (three benign PT, one borderline PT, and four malign PT), one single distant metastasis (malign PT), and two LR plus distant metastasis (malign PT) occurred in follow-up, with a total of 10 LR. One LR developed following mastectomy, and the remaining nine following BCS. There is no relationship between recurrence and patient age (p=0.53). Large tumor size, tumor grade of three, high mitosis score, marked stromal atypia, cellular pleomorphism, stromal overgrowth, tumoral heterogeneity, tumor margin irregularity, and high ki-67 index had a role in the development of recurrence in univariate analyses. Among the factors affecting recurrence according to univariate analyses, other than large tumor size and tumor grade of three, others were also determined as independent significant risk factors in multivariate analysis. There was no difference in the recurrence rate following overall mastectomy and BCS (p=0.299). Seven patients developed LR with a surgical margin \geq 1 cm that could not be obtained, and three patients with a 1 cm clear margin (p=0.045). Therefore, a surgical margin of \geq 1 cm was critical in the LR. Tables 3 and 4 summarize the factors of recurrence.

Table 3. Features of recurrent phyllodes tumors

| Local recurrence | | No n=54 | Yes n=10 | p |
|------------------------------------|----------------|----------------------|----------------------|--------|
| Age, years, mean | | 39.22 (\pm 11.91) | 36.62 (\pm 11.92) | 0.532 |
| Tumor size, mm, mean | | 47.12 (\pm 41.93) | 85.51 (\pm 56.53) | 0.019 |
| Tumor grade | 1-2 | 42 (77.82%) | 5 (50.0%) | <0.001 |
| | 3 | 12 (22.18%) | 5 (50.0%) | |
| Mitotic number of Per 10 HPF, mean | | 8.22 (\pm 11.41) | 25.12 (\pm 20.91) | 0.001 |
| Stromal atypia | Mild/ Moderate | 43 (79.63%) | 5 (50.0%) | 0.06 |
| | Marked | 11 (20.37%) | 5 (50.0%) | |
| Cellular pleomorphism | No | 45 (83.32%) | 4 (40.0%) | 0.008 |
| | Yes | 9 (16.69%) | 6 (60.0%) | |
| Stromal overgrowth | No | 43 (79.64%) | 4 (40.0%) | 0.017 |
| | Yes | 11 (20.36%) | 6 (60.0%) | |
| Tumoral heterogeneity | No | 42 (77.83%) | 4 (40.0%) | 0.024 |
| | Yes | 12 (22.17%) | 6 (60.0%) | |
| Tumor margin irregularity | No | 37 (68.52%) | 0 | <0.001 |
| | Yes | 17 (31.53%) | 10 (100.0%) | |
| Ki-67, mean | | 6.12 (\pm 6.61) | 17.82 (\pm 15.31) | 0.001 |
| Overall surgery | BCS | 41 (82.0%) | 9 (90.0%) | 0.299 |
| | Mastectomy | 13 (18.0%) | 1 (10.0%) | |
| Margin | 2-10 mm | 19 (35.22%) | 7 (70.0%) | 0.045 |
| | >10 mm | 35 (64.78%) | 3 (30.0%) | |

HPF: high-power field, BCS: breast-conserving surgery

Table 4. Multivariate analysis on recurrence

| | Odds Ratio | p | 95% C.I. for EXP(B) | |
|--|------------|-------|---------------------|-------|
| | | | Lower | Upper |
| Tumor size ≥ 50 mm | 1.27 | 0.071 | 0.88 | 1.43 |
| Tumor grade 1-2 vs. 3 | 1.25 | 0.082 | 0.86 | 1.41 |
| Mitotic number of ≥ 20 per 10 HPF | 1.76 | 0.025 | 1.40 | 2.44 |
| Cellular pleomorphism | 2.02 | 0.015 | 1.75 | 3.21 |
| Stromal overgrowth | 1.77 | 0.017 | 1.41 | 2.45 |
| Tumoral heterogeneity | 1.66 | 0.022 | 1.27 | 2.68 |
| Tumor margin irregularity | 2.98 | 0.004 | 0.22 | 6.72 |
| Ki-67 ≥ 20 | 2.04 | 0.014 | 1.76 | 3.25 |
| Nagelkerke R Square | 0.63 | | | |
| Hosmer and Lemeshow Test | 0.97 | | | |
| HPF: high-power field, CI: 95% confidence interval | | | | |

Among patients with malign PT, two patients received adjuvant CT plus RT, and one patient received only CT following mastectomy. Three patients who underwent conservative surgery had CT and RT, and four received only RT. Lung metastasis developed in the eleventh month, and bone metastasis in the eighth month after surgery. Three recurrences developed in patients following conservative surgery who received RT. Nine of 17 patients with malign PT in our series received RT. Three of six malignant phyllodes cases with LR were among the patients who received adjuvant RT, and three LRs developed in the remaining 11 cases with malign PT who did not receive RT. In addition, LR developed in two of six patients who received adjuvant CT during the follow-up.

Study endpoint

Regarding recurrent phyllodes tumors, a common tumor feature to predict recurrence for benign & borderline and also for malign tumors was tumor margin irregularity. In addition, LR developed in three of four benign phyllodes tumors and one of four borderline tumors with tumor margin irregularity based on definitive pathological examination. The median recurrence time was 29.5 (range: 10–64) months. Five re-excisions could be performed in patients with recurrence within the first three years (mean, 13.82 months) after conservative surgery. However, patients required four mastectomies (mean, 50.52 months) due to the prolonged recurrence detection process. A possible explanation was that it was due to the rapid growth pattern of these tumors. All recurrent benign & borderline tumors underwent conservative surgeries, and excisions were within a 2–5 mm surgical margin, which led to the interpretation that this surgical margin may not be sufficient for benign and borderline tumors with margin irregularity. Features of recurrent phyllodes tumors are shown in Table 5.

Table 5. Recurrent phyllodes tumors

| Tumor type | Age | Size, mm | Grade | Mitotic number | P/O/H | M.I. | Surgery | Margin, mm | LRFS, months | Overall surgery |
|------------|-----|----------|-------|----------------|-------|------|---------|------------|--------------|-----------------|
| Benign | 26 | 23 | 1 | 1 | - | + | BCS | 2–5 | 10 | Rx |
| Benign | 28 | 40 | 1 | 1 | - | + | BCS | 2–5 | 18 | Rx |
| Benign | 33 | 130 | 1 | 1–2 | - | + | BCS | 2–5 | 43 | Mas |
| Borderline | 27 | 20 | 1 | 5 | - | + | BCS | 2–5 | 56 | Mas |
| Malign | 43 | 54 | 3 | 45 | + | + | BCS | >10 | 14 | Rx |
| Malign | 29 | 110 | 3 | 40 | + | + | BCS | 5–10 | 39 | Mas |
| Malign | 53 | 210 | 3 | 50 | + | + | Mas | 5–10 | 26 | Rx-Mas |
| Malign | 41 | 70 | 3 | 50 | + | + | BCS | >10 | 11 | Rx |
| Malign | 33 | 40 | 3 | 20 | + | + | BCS | >10 | 64 | Mas |
| Malign | 38 | 55 | 3 | 40 | + | + | BCS | 5–10 | 16 | Rx |

LRFS: local recurrence-free survival, BCS: breast-conserving surgery, Rx: re-excision, mm: millimeter, Mas: mastectomy, P/O/H: pleomorphism, overgrowth, heterogeneity, M.I.: margin irregularity

DISCUSSION

Phyllodes tumors account for 0.5% of all breast neoplasms.¹⁸ These tumors peak between 35–49 years of age, while fibroadenomas (FA), which can be difficult to differentiate diagnostically, are usually observed at a younger age.¹⁹ The median age of our series was 41 (range: 26–63) years. In addition, patients with malign PT were older than patients with other PT subtypes.

Typically a PT appears on ultrasound and mammography as a clinically fast-growing mass with a smoothly circumscribed or slightly lobulated contour.²⁰ All patients in this series underwent USG and MG, except in some cases MG due to young age. In some studies performed with MRI, there were no significant differences between benign PT and FA. However, malignant PT usually had a higher contrast enhancement pattern in T1-weighted sections than benign PT.²¹ In our series, all patients with preoperative diagnosis of mixed histology or malignant PT underwent a magnetic resonance imaging, but not in all cases with benign PT diagnosis. In this study, marked stromal atypia, cellular pleomorphism, stromal overgrowth, tumoral heterogeneity, and tumor margin irregularity tended significantly more to exist in malign tumors compared with benign & borderline ones. In addition, while 60–70% of these tumors were benign in other series, this rate was 56.3% in our series, with a relatively lower rate of benign tumors.²² A possible explanation was due to the tendency of surgeons to probably not refer patients diagnosed with benign PT to a cancer center.

The literature indicates that the average size of phyllodes tumors typically ranges from 4 to 7 cm.²³ Additionally, Mallick et al. noted that the median size of malignant tumors can reach as high as 13.6 cm.²⁴ In our study, the median tumor size was 52 (range: 11–210) mm, with malignant tumors measuring larger (75 mm) compared to the benign and borderline subtypes (42 mm).

According to the National Comprehensive Cancer Network (NCCN), the standard approach involves excision with a safe margin of at least 1 cm, without axillary staging. Ensuring a wide margin during excision is essential, as narrower surgical margins are linked to an increased risk of local recurrence.²⁵ A simple mastectomy may be necessary whenever margin control may not be sufficient or large or multiple tumors.^{25,26} Demian et al. reported a mastectomy rate of 48.5%. Patients in this report underwent 56/64 (87.5%) BCS and 14/64 (21.8%) mastectomy. These small tumor sizes and relatively low mastectomy rates may be due to the rapid presentation of patients and successful screening programs in our case series. In the same study, the positive margin rate was 24% and 15% for malignant tumors and borderline subtypes, respectively.²⁷ In our study, the likelihood of margin positivity following breast-conserving surgery (BCS) was significantly greater in patients with malignant phyllodes tumors

compared to those with benign and borderline tumors (45% versus 9%). This higher rate of margin positivity may be attributed to our inclination to perform BCS (with or without reconstruction) and the inability to achieve a clear surgical margin of 1 cm in all cases of malignant phyllodes tumors.

Although studies show that adjuvant RT contributes to decreasing the recurrence rate for malignant tumors, it is still controversial. In this series, LR developed in one patient who underwent a mastectomy and received RT, and three LR developed in patients following conservative surgery who received RT. Nine of 17 patients with malignant PT in our series received RT. Three of six malignant phyllodes cases with LR were among the patients who received adjuvant RT, and three LR developed in the remaining 11 cases with malignant PT who did not receive RT. During the follow-up period, LR occurred in two out of six patients who received adjuvant CT. The effectiveness of CT remains a contentious issue. In our series, four patients with malignant phyllodes tumors underwent CT, with two developing distant metastasis and one experiencing local recurrence. As a result, this study could not definitively demonstrate a positive impact of RT and CT.

The overall rate of local recurrence in our study was 15.6% (10 out of 64 patients), and 18% (nine out of 50 patients) following breast-conserving surgery, which is relatively high compared to the literature, which reports rates ranging from 8% to 19%.²⁸ According to the National Comprehensive Cancer Network (NCCN) guidelines, a minimum negative surgical margin of 1 cm is recommended to lower the risk of recurrence.²⁶ In our retrospective study, the threshold for a clear tumor-free margin for re-excision was set at 2 mm, resulting in none of the cases having a clear margin of 1 cm. This finding may account for the elevated recurrence rate observed.

A large meta-analysis by Yu C-Y et al. identified several risk factors for recurrence, including stromal atypia, high cellularity, stromal overgrowth, a mitotic count of five or more, border irregularity, and margin positivity, in addition to tumor size exceeding 5 cm.²⁹ Our study corroborated these potential risk factors associated with the occurrence of local recurrence.

Again, according to the NCCN guidelines, the recommendation for borderline and malignant tumors was close follow-up for three years.²⁵ In our study, re-excision is sufficient instead of mastectomy in recurrences detected in the first three years. In our series, patients underwent mastectomy in relapses exceeding three years, possibly due to rapid growth patterns. In conclusion, our study may support the interpretation that all types of PT require a 3-year close follow-up after surgery.

Of course, the limitation of our study is that contrary to the current guidelines, there was no surgical margin of 1 cm in all borderline or malignant PT cases. This finding may present insufficient information regarding post-surgical outcomes or possible CT and RT contributions.

CONCLUSION

Phyllodes tumors are rare fibroepithelial neoplasms with substantial potential for local recurrence and distant metastasis. In particular, the recommendation should be to remove a malignant PT with a surgical margin of at least 1 cm in line with current guidelines. In addition, LR developed in three of four benign tumors and one of four borderline tumors with tumor margin irregularity based on definitive pathological examination. These surgical margins were within a 1 cm surgical margin. Therefore, the study may suggest that the excision of benign or borderline tumors should be in the same way as a malignant PT, at least to provide a clear surgical margin of 1 cm macroscopically. In addition, for patients with benign and borderline PT, even if the patient is young, especially if tumor margin irregularity is detected as a result of definitive pathological examination because recurrences generally occur in a short period, the study may extrapolate that a minimum of three years of close follow-up should be kept to avoid mastectomy due to recurrence, perhaps.

Acknowledgments: We would like to acknowledge Dr. Süleyman Bademler for his guidance and direction in this article. No financial support was received from any institution or individual for this study.

Conflicts of Interest: There are no conflicts of interest to disclose.

Author Contributions: Concept, design, data collection and analysis: B.İ., conducting a literature review and composing the article: B.K.

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