Ann Surg Oncol (2019) 26:2136–2143
https://doi.org/10.1245/s10434-019-07210-4

Annals of
SURGICAL ONCOLOGY
OFFICIAL JOURNAL OF THE SOCIETY OF SURGICAL ONCOLOGY

ORIGINAL ARTICLE – BREAST ONCOLOGY

Long-Term Outcomes After Surgical Treatment of Malignant/Borderline Phyllodes Tumors of the Breast

Philip M. Spanheimer, MD[1], Melissa P. Murray, DO[2], Emily C. Zabor, MS[3], Michelle Stempel, MPH[1], Monica Morrow, MD[1], Kimberly J. Van Zee, MD, MS[1], and Andrea V. Barrio, MD[1]

[1]Breast Service, Department of Surgery, Memorial Sloan Kettering Cancer Center, New York, NY; [2]Breast Pathology Service, Department of Pathology, Memorial Sloan Kettering Cancer Center, New York, NY; [3]Biostatistics Service, Department of Epidemiology and Biostatistics, Memorial Sloan Kettering Cancer Center, New York, NY

ABSTRACT

Background. Malignant/borderline phyllodes tumors (PTs) are rare, and little is known about their long-term prognosis. This study sought to evaluate recurrence rates and identify factors associated with local and distant failure.

Methods. From 1957 to 2017, we identified 124 patients with 125 PTs (86 malignant and 39 borderline). Recurrence rates and survival were assessed using the Kaplan–Meier method, and correlated with clinicopathologic factors using the log-rank test.

Results. The median age of the patients was 44 years, and the median tumor size was 5 cm. Breast-conserving surgery was performed for 57% of the patients. At a median follow-up of 7.1 years, 14 patients experienced a locoregional recurrence (LRR), with a 10-year cumulative LRR incidence of 12%. On univariable analysis, age younger than 40 years ($p = 0.02$) and close/positive margins ($p = 0.001$) were associated with increased risk of LRR. Seven patients developed distant disease, all occurring in malignant PTs. The 10-year distant recurrence-free survival was 94%. Uniformly poor pathologic features consisting of marked stromal cellularity, stromal overgrowth, infiltrative borders, and 10 or more mitoses per 10 high-power fields (hpf) were identified in 25 PTs (20%), and all distant recurrences occurred in this group. For the patients who did not have uniformly poor features, the 10-year disease-specific survival was 100%, and the overall survival was 94% compared with 66% and 57%, respectively, among those with poor features.

Conclusion. Malignant/borderline PTs without uniformly poor histologic features have an excellent prognosis after surgical resection, with a 10-year disease-specific survival of 100%. The presence of uniformly poor pathologic features predicts a poor prognosis. Efforts should be directed toward new treatment approaches for these tumors.

Malignant phyllodes tumors (PTs) are rare neoplasms of the breast, with an estimated annual incidence of 2.1 cases per 1,000,000 women.[1] The primary treatment for malignant PT is complete surgical excision with either breast-conserving surgery (BCS) or mastectomy,[2,3] with little known benefit from adjuvant chemotherapy or radiation therapy.[4–6]

Due to the rarity of malignant PT, little is known about its long-term prognosis, with local and distant failure rates reported to range from 10–65% and 5–30%, respectively.[7–13] Furthermore, clinicopathologic factors associated with recurrence are inconsistent in the literature, providing little guidance on how patients should be counseled regarding prognosis after surgical excision. Current single-institution data are limited by small sample size,[4,14,15] and publications using larger national databases lack detailed pathologic data that can be linked to outcomes.[2,5]

Notably, the boundary between malignant and borderline PT is ill defined because these tumors demonstrate overlapping histologic features.[16] In addition, the grading of PT has changed over time, so the uncertainties concerning the prognosis and management of malignant PT are

Presented in poster format at the 19th Annual Meeting of the American Society of Breast Surgeons, 2–6 May 2018, Orlando, FL, USA.

First Received: 6 September 2018;
Published Online: 19 February 2019

A. V. Barrio, MD
e-mail: barrioa@mskcc.org

equally applicable to borderline tumors. In this report, we review our single-institution experience with malignant/borderline PTs during a 50-year period to evaluate recurrence rates and survival, and to identify factors associated with local and distant failure.

METHODS

After institutional review board approval, we reviewed the cancer registry records at Memorial Sloan Kettering Cancer Center (MSK) for patients with malignant/borderline PT. Between April 1957 and July 2017, we identified 124 patients with 125 malignant/borderline PTs who had definitive surgery at MSK. Clinical, pathologic, and follow-up data were obtained by chart review.

Available pathology slides (43 of 125 cases, 34%) were re-reviewed by a breast pathologist. One of these cases was reclassified from malignant to borderline. For the remaining cases, characterization of the tumors was based on the original pathology report.

Tumors were classified as borderline or malignant based on different grading schemes throughout the study period using pathologic characteristics such as stromal cellularity, stromal overgrowth, tumor borders, number of mitoses, and necrosis. Stromal cellularity was categorized as marked if there were confluent areas of densely overlapping stromal nuclei, or as mild to moderate if there was a slight to intermediate increase in stromal cells with evenly spaced nuclei or some overlapping nuclei. Stromal overgrowth was defined as the presence of stroma without epithelium in at least one low-power field as observed with a 4x microscopic objective.

The tumor border was characterized as infiltrative if invasion was noted, or as circumscribed/pushing if there was displacement of the breast parenchyma without invasion or no breast parenchyma displacement. Mitotic count was calculated as the number of mitoses observed over 10 high-power fields (hpf) and stratified according to a cutoff of 10 or more mitoses per 10 hpf. Tumor necrosis was defined as the presence of ghosts of tumor cells retaining phyllodes architecture within the tumor.

The excision margin was recorded as close/positive if the tumor was present at or within 1 mm of the inked tissue edge. Margins of 1 mm or wider were recorded as negative. Margin status was determined from the last surgical procedure.

Locoregional recurrence was defined as recurrence in the breast or chest wall, or within the ipsilateral regional nodal basins. Distant disease was defined as metastatic disease or inoperable locoregional disease extending directly into the chest cavity. Time to recurrence or death was calculated from the date of surgical resection.

Continuous variables were summarized using median (range), and categorical variables were summarized using frequency (%). Comparisons between borderline and malignant histology groups were tested using the Kruskal–Wallis test for continuous variables, and Fisher's exact test for categorical variables. The Kaplan–Meier method was used to estimate distant recurrence-free survival (DRFS), disease-specific survival (DSS) defined as time from surgery to death from disease, and overall survival (OS). The cumulative incidence of local recurrence (LR) was estimated using one minus the Kaplan–Meier estimate of local recurrence-free survival. The log-rank test was used for comparisons between borderline and malignant histology groups. Univariable hazard ratios were estimated using Cox regression. Patients with uniformly poor pathologic features were defined as those with marked stromal cellularity, stromal overgrowth, infiltrative borders, and 10 mitoses or more per 10 hpf. A p value less than 0.05 was considered statistically significant. All statistical analyses were performed using R version 3.4.2 (R Core Development Team, Vienna, Austria).

RESULTS

Clinicopathologic Characteristics

Of the 124 patients with malignant/borderline PT, 1 had a bilateral tumor, for a total of 125 cases, of which 86 were malignant and 39 were borderline. Table 1 shows the clinicopathologic characteristics of the study cohort overall and stratified by malignant and borderline histology.

The median patient age was 44 years (range 13–83 years), and the median pathologic tumor size was 5 cm (range 0.9–35 cm). Patients with malignant PT had larger tumors than those with borderline PT (median 5.3 vs 3 cm; $p < 0.001$), and were more likely to have poor pathologic features including marked stromal cellularity ($p < 0.001$), stromal overgrowth ($p = 0.001$), infiltrative borders ($p = 0.006$), and 10 or more mitoses per 10 hpf ($p < 0.001$).

Overall, 57% of the patients were treated with BCS and 43% with mastectomy. The majority (87%) had a negative final excision margin. Adjuvant chemotherapy and radiotherapy were rarely used (1.6% and 0.8%, respectively).

Locoregional Recurrence

At a median follow-up of 7.1 years (range 0–32.2 years), 14 patients had experienced a locoregional recurrence (LRR), of which 12 were local, 1 was locoregional (breast + ipsilateral axilla), and 1 was regional (ipsilateral axilla). The 5- and 10-year cumulative

TABLE 1 Clinicopathologic characteristics of the study cohort stratified by histology

Characteristic	Total (n = 125)	Malignant (n = 86)	Borderline (n = 39)	p value
Median age: years (range)	44 (13–83)	43 (13–83)	44 (14–77)	0.8
Median pathologic tumor size: cm (range)	5 (0.9–35)	5.3 (0.9–35)	3 (0.9–22)	< 0.001
Stromal cellularity[a], n (%)				< 0.001
Mild/moderate	37 (30)	16 (19)	21 (54)	
Marked	70 (56)	55 (64)	15 (39)	
Stromal overgrowth[a], n (%)				0.001
No	58 (46)	31 (36)	27 (69)	
Yes	45 (36)	38 (44)	7 (18)	
Borders[a], n (%)				0.006
Circumscribed/pushing	43 (34)	23 (27)	20 (51)	
Infiltrative	68 (54)	54 (63)	14 (36)	
Mitosis[a], n (%)				< 0.001
< 10	53 (42)	24 (28)	29 (74)	
≥ 10	48 (38)	44 (51)	4 (10)	
Necrosis[a], n (%)				0.03
No	93 (74)	58 (67)	35 (90)	
Yes	19 (15)	17 (20)	2 (5)	
Uniformly poor pathologic features[a], n (%)				< 0.001
No	67 (54)	38 (44)	29 (74)	
Yes	25 (20)	25 (29)	0 (0)	
Surgery, n (%)				0.003
Breast-conserving surgery	71 (57)	41 (48)	30 (77)	
Mastectomy	54 (43)	45 (52)	9 (23)	
Final margin, n (%)				0.09
Negative	109 (87)	78 (91)	31 (79)	
Close/positive	16 (13)	8 (9)	8 (21)	

[a]Unknown, stromal cellularity (n = 18), stromal overgrowth (n = 22), borders (n = 14), mitosis (n = 24), necrosis (n = 13), uniformly poor pathologic features (n = 33)

incidence of LRR for the entire cohort was 11% (95% confidence interval [CI], 5–17%) and 12% (95% CI 6–19%), respectively (Fig. 1a), with a similar 10-year incidence of LRR between patients with borderline (11%) and malignant (13%) PTs (log-rank p = 0.87) (Fig. 1b).

Of 14 LRRs, 13 developed within 6 years, with the final LRR occurring nearly 14 years after surgery. On univariable analysis, factors associated with a higher incidence of LRR included age younger than 40 years (10-year cumulative incidence: 21% [age < 40] vs 7% [age ≥ 40], log-rank p = 0.02) and close/positive margins (10-year cumulative incidence: 33% [close/positive] vs 9% [negative], log-rank p = 0.001). There was no significant association between age and type of surgery (p = 0.26) or age and margin status (p = 0.26). Individual histologic characteristics were not associated with LRR (Table 2). Overall, BCS demonstrated a higher 10-year cumulative incidence of LRR (16%) than mastectomy (8%), but this difference was not statistically significant (log-rank p = 0.11) (Table 2). Among those with a negative final margin, the 10-year cumulative incidence of LRR was 12% with BCS versus 6% with mastectomy (log-rank p = 0.17).

Distant Metastasis and Survival

Of the 124 patients, 7 developed distant disease, 6 within 5 years of surgery. Two of the seven distant recurrences (DRs) were preceded by an LR. The distant metastatic sites included lung, brain, bone, epidural space, and direct local extension to the parasternal region/mediastinum. Overall, the 5- and 10-year DRFS was 95% (95% CI 91–99%) and 94% (95% CI 89–98%), respectively (Fig. 2), and DR was not observed in patients with borderline histology. DR occurred only in patients whose tumors had uniformly poor pathologic features, including marked stromal cellularity, stromal overgrowth, infiltrative

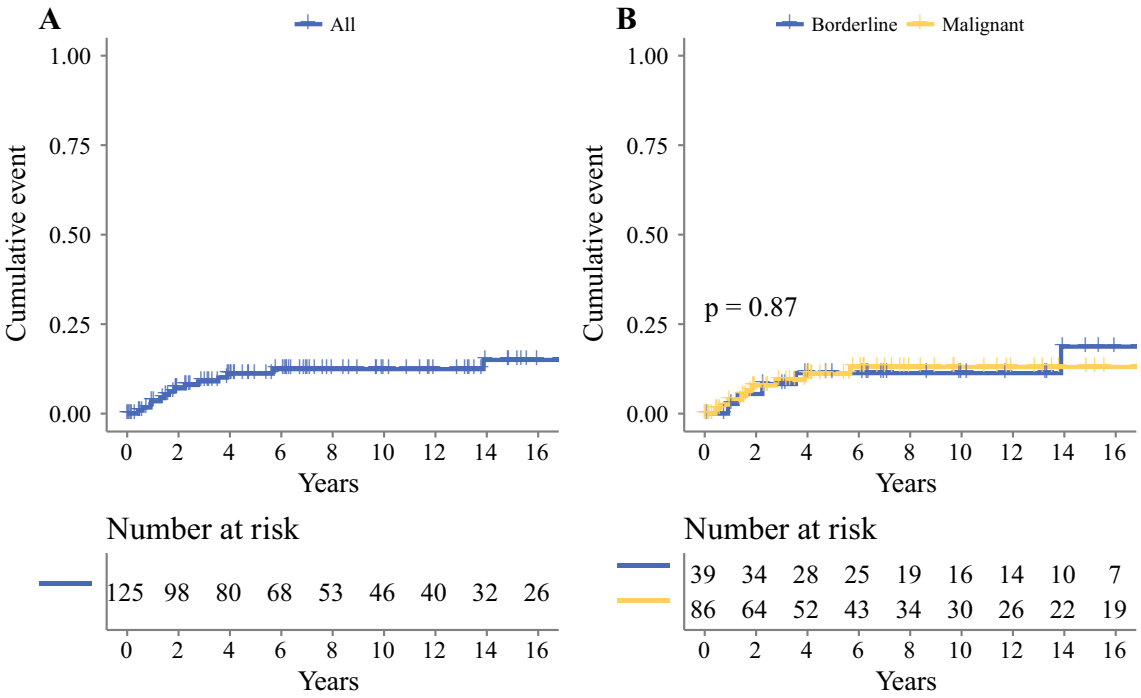

FIG. 1 Cumulative incidence of locoregional recurrence **a** for all patients and **b** stratified by malignant versus borderline histology

borders, and 10 or more mitoses per 10 hpf. These features were identified in only 25 (29%) of 86 malignant PTs overall. None of the patients without uniformly poor pathologic features (100 patients altogether, and 66 patients with complete data) developed distant disease.

Six of the seven patients with distant disease died of their disease a median of 5 months (range, 1–10 months) after diagnosis of metastasis. For the entire cohort, the 10-year DSS was 94% (95% CI 90–99%), and the 10-year OS was 90% (95% CI 83–96%). In the patients without uniformly poor pathologic features, the 10-year DSS and OS were 100% and 94% (95% CI 87–100%), respectively, compared with 66% (95% CI 45–97%) and 57% (95% CI 37–88%), respectively, in the patients with uniformly poor features (Fig. 3).

DISCUSSION

Given the rarity of malignant/borderline PTs, it often is difficult to counsel patients about appropriate surgical management and prognosis after surgical excision, and the long-term incidence of local and distant relapse remains uncertain. The purpose of our study was to evaluate a large cohort of patients with malignant/borderline PT from a single institution to better understand the incidence and patterns of LR and DR, and to identify reproducible factors associated with recurrence.

Overall, the 10-year incidence of LRR was approximately 12% and did not vary between tumors classified as borderline versus malignant, suggesting that individual histologic characteristics were not important predictors of local failure. However, LRR incidence was significantly higher for the patients younger than 40 years of age and for those with close/positive final surgical margins. Due to the small number of local failures, multivariable analysis could not be performed. However, we found no association between age and either surgery type or margin status, suggesting that these factors are not potential confounders of the association between age and LRR.

In a study of 192 patients with PT, Wei et al.[17] similarly demonstrated a three-fold increase in LRR among patients diagnosed before the age of 35 years compared with older patients, although this has not been reported in other studies.[18–20] Given the small number of patients in our study younger than 40 years of age ($n = 42$), we do not suggest that these patients warrant more aggressive surgical management other than obtaining negative surgical margins. However, patients younger than 40 years of age should undergo continued surveillance with annual breast imaging, as recommended for women 40 years of age or older, to monitor for LR.

Similar to our study, several other studies have demonstrated that close or positive margins are associated with an increased risk of LR among patients with PTs.[10,13,19,21] Consequently, the National Comprehensive Cancer Network (NCCN) guidelines recommend excision

TABLE 2 Factors associated with locoregional recurrence

Characteristic	10-year LRR cumulative incidence % (95% CI)	HR (95% CI)	*p* value
Age (years)			0.02
< 40	21 (7–33)	1.00	
≥ 40	7 (1–13)	0.3 (0.1–0.89)	
Histology			0.87
Borderline	11 (0–21)	1.00	
Malignant	13 (5–21)	0.91 (0.31–2.72)	
Stromal cellularity			0.25
Mild/moderate	8 (0–17)	1.00	
Marked	17 (6–26)	2.11 (0.58–7.67)	
Stromal overgrowth			0.79
No	11 (2–19)	1.00	
Yes	13 (0–24)	0.84 (0.25–2.9)	
Borders			0.55
Circumscribed/pushing	15 (3–26)	1.00	
Infiltrative	13 (3–22)	0.73 (0.26–2.08)	
Mitosis			0.93
< 10	12 (3–21)	1.00	
≥ 10	15 (1–27)	1.06 (0.33–3.35)	
Necrosis			0.47
No	12 (5–19)	1.00	
Yes	32 (0–62)	1.75 (0.38–8.13)	
Surgery			0.11
Breast-conserving surgery	16 (6–24)	1.00	
Mastectomy	8 (0–16)	0.37 (0.1–1.31)	
Final margin			0.001
Negative	9 (3–15)	1.00	
Close/positive	33 (5–53)	4.97 (1.66–14.88)	

LRR, locoregional recurrence; CI, confidence interval; HR, hazard ratio

of PT with a margin of 1 cm or wider[3] to minimize the risk of LR. Although our study also demonstrated an increased risk of LR with close (defined as < 1 mm) or positive margins, the ideal negative margin width after excision of PT has yet to be defined.

Among patients with benign PT, the 1 cm margin recommendation has been challenged, with several recent studies demonstrating similar rates of LR with narrow versus wider margins.[15,22,23] However, these data cannot be extrapolated to malignant/borderline PT. Based on our data, at minimum, a margin of at least 1 mm after BCS or mastectomy was associated with a significantly lower 10-year risk of LR (9%) compared to a margin smaller than 1 mm or a positive margin (33%) ($p = 0.001$), a finding also observed in a recent multicenter Korean study of malignant and borderline PT.[19] Efforts should be made to achieve a margin of at least 1 mm when feasible to minimize the risk of LR.

We also found no significant reduction in LR with mastectomy, which potentially has the widest negative margin that can be obtained, compared with BCS, for patients with malignant/borderline PT. Although the 10-year incidence of LR was numerically higher for the patients undergoing margin-negative BCS than for those undergoing mastectomy (12% vs 6%; log-rank $p = 0.17$), the rates of LR were acceptably low with either treatment. These findings suggest that even among patients with malignant/borderline PT, BCS is an appropriate treatment option provided that negative margins can be achieved with an acceptable cosmetic outcome.

Most of our patients did not receive adjuvant radiotherapy, so we were unable to draw definitive conclusions regarding this treatment. However, given the low rates of LR observed in our study among patients with negative margins after BCS and mastectomy without radiotherapy, it

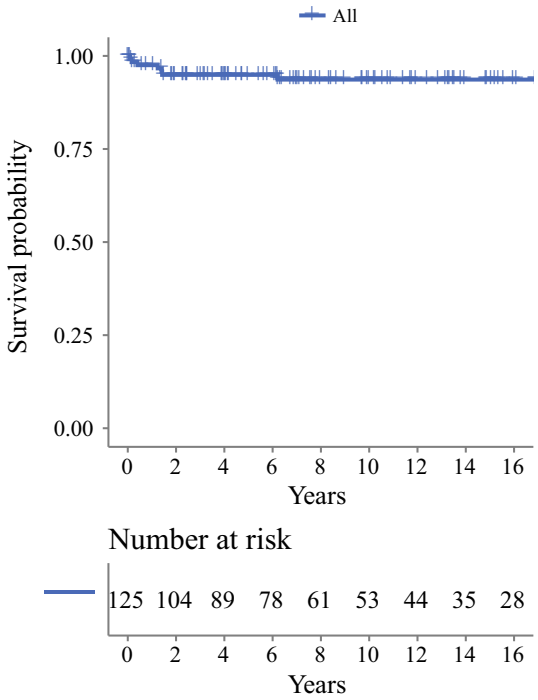

FIG. 2 Distant recurrence-free survival for the entire cohort

is unlikely that adjuvant radiotherapy would provide additional meaningful benefit for these patients, which is in keeping with observations from other studies.[2,5]

Overall, we found a low rate of DR for patients with malignant/borderline PT (10-year DRFS, 94%). However, unlike local failures, which were not influenced by histologic features, all DRs occurred in patients with malignant PT whose tumors had uniformly poor pathologic features including marked stromal cellularity, stromal overgrowth, infiltrative borders, and 10 or more mitoses per 10 hpf. The majority (80%) of the patients with malignant/borderline PT did not have uniformly poor histologic features, and those patients had a 10-year DSS of 100% and an OS of 94%, suggesting that surgery alone results in a negligible risk of distant failure for this subset.

The presence of uniformly poor pathologic features was seen in 29% of patients with malignant PT and predicted a poor prognosis, with a 10-year DSS of 63% and a 10-year OS of 57%. Additionally, the development of distant metastasis led to death in six of seven patients at a median of 5 months after diagnosis of distant disease. The difference in prognosis observed between patients with and without uniformly poor features suggests that the current classification system may be inadequate for prognostication. Consideration should be given to creation of a new classification system whereby only tumors with uniformly poor features are considered "malignant" given their significant metastatic potential, and those lacking these features can be reclassified into a different "non-malignant" category.

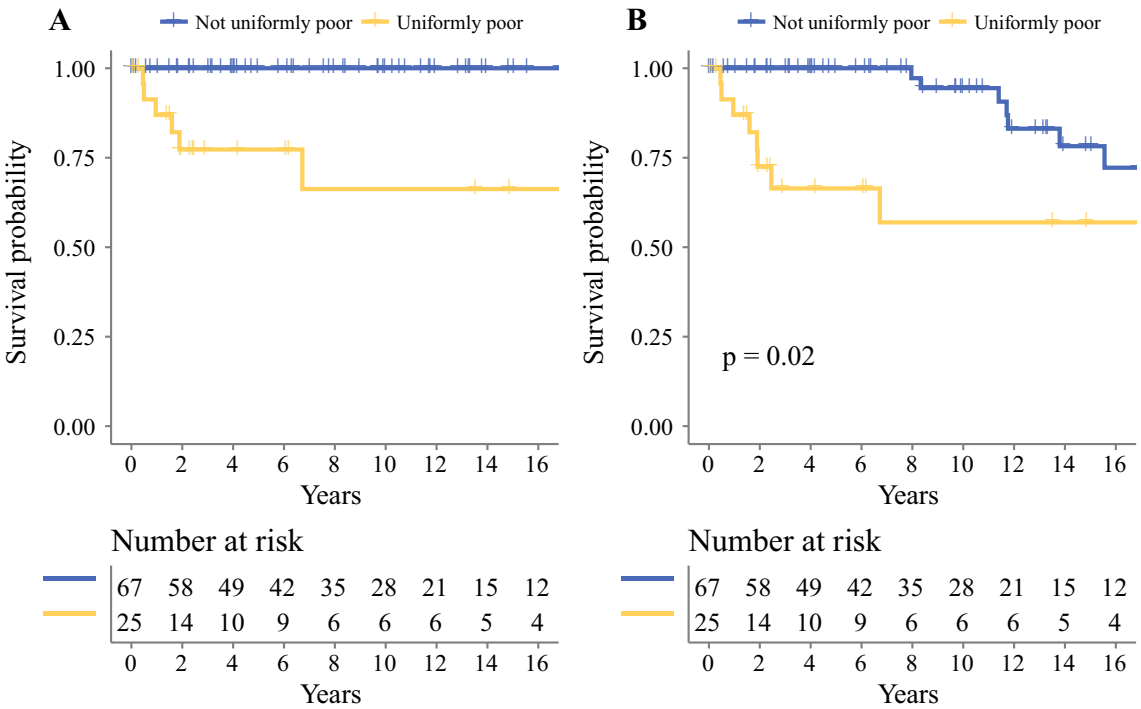

FIG. 3 **a** Disease-specific survival and **b** overall survival by pathologic features

Although the presence of uniformly poor pathologic features can be used to identify patients at high risk for distant failure, there is currently no systemic therapy regimen that is known to improve outcome in patients with malignant PT. Further study of these patients on a molecular level is needed to potentially identify unique genetic alterations that could be targeted with novel therapies in the future.

Our study was limited by its retrospective nature and small sample size, which was largely related to the rarity of malignant/borderline PT in the population. Additionally, we included patients with borderline histology in our study cohort due to the histologic similarities between borderline and malignant PT, and differences in grading schemes during the long study period. Although the LRR rates between borderline and malignant PT were similar, DR occurred only in malignant PT with uniformly poor features. However, DR was not observed in patients with malignant/borderline PT who did not have uniformly poor features, arguing that the presence of multiple poor features is more important in determining prognosis than the histologic designation. Margin width was dichotomized in our study as less than 1 mm (close) or 1 mm or wider (negative), and, as a result, the relationship between local recurrence and margin width could not be examined.

Finally, only about one-third of pathology slides were available for re-review by a breast pathologist. Because histologic definitions for PT have changed over time, re-review of additional slides may have resulted in a revised histologic diagnosis for a proportion of cases, which could have had an impact on the study findings.

CONCLUSIONS

Overall, patients with malignant/borderline PT have a low LRR rate after surgical excision without adjuvant therapy, with similar rates observed for patients with borderline versus malignant histologies. Higher rates were observed for patients younger than 40 years of age and those with close/positive margins. Young age does not mandate mastectomy for patients with malignant/borderline PT. However, young women should be monitored closely for recurrence after excision with annual breast imaging. Efforts should be made to achieve negative margins for all patients after surgery for malignant/borderline PT to minimize the risk of local failure. The ideal negative margin width has yet to be defined, but should be at least 1 mm. In this study, DR was rare and occurred only in patients with uniformly poor pathologic features, such as marked stromal cellularity, stromal overgrowth, infiltrative borders, and 10 or more mitoses per 10 hpf. Malignant/borderline PTs without multiple poor histologic features have an excellent prognosis after surgical resection, with a 10-year DSS of 100%. Uniformly poor pathologic features predict poor prognosis and represent a group of patients who require further study and novel treatment strategies.

ACKNOWLEDGMENT The preparation of this manuscript was funded in part by NIH/NCI Cancer Center Support Grant No. P30 CA008748 to Memorial Sloan Kettering Cancer Center.

DISCLOSURE Dr. Monica Morrow has received speaking honoraria from Roche and Genomic Health, and Dr. Andrea V. Barrio has received speaking honorarium from Roche.

REFERENCES

1. Bernstein L, Deapen D, Ross RK. The descriptive epidemiology of malignant cystosarcoma phyllodes tumors of the breast. *Cancer*. 1993;71:3020–4.
2. Macdonald OK, Lee CM, Tward JD, Chappel CD, Gaffney DK. Malignant phyllodes tumor of the female breast: association of primary therapy with cause-specific survival from the Surveillance, Epidemiology, and End Results (SEER) program. *Cancer*. 2006;107:2127–33.
3. National Comprehensive Cancer Network. Phyllodes Tumor. Version 1.2018. Retrieved 20 June 2018 at https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf.
4. Barth RJ Jr, Wells WA, Mitchell SE, Cole BF. A prospective, multi-institutional study of adjuvant radiotherapy after resection of malignant phyllodes tumors. *Ann Surg Oncol*. 2009;16:2288–94.
5. Gnerlich JL, Williams RT, Yao K, Jaskowiak N, Kulkarni SA. Utilization of radiotherapy for malignant phyllodes tumors: analysis of the National Cancer Data Base, 1998–2009. *Ann Surg Oncol*. 2014;21:1222–30.
6. Morales-Vasquez F, Gonzalez-Angulo AM, Broglio K, Lopez-Basave HN, Gallardo D, Hortobagyi GN, De La Garza JG. Adjuvant chemotherapy with doxorubicin and dacarbazine has no effect in recurrence-free survival of malignant phyllodes tumors of the breast. *Breast J*. 2007;13:551–6.
7. Abdalla HM, Sakr MA. Predictive factors of local recurrence and survival following primary surgical treatment of phyllodes tumors of the breast. *J Egypt Natl Cancer Inst*. 2006;18:125–33.
8. Asoglu O, Ugurlu MM, Blanchard K, Grant CS, Reynolds C, Cha SS, Donohue JH. Risk factors for recurrence and death after primary surgical treatment of malignant phyllodes tumors. *Ann Surg Oncol*. 2004;11:1011–7.
9. Barrio AV, Clark BD, Goldberg JI, Hoque LW, Bernik SF, Flynn LW, Susnik B, et al. Clinicopathologic features and long-term outcomes of 293 phyllodes tumors of the breast. *Ann Surg Oncol*. 2007;14:2961–70.
10. Barth RJ Jr. Histologic features predict local recurrence after breast-conserving therapy of phyllodes tumors. *Breast Cancer Res Treat*. 1999;57:291–5.
11. Guillot E, Couturaud B, Reyal F, Curnier A, Ravinet J, Lae M, Bollet M, et al. Management of phyllodes breast tumors. *Breast J*. 2011;17:129–37.
12. Pezner RD, Schultheiss TE, Paz IB. Malignant phyllodes tumor of the breast: local control rates with surgery alone. *Int J Radiat Oncol Biol Phys*. 2008;71:710–3.
13. Reinfuss M, Mitus J, Duda K, Stelmach A, Rys J, Smolak K. The treatment and prognosis of patients with phyllodes tumor of the breast: an analysis of 170 cases. *Cancer*. 1996;77:910–6.

14. Onkendi EO, Jimenez RE, Spears GM, Harmsen WS, Ballman KV, Hieken TJ. Surgical treatment of borderline and malignant phyllodes tumors: the effect of the extent of resection and tumor characteristics on patient outcome. *Ann Surg Oncol*. 2014;21:3304–9.
15. Yom CK, Han W, Kim SW, Park SY, Park IA, Noh DY. Reappraisal of conventional risk stratification for local recurrence based on clinical outcomes in 285 resected phyllodes tumors of the breast. *Ann Surg Oncol*. 2015;22:2912–8.
16. Tan BY, Acs G, Apple SK, Badve S, Bleiweiss IJ, Brogi E, Calvo JP, et al. Phyllodes tumours of the breast: a consensus review. *Histopathology*. 2016;68:5–21.
17. Wei J, Tan YT, Cai YC, Yuan ZY, Yang D, Wang SS, Peng RJ, et al. Predictive factors for the local recurrence and distant metastasis of phyllodes tumors of the breast: a retrospective analysis of 192 cases at a single center. *Chin J Cancer*. 2014;33:492–500.
18. Belkacemi Y, Bousquet G, Marsiglia H, Ray-Coquard I, Magne N, Malard Y, Lacroix M, et al. Phyllodes tumor of the breast. *Int J Radiat Oncol Biol Phys*. 2008;70:492–500.
19. Choi N, Kim K, Shin KH, Kim Y, Moon HG, Park W, Choi DH, et al. Malignant and borderline phyllodes tumors of the breast: a multicenter study of 362 patients (KROG 16-08). *Breast Cancer Res Treat*. 2018;171:335–44.
20. Jang JH, Choi MY, Lee SK, Kim S, Kim J, Lee J, Jung SP, et al. Clinicopathologic risk factors for the local recurrence of phyllodes tumors of the breast. *Ann Surg Oncol*. 2012;19:2612–7.
21. Tan PH, Thike AA, Tan WJ, Thu MM, Busmanis I, Li H, Chay WY, et al. Predicting clinical behaviour of breast phyllodes tumours: a nomogram based on histological criteria and surgical margins. *J Clin Pathol*. 2012;65:69–76.
22. Kim S, Kim JY, Kim DH, Jung WH, Koo JS. Analysis of phyllodes tumor recurrence according to the histologic grade. *Breast Cancer Res Treat*. 2013;141:353–63.
23. Moo TA, Alabdulkareem H, Tam A, Fontanet C, Lu Y, Landers A, D'Alfonso T, et al. Association between recurrence and re-excision for close and positive margins versus observation in patients with benign phyllodes tumors. *Ann Surg Oncol*. 2017;24:3088–92.