The Breast 81 (2025) 104455

Contents lists available at ScienceDirect

The Breast

journal homepage: www.journals.elsevier.com/the-breast

Prognostic factors and treatment insights for metastatic malignant phyllode tumors

Mengjia Han [a,b,1], Yunyi Zhang [a,b,1], Rong Lei [a,b,1], Zijia Lai [a,b], Zilin Zhuang [a,b], Yulu Zhang [c], Xun Li [a,b], Xiaojun Li [a,b], Rurong Jia [d], Qiongchao Jiang [e,*], Feng Ye [f,**], Yan Nie [a,b,***]

[a] Guangdong Provincial Key Laboratory of Malignant Tumor Epigenetics and Gene Regulation, Guangdong-Hong Kong Joint Laboratory for RNA Medicine, Medical Research Center, Sun Yat-sen Memorial Hospital, Sun Yat-sen University, Guangzhou, 510120, Guangdong, China
[b] Breast Tumor Center, Sun Yat-sen Memorial Hospital, Sun Yat-sen University, Guangzhou, 510120, Guangdong, China
[c] Department of Breast Surgery, Third Hospital of Nanchang, Nanchang, 330009, JiangXi, China
[d] School of Basic Medical Science, Southern Medical University, Guangzhou, 510515, China
[e] Department of Ultrasound, Sun Yat-sen Memorial Hospital, Sun Yat-sen University, Guangzhou, 510120, Guangdong, China
[f] Department of Breast Oncology, State Key Laboratory of Oncology in South China, Sun Yat-Sen University Cancer Center, Guangzhou, 510060, Guangdong, China

ARTICLE INFO

Keywords:
Metastatic malignant phyllode tumor
Chemotherapy
Metastasectomy
MFS
Prognostic factors

ABSTRACT

Background: The aim of this study is to contribute a better understanding of metastatic malignant phyllode tumors (MMPTs) by exploring its prognostic factors, describing treatment landscape, and providing optimal treatment choices.

Methods: This retrospective multicentric study was included 43 patients with MMPTs who received treatment from 2009 to 2023 in four centers. The primary endpoint of the study was overall survival (OS).

Results: The median overall survival of these patients was 7.27 months (range: 0.63–118.53) and the median follow-up time was 16.8 months (range: 2–188). The median age of these patients were 49 years. The median metastasis-free survival (MFS, it is the time between initial diagnosis and diagnosis of metastatic disease) was 7.27 months, and the most common site of metastasis was lung (35/43, 81.4 %). Treatment for MMPTs primarily consisted of systemic chemotherapy and metastasectomy.

Multivariate analysis revealed that chemotherapy after metastasis (HR = 0.250, 95 % CI 0.109–0.571; $P = 0.001$) and MFS >6 months (HR = 0.407, 95 % CI 0.198–0.836; P = 0.014) were independently associated with OS. The most common chemotherapy regimen was anthracyclines along with ifosfamide (AI), with the median progression-free survival of 5.5 months. Metastasectomy did not significantly improve OS.

Conclusion: The study findings highlight the significance of systemic treatment (chemotherapy) and the impact of MFS on prognosis of MMPTs. For these patients, systemic treatment may improve survival outcomes. And patients with MFS <6 months appear to have a poorer prognosis.

1. Background

Phyllodes tumors (PTs) of the breast are rare tumors, comprising less than 1 % of all breast tumors. PTs were classified as benign, borderline, or malignant by the World Health Organization based on histological features including stromal cell atypia, mitotic activity, stromal overgrowth, and tumor margin type. Most PTs are benign, and malignant phyllodes tumors (MPTs) account for approximately 10–20 % of all PT

* Corresponding author. Department of Ultrasound, Sun Yat-sen Memorial Hospital, Sun Yat-sen University, No. 107 Yanjiang West Road, Guangzhou 510120, Guangdong, China.
** Corresponding author. Department of Breast Oncology, State Key Laboratory of Oncology in South China, Sun Yat-Sen University Cancer Center, 651 Dongfeng East Road, Guangzhou, 510060, Guangdong, China.
*** Corresponding author. Guangdong Provincial Key Laboratory of Malignant Tumor Epigenetics and Gene Regulation, Breast Tumor Center, Sun Yat-sen Memorial Hospital, Sun Yat-sen University, No. 107 Yanjiang West Road, Guangzhou, 510120, China.
E-mail addresses: jiangqch3@mail.sysu.edu.cn (Q. Jiang), yefeng@sysucc.org.cn (F. Ye), nieyan7@mail.sysu.edu.cn (Y. Nie).
[1] Have contributed equally to this work.

https://doi.org/10.1016/j.breast.2025.104455
Received 4 September 2024; Received in revised form 11 February 2025; Accepted 19 March 2025
Available online 19 March 2025

cases [1,2]. MPTs are insensitive to radiotherapy and chemotherapy, so surgical resection is the mainstay of treatment. The NCCN guidelines recommend a surgical negative margin of at least 1 cm [3]. Generally, five-year OS is about 54–89 % for MPTs [4]. Local recurrence and metastasis of the tumor are the main causes of treatment failure. Recent studies have shown that MPT has a local recurrence rate of approximately 6.9 %–18 % [8,11,29]. Early report indicated that the recurrence rate could be as high as 53 % [7]. The metastasis rate of MPTs is approximately 10–50 % [1,5–8].

Metastatic malignant phyllodes tumors (MMPTs) have a particularly poor prognosis due to tumors are not sensitive to radiotherapy/chemotherapy, and lack of targeted therapeutic drugs. Literature suggests that the median MFS (metastasis-free survival, it is the time between initial diagnosis and diagnosis of metastatic disease) is around 13 months, and the reported survival time for MMPTs is approximately 10.7–15.2 months [9,10]. Due to the rarity of MMPTs, our current understanding of this disease is limited and primarily based on small retrospective studies and case reports. Therefore, further exploration is necessary to better comprehend the survival outcomes and treatment strategies for MMPTs. The purpose of this study is to describe the survival status and treatment options of patients with MMPTs, while providing clinically meaningful prognostic information.

2. Patients and methods

2.1. Patients selection and study design

We implemented a retrospective analysis of medical records from four centers: Sun Yat-sen Memorial Hospital, Sun Yat-Sen University Cancer Center, Third Hospital of Nanchang and Peking University Shenzhen Hospital, covering the period from January 2009 to June 2023. This research collected relevant clinical features, treatment regimens, and outcomes of patients diagnosed with MMPTs. We reviewed the patients' clinical records, reassessed histopathological slides, and classified the tumors according to the WHO classification.

The inclusion criteria were as follows: (1) confirmed diagnosis of MPT through histological examination, (2) presence of at least one site of metastasis during treatment (including axillary lymph nodes), (3) absence of concurrent uncontrolled cancers, and (4) availability of complete medical records. Patients without metastasis and those with significant missing follow-up data were excluded.

2.2. Assessments

The primary study endpoints were survival time and OS. Overall survival (OS) is defined as the time from the date of confirmed metastasis until the patient's death or a censoring event (such as loss to follow-up or remaining alive at the end of the follow-up period). Metastasis confirmation involves three methods: 1) Pathological examination confirms the lesion as a metastatic tumor site. 2) The imaging features of new lesions are consistent with the primary tumor: the newly emerged tumor lesions have similar imaging characteristics (such as density, signal intensity, enhancement pattern, etc.) to the primary tumor. 3) Changes in the imaging features of existing lesions: the size, number, or imaging features of the existing lesions have changed significantly during tumor treatment, and the magnitude of change exceeds the measurement error. Metastasis-free survival (MFS) was defined as the interval from the initial diagnosis of MPTs to the first metastasis. Multiorgan metastases refers to metastasis present in more than one organ. Progression-Free Survival (PFS) refers to the length of time during and after treatment in which a patient's disease does not worsen or progress. In this study, it refers to the time after MMPTs receive systemic treatment without disease progression. Disease control rate (DCR) refers to the percentage of patients who are classified as stable, partially relieved, or completely relieved based on their response to treatment after receiving treatment. In this study, patients will be defined according to response Evaluation Criteria in Solid Tumors Committee (RECIST) criteria. Other collected clinical information includes age at metastasis diagnosis, Eastern Cooperative Oncology Group (ECOG) performance status, treatment measures after initial diagnosis, history of recurrence prior to metastasis, treatment regimens received after metastasis (including surgical interventions for metastatic disease), chemotherapy data (regimen, disease control rate), and radiotherapy management. Treatment response for patients receiving chemotherapy is determined by treating physicians and radiology experts based on clinical information and confirmed through imaging data after study inclusion. Each treatment regimens' effectiveness is considered independent of previous treatments, accounting for patients undergoing multiple regimens. The last follow-up date is determined as the date of death or the specified cutoff date set by the researchers.

2.3. Statistical analyses

Descriptive statistics were used to calculate the median and range for continuous variables. OS was assessed using the Kaplan-Meier method, and differences in survival between different groups were evaluated using the log-rank test. Median follow-up time was estimated for the whole cohort of 43 patients using the descriptive statistics. The log-rank test was employed to compare survival differences and identify potential prognostic factors. Factors demonstrating significant statistical significance were included in the multivariate analysis, utilizing the Cox proportional hazards model to assess their impact on adjusted survival rates. All tests were two-sided, and a P-value <0.05 was considered statistically significant. Statistical analyses were performed using SPSS (version 25, IBM Corp., Armonk, NY, USA) and Prism (version 9, GraphPad Software, San Diego, CA, USA).

3. Results

3.1. Patients' characteristics

A total of 43 patients with MMPTs were included in this study. The median age when first metastasis site was diagnosed was 49 years (range: 20–77), and the median follow-up time was 16.8 months (range: 2–184). Almost all patients underwent surgical treatment at the initial diagnosis of MPT. Only 10 patients (23.3 %) received chemotherapy, and 7 patients (16.3 %) received radiotherapy prior to metastasis. The majority of patients (27/43, 62.8 %) experienced metastasis more than 6 months after the initial diagnosis.

The median MFS was 7.27 months (range: 0–114.5). Of the patients diagnosed with MMPTs, 62.8 % (27/43) received treatment, including metastasectomy (37.2 %) and chemotherapy (46.5 %). Most patients (29/43, 67.4 %) had experienced local recurrence of MPT before metastasis. The lung was the most common site of metastasis (35/43, 81.4 %), followed by bone metastasis (11/43, 18.6 %). Detailed patient and tumor characteristics were provided in Table 1.

3.2. Survival outcomes

3.2.1. Overall survival

The median survival time was 7.27 months (95 % CI: 0.63–118.53). Out of the total 43 patients, 41 died during the study period, while 2 patients were still alive at the last follow-up in May 2024. The OS curve for all patients is illustrated in Fig. 3. The median follow-up time was 16.8 months (range: 2–188).

3.2.2. Treatment Modality analysis

The patients were divided into two groups: the intervention group (patients receiving treatment after metastasis) and the non-intervention group (patients who did not receive any treatment after metastasis). The median survival time was 2.43 months in the non-intervention group and 8.50 months in the intervention group. (Fig. 1). The survival

Table 1
Patient characteristics.

		N	Range or percentage
Age (median, years)		43	49.29 (20–77)
ECOG Performance Status		43	
	0–1	34	79.1 %
	≥2	9	20.9 %
Chemotherapy at first diagnosis		43	
	Yes	10	23.3 %
	No	33	76.7 %
Radiotherapy at first diagnosis		43	
	Yes	7	16.3 %
	No	36	83.7 %
Metastasis-free survival (median, months)		43	7.27 (0–114.5)
	≤6 months	16	37.2 %
	>6 months	27	62.8 %
Chemotherapy after metastasis		43	
	Yes	22	51.2 %
	No	21	44.8 %
Metastasectomy		43	
	Yes	16	37.2 %
	No	27	62.8 %
Experience recurrence before metastasis		43	
	Yes	29	67.4 %
	Once	15	51.7 %
	More than once	14	48.3 %
	No	14	32.6 %
Organ of metastasis			
	lung	35	81.4 %
	bone	11	18.6 %
	others	10	23.3 %
Multiorgan metastases		43	
	1	27	62.8 %%
	≥2	16	37.2 %

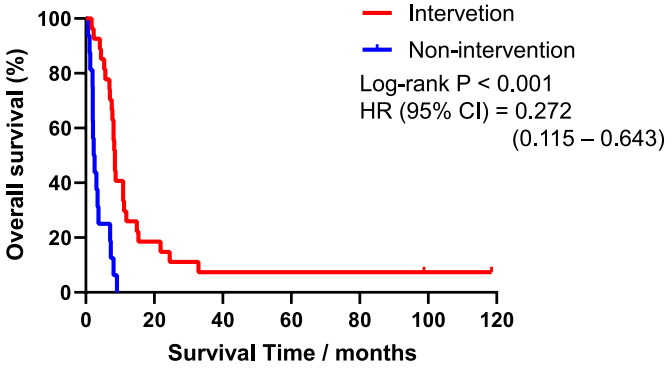

Fig. 1. Impact of treatment intervention on OS Kaplan-Meier curves of OS for all MMPTs who did and did not receive treatment intervention after metastasis. Abbreviations: OS, overall survival; MMPTs, metastatic malignant phyllode tumors; HR, hazard ratio.

analysis of the two groups suggests that active intervention through metastatic tumor resection or chemotherapy may have a trend towards improving patient overall survival. Among the 27 patients of MMPTs who received treatment after metastasis, there appeared to be variability in survival outcomes depending on the treatment method used. (Table 2). 11 patients underwent both metastasectomy and systemic chemotherapy, 5 patients had only metastasectomy, and 11 patients received chemotherapy alone. Among them, patients who underwent both metastasectomy and systemic treatment had a longer median survival time of 10.8 months. Although these patients' survival was better than those who only received metastasectomy alone (P = 0.042, Fig. 2), there was no significant difference in survival time among Chemotherapy alone group (P > 0.05, Fig. 2).

51.4 % (18/35) of cases had only pulmonary metastases. The median survival time for patients with only pulmonary metastases was 8.40 months (range: 1.73–118.53). Among these eighteen patients, eight received pulmonary metastasectomy (three patients also received chemotherapy), these eight patients were metastasectomy group. Ten patients received chemotherapy along (non-metastasectomy group). The one-year OS was about 40.0 % in the metastasectomy group, whereas it was only 10.0 % in the non-metastasectomy group. However, this difference did not achieve statistical significance (HR = 0.547, 95 % CI: 0.205 to 1.458, Fig. 5).

3.2.3. *Prognostic factors*

Factors potentially influencing the prognosis of MMPTs were analyzed. In the univariate logistic regression analysis, MFS (HR = 0.342, 95 % CI: 0.172–0.678), metastasectomy (HR = 0.408, 95 % CI: 0.208–0.800), chemotherapy after metastasis (HR = 0.203, 95 % CI: 0.095–0.437), and presence of lung metastasis (HR = 0.392, 95 % CI: 0.172–0.890) were independently associated with OS (Table 3). Previous treatment methods (radiotherapy or chemotherapy), recurrence

Table 2
Different treatment for Patients with MMPTs.

Intervention after Metastasis	*n*	*Median survival time/months*	*Range*	*P* value
Metastasectomy plus Chemotherapy	11	10.87	5.37–118.53	<0.05
Chemotherapy alone	11	8.07	2.30–32.90	
Metastasectomy alone	5	7.77	1.73–8.50	
	27	8.50	1.73–118.53	

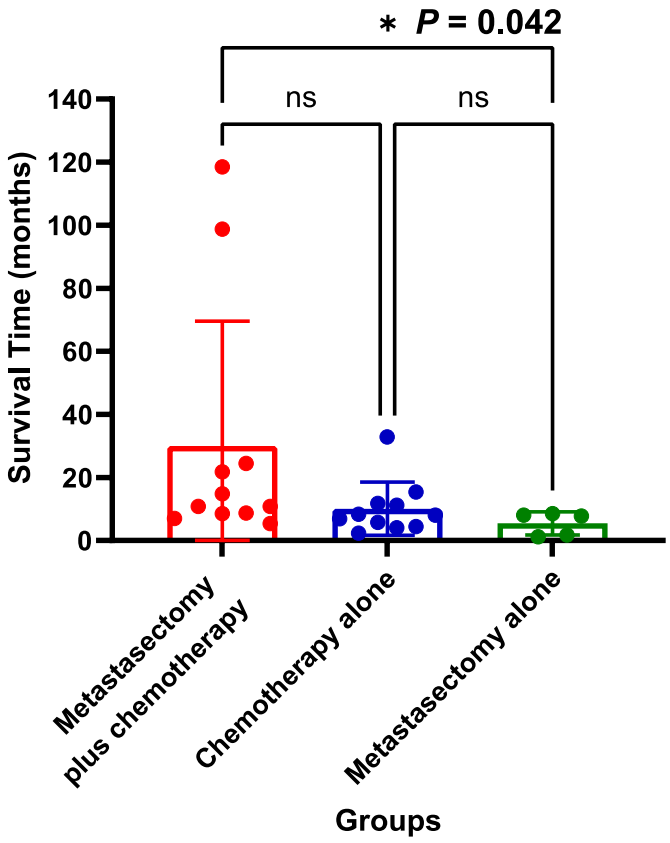

Fig. 2. Overall Survival Time Among Patients with MMPTs by Treatment Modality
Comparation of survival time among three groups: patients treated with metastasectomy plus chemotherapy, chemotherapy along and metastasectomy along. Metastasectomy plus chemotherapy group and metastasectomy along group exhibit notable differences (P = 0.042).

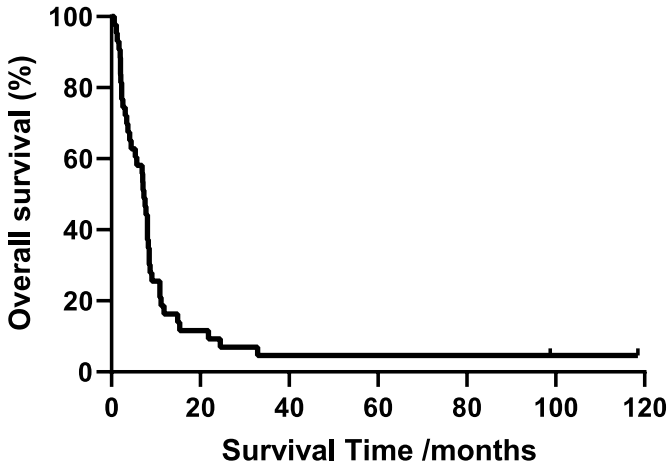

Fig. 3. Kaplan-Meier Overall Survival Curves for All Patients
Survival status of all MMPTs. The median survival time was 7.27 months (95 % CI: 0.63–118.53).

Table 3
Univariate analysis of prognostic factors for MMPTs.

Predictor	N	*P* value	HR	95 % CI
Age	43	0.158	1.020	0.992–1.048
ECOG Performance Status	43	0.348	1.191	0.827–1.713
Radiotherapy at first diagnosis	43			
No	36	Ref		
Yes	7	0.349	0.675	0.296–1.538
Chemotherapy at first diagnosis	43			
No	33	Ref		
Yes	10	0.771	1.114	0.537–2.312
Recurrence	43			
No	14	Ref		
Yes	29	0.358	0.736	0.383–1.414
Metastasis-free survival	43			
≤6 months	16	Ref		
>6 months	27	0.002	0.342	0.172–0.678
Multiorgan metastases	43			
No	27	Ref		
Yes	16	0.960	1.017	0.534–1.937
Metastasectomy	43			
No	27	Ref		
Yes	16	0.009	0.408	0.208–0.800
Chemotherapy after metastasis	43			
No	23	Ref		
Yes	20	<0.001	0.203	0.095–0.437
Lung metastasis	43			
No	8	Ref		
Yes	35	0.025	0.392	0.172–0.890
Bone metastasis	43			
No	32	Ref		
Yes	11	0.366	1.380	0.686–2.775

Abbreviation: HR, hazard ratio; Ref, reference group.

before metastasis, and multiorgan metastases did not significantly impact OS.

Further multivariate regression analysis revealed that the MFS (HR = 0.407, 95 % CI: 0.198–0.836) and chemotherapy after metastasis (HR = 0.250, 95 % CI: 0.109–0.571) independently influenced OS. The multivariate analysis indicated that patients who experienced metastasis within 6 months after the initial diagnosis had a poorer prognosis (Table 4, Fig. 4).

3.2.4. Chemotherapy regimen details

The role of chemotherapy in MMPTs lacked validation from large-scale prospective randomized controlled studies. Our findings indicated that chemotherapy in MMPTs could indeed improve survival outcomes after metastasis. Due to the lack of consensus or guidelines for

Table 4
Multivariate analysis of prognostic factors for MMPTs.

Predictor	N	*P* Value	HR (95 % CI)
Metastasis-free survival	43		
≤6 months	16	Ref	
>6 months	27	0.014	0.407 (0.198–0.836)
Metastasectomy	43		
No	27	Ref	
Yes	16	0.110	0.554 (0.268–1.143)
Chemotherapy after metastasis	43		
No	23	Ref	
Yes	20	0.001	0.250 (0.109–0.571)
Lung metastasis	43		
No	8	Ref	
Yes	35	0.616	1.270 (0.498–3.238)

Abbreviation: HR, hazard ratio; Ref, reference group.

the treatment of MMPTs, various chemotherapy regimens were used. The most commonly used treatment regimen **was** the AI regimen, which was administered to 10 cases (37.0 %) of patients. Among them, 2 patients achieved PR (PFS were 5.0 and 6.0 months), and 2 patients maintained SD (PFS were 5.0 and 7.0 months). Four patients (14.8 %) received paclitaxel-based systemic treatment, with 2 patients showing disease stabilization (PFS = 3.0, 4.0 months). Another three cases (11.1 %) received gemcitabine-based regimens, including 1 patient had disease stabilization (PFS = 4.0 months).

Additionally, there was one patient who received zoledronate and another patient who received the UTD-1 + capecitabine + xindilizumab + etamine regimen, both of whom also experienced a brief PFS of 4.00 and 3.00 months (Table 5).

4. Discussions

In this study, we found a median OS of 7.27 months (95 % CI: 0.63–118.53) and median MFS of 7.27 months (range: 0–114.5) in MMPT patients. Compared with the OS (10.7–15.2 months) reported in previous literature for patients receiving treatment [9,10], our lower OS may be due to including 37.2 % of patients who did not receive intervention after transfer were included in this cohort, and their prognosis was extremely poor (median OS was only 2.43 months), directly affecting overall survival rate. Additionally, Neron et al. reported a median MFS of 13 months [9], highlighting population differences that likely contributed to different OS data.

There is ongoing controversy regarding the use of chemotherapy in non-metastasis MPTs, and the majority of studies suggested that it does not improve prognosis [9,12,13]. So the NCCN guidelines don't recommended it as a standard treatment [3,12,18]. However, our analysis indicates that for MMPTs, chemotherapy could potentially prolong survival after metastasis (HR = 0.250, 95 % CI: 0.109–0.571; *P* = 0.001). The AI regimen is the most commonly used treatment for MMPTs, and elicit a better response in MMPTs compared to other treatment regimens. This was also consistent with the recommendations in the NCCN guidelines. For MMPTs, NCCN guidelines suggest using the chemotherapy regimens for sarcomas as a reference, and the first-line regimen recommendation includes the AI regimen [14]. In an analysis of 56 MMPTs receiving chemotherapy, Palassini E et al. reported a DCR of 66.7 % (18/56, 1 CR, 11 PR, 6 SD) with the AI regimen [19]. Moreover, Parkes A et al. discovered that MMPTs treated with the AI regimen achieved a longer PFS of 9.10 months (95 % CI: 5.03–14.2), compared to 2.80 months (95 % CI: 1.83–4.60) with gemcitabine, and 1.67 months (95 % CI: 1.83–4.60, 7.77) with other regimens [10]. Tyrosine kinase inhibitor drugs (TKIs) had become popular medications in cancer treatment, significantly improving survival rates and quality of life for various solid tumors, such as breast cancer, colorectal cancer, and gastrointestinal stromal tumors [15,16]. Ng et al. found that pazopanib, a type of TKI, achieved the best response in a case of lung metastasis in a PT patient, providing evidence for the clinical use of TKIs in the

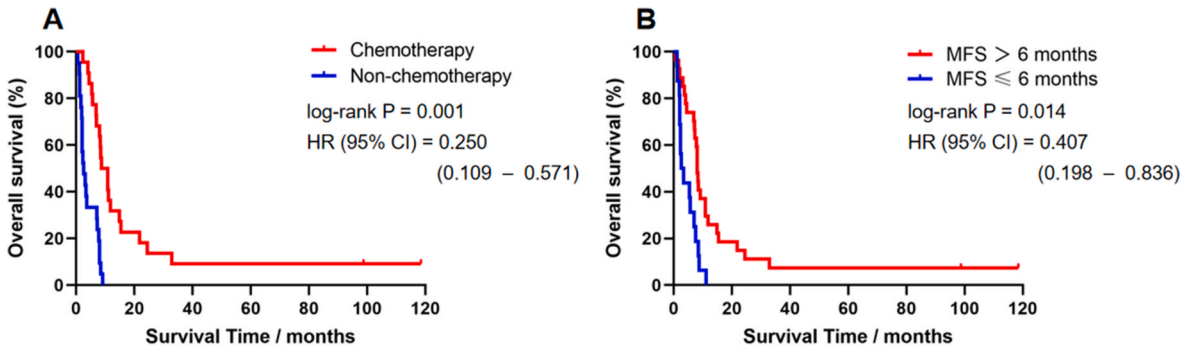

Fig. 4. Impact of chemotherapy utilization and MFS on OS
Kaplan-Meier survival curves for all MMPTs, stratified by chemotherapy utilization (A) and MFS (B).

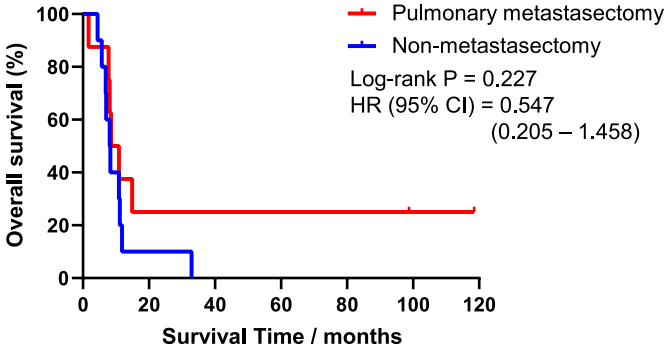

Fig. 5. Impact of pulmonary metastasectomy on OS
Kaplan-Meier curves of OS for MMPTs who only pulmonary metastases had, divided into pulmonary metastasectomy group (eight patients who received pulmonary metastasectomy, and three of them also received chemotherapy) and non-metastasectomy group (ten patients received chemotherapy along).

Table 5
Chemotherapy regimens received by each patient.

Chemotherapy regimens*	N	Outcomes	Median PFS/ months
AI	10	2 PR + 2 SD	5.5
Other Anthracycline or Ifosfamide Regimens	3	0	/
Adriamycin + Carboplatin			
Adriamycin + Cisplatin			
Ifosfamide + Etoposide			
Paclitaxel-Based Regimens	4	2 SD	3.5
Paclitaxel		SD	3
Paclitaxel + Carboplatin + Sintilimab		SD	4
Paclitaxel + Carboplatin			
Docetaxel + Cisplatin			
Gemcitabine-Based Regimens	3	1 SD	4
Gemcitabine + Paclitaxel + Apatinib		SD	4
Gemcitabine + Abemaciclib			
Gemcitabine + Ivolimus			
TKIs	4	0	/
Pezopanib			
Apatinib			
Anlotinib			
Other Regimens	3	2 SD	3.5
Zoledronate*		SD	4
UTD-1 + Capecitabine + Xindilizumab + Apatinib		SD	3
Vinorelbine + Xindilizumab + Anlotinib			

*Each treatment regimens' effectiveness is considered independent of previous treatments, accounting for patients may undergoing multiple regimens.
*Zoledronate is a bisphosphonate agent that, through its binding to bone mineral in the body, suppresses osteoclast activity, thereby enabling the treatment of osteoporosis and tumor-related bone metastases. In a clinical study (ChiCTR1800017822), zoledronate was used as a therapy for PTs.
Abbreviation: PFS, progression-free survival; DCR, disease control rate; AI, anthracycline plus ifosfamide; TKIs, tyrosine kinase inhibitors; SD, stable disease; PR, partial response.

treatment of MPTs [17]. However, in our study, TKI drugs did not produce the desired effects.

Surgery is the primary treatment for early-stage PTs, but there is no consensus on the application of metastasectomy. Our study did not find that metastasectomy provided a survival benefit to patients (HR = 0.554, 95 % CI: 0.268–1.143, Table 4). Several studies have suggested that metastasectomy may increase the treatment burden and the likelihood of postoperative complications, while its effect on improving OS remains uncertain [20,21]. However, in soft tissue sarcomas (STS), metastasectomy of pulmonary metastases appears to improve patients' OS [22–24]. A study involving 48 STS patients who underwent pulmonary metastasectomy demonstrated a significantly better 5-year OS compared with those who did not (52 % vs 14–40 %). This difference suggested that these patients may benefit from pulmonary metastasectomy [25]. Due to the small sample size in this study, although a higher 1-year OS was observed in the metastasectomy group, the difference between the two was not statistically significant.

Limited research has investigated the association between the timing of metastasis and patient outcomes. Study found that for colorectal cancer, no difference in median survival was observed between synchronous metastases and metachronous metastases [26]. Rahbari et al. subsequently validated these findings, demonstrating that early or immediate metastasis (occurring within 6 months of initial diagnosis) was not associated with a poor prognosis [27]. However, different subtypes of tumors can lead to completely contradictory findings. Majority of scholars believed that faster metastasis indicates a more aggressive tumor and a poorer prognosis. This is consistent with our findings. In the multivariate Cox regression analysis, we found that MFS was associated with survival in MMPTs, Patients who develop metastasis within 6 months exhibit a worse prognosis. (Table 4). Previous research and our data indicate that the peak period for MPT metastasis is approximately 3–24 months, with the lungs being the most common site of metastasis. Therefore, in order to detect tumor metastasis in a more timely, special attention should be given to this high-risk period during follow-up, focusing on monitoring for metastases in the lungs, bones, and other areas.

As a retrospective study, there may have been some missing data during the collection process. Factors such as tumor size, mitotic rate, and stromal involvement at initial diagnosis were not examined in relation to prognosis, potentially introducing bias. What's more, the limited number of patients receiving chemotherapy hindered the ability to compare survival under different regimens. We were unable to further analyze the treatment and survival characteristics of oligometastatic patients in MPT, either. With the advancement of precision medicine, the concept of "oligometastasis" has emerged as a crucial factor in

clinical decision-making. It is defined as a specific metastatic state characterized by ≤ 5 metastatic lesions and relatively inert biological behavior [28]. Study have shown that stereotactic ablative radiotherapy (SBRT) can improve patients' survival of oligometastatic cancers [29]. A retrospective analysis of STS patients with pulmonary metastases demonstrated superior outcomes with SBRT: the oligometastatic subgroup ($n = 5$) achieved a 40.7-month median overall survival, indicating that local treatment can yield significant results for those with limited metastasis [30]. Another cohort study compared the efficacy of lung metastasectomy and SBRT in 110 patients with pulmonary oligometastases and found that the 5-year overall survival rates were 41 % for the metastasectomy group and 45 % for the SBRT group (HR = 1.1, 95 % CI: 0.70–1.75) [31], suggesting that for treating oligometastases in specific anatomical sites, SBRT can achieve disease control effects comparable to those of surgical resection. Further exploration of local treatment for MPT oligometastatic patients is needed in the future.

Although our study only included 43 patients, this study is the largest investigation focused on patients with MMPTs in Asia and is the first study to highlight the effect of the MFS on the prognosis of MMPTs. Studies on MMPTs are rare, our study can serve as a good supplement to the previous article which paid more attention to borderline and malignant phyllode tumor rather than MMPTs [32]. We can help researchers gain a more comprehensive understanding of phyllode tumors of the breast. Our results highlight the impact of MFS and chemotherapy on the survival of MMPTs, providing valuable guidance for the treatment to some extent. The prognosis of MMPT patients is generally poor, especially for patients developing metastasis within 6 months of initial diagnosis. Current evidence suggests systemic therapy may offer limited survival benefits for MMPT patients. local therapy (such as Metastasectomy) provided no survival advantage, so it should be used cautiously to avoid increasing the treatment burden. It is essential to explore more treatment options that could improve the prognosis for MMPT patients in the future.

CRediT authorship contribution statement

Mengjia Han: Writing – original draft, Visualization, Methodology, Formal analysis, Data curation. **Yunyi Zhang:** Writing – original draft, Formal analysis, Data curation. **Rong Lei:** Writing – original draft, Formal analysis, Data curation. **Zijia Lai:** Writing – review & editing, Visualization. **Zilin Zhuang:** Resources, Data curation. **Yulu Zhang:** Resources, Data curation. **Xun Li:** Writing – review & editing, Data curation. **Xiaojun Li:** Writing – review & editing, Resources. **Rurong Jia:** Writing – review & editing, Resources. **Qiongchao Jiang:** Writing – review & editing, Supervision. **Feng Ye:** Writing – review & editing, Supervision. **Yan Nie:** Writing – review & editing, Project administration, Methodology, Funding acquisition, Conceptualization.

Ethics statement

The experimental protocol was established, according to the ethical guidelines of the Helsinki Declaration and was approved by the Human Ethics Committee of Sun Yat-sen Memorial Hospital, Sun Yat-sen University, Guangzhou, China (Approval Number: SYSKY-2024-522-01). Written informed consent was obtained from individual or guardian participants.

Data availability statement

The data that support the findings of this study are available on request from the corresponding author, Yan Nie, e-mail: nieyan7@mail.sysu.edu.cn, upon reasonable request.

Funding

This work was supported by the National Natural Science Foundation of China (82173054), the Guangdong Basic and Applied Basic Research Foundation (2022B1515020048, China).

Declaration of competing interest

The authors declare no conflict of interest.

Acknowledgements

We thank all members of the breast cancer center for helpful suggestions. We also appreciate the assistance from the Disease Registry Department of Sun Yat-Sen sen Memorial Hospital, Sun Yat-sen University.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.breast.2025.104455.

References

[1] Chaney AW, et al. Primary treatment of cystosarcoma phyllodes of the breast. Cancer 2000;89(7):1502–11.
[2] Parker SJ, Harries SA. Phyllodes tumours. Postgrad Med J 2001;77(909):428–35.
[3] Gradishar WJ, et al. Breast cancer, version 3.2024, NCCN clinical practice guidelines in Oncology. J Natl Compr Canc Netw 2024;22(5):331–57.
[4] Gutnik L, et al. Malignant phyllodes tumor and primary breast sarcoma; distinct rare tumors of the breast. J Surg Oncol 2022;125(6):947–57.
[5] Barth RJ. Histologic features predict local recurrence after breast conserving therapy of phyllodes tumors. Breast Cancer Res Treat 1999;57(3):291–5.
[6] Tan BY, et al. Phyllodes tumours of the breast: a consensus review. Histopathology 2016;68(1):5–21.
[7] Ramakant P, et al. Challenges in management of phyllodes tumors of the breast: a retrospective analysis of 150 patients. Indian J Cancer 2013;50(4):345–8.
[8] Valenza C, et al. Primary malignant phyllodes tumors of the breast: a retrospective analysis from a referral center. Eur J Cancer 2024;196:113423.
[9] Neron M, et al. Impact of metastasis surgery and alkylating-agent-based chemotherapy on outcomes of metastatic malignant phyllodes tumors: a multicenter retrospective study. Ann Surg Oncol 2020;27(5):1693–9.
[10] Parkes A, et al. Outcomes of systemic therapy in metastatic phyllodes tumor of the breast. Breast Cancer Res Treat 2021;186(3):871–82.
[11] Rosenberger LH, et al. Contemporary multi-institutional cohort of 550 cases of phyllodes tumors (2007-2017) demonstrates a need for more individualized margin guidelines. J Clin Oncol 2021;39(3):178–89.
[12] Morales-Vasquez F, et al. Adjuvant chemotherapy with doxorubicin and dacarbazine has no effect in recurrence-free survival of malignant phyllodes tumors of the breast. Breast J 2007;13(6):551–6.
[13] Chao X, et al. Adjuvant radiotherapy and chemotherapy for patients with breast phyllodes tumors: a systematic review and meta-analysis. BMC Cancer 2019;19(1):372.
[14] von Mehren M, et al. Soft tissue sarcoma, version 2.2022, NCCN clinical practice guidelines in Oncology. J Natl Compr Canc Netw 2022;20(7):815–33.
[15] Ruan R, et al. Unleashing the potential of combining FGFR inhibitor and immune checkpoint blockade for FGF/FGFR signaling in tumor microenvironment. Mol Cancer 2023;22(1):60.
[16] Huang L, Jiang S, Shi Y. Tyrosine kinase inhibitors for solid tumors in the past 20 years (2001-2020). J Hematol Oncol 2020;13(1):143.
[17] Ng D, et al. Therapeutic and immunomodulatory potential of pazopanib in malignant phyllodes tumor. NPJ Breast Cancer 2022;8(1):44.
[18] Zhuang Z, et al. The impact of adjuvant chemotherapy on the long-term prognosis of breast malignant phyllodes tumors: a propensity score-matched study. J Natl Compr Canc Netw 2024;22(7).
[19] Palassini E, et al. Systemic treatment in advanced phyllodes tumor of the breast: a multi-institutional European retrospective case-series analyses. Breast Cancer Res Treat 2022;192(3):603–10.
[20] Treasure T, et al. The Pulmonary Metastasectomy in Colorectal Cancer (PulMiCC) burden of care study: analysis of local treatments for lung metastases and systemic chemotherapy in 220 patients in the PulMiCC cohort. Colorectal Dis 2021;23(11):2911–22.
[21] Rajwa P, et al. Surgical metastasectomy for visceral and bone prostate cancer metastases: a mini-review. Eur Urol Focus 2023;9(2):232–5.
[22] Rehders A, et al. Benefit of surgical treatment of lung metastasis in soft tissue sarcoma. Arch Surg 2007;142(1):70–5. discission 76.
[23] Pfannschmidt J, et al. Pulmonary metastasectomy for soft tissue sarcomas: is it justified? Recent Results. Cancer Res 2009;179:321–36.
[24] Pfannschmidt J, et al. Pulmonary metastasectomy in patients with soft tissue sarcomas: experiences in 50 patients. Thorac Cardiovasc Surg 2006;54(7):489–92.
[25] Predina JD, et al. Improved survival after pulmonary metastasectomy for soft tissue sarcoma. J Thorac Oncol 2011;6(5):913–9.

[26] Mekenkamp LJ, et al. Clinicopathological features and outcome in advanced colorectal cancer patients with synchronous vs metachronous metastases. Br J Cancer 2010;103(2):159–64.
[27] Rahbari NN, et al. Time of metastasis and outcome in colorectal cancer. Ann Surg 2019;269(3):494–502.
[28] Guckenberger M, et al. Characterisation and classification of oligometastatic disease: a European society for radiotherapy and Oncology and European organisation for research and treatment of cancer consensus recommendation. Lancet Oncol 2020;21(1):e18–28.
[29] Palma DA, et al. Stereotactic ablative radiotherapy versus standard of care palliative treatment in patients with oligometastatic cancers (SABR-COMET): a randomised, phase 2, open-label trial. Lancet 2019;393(10185):2051–8.
[30] Lee TH, et al. Treatment outcomes of stereotactic body radiation therapy for pulmonary metastasis from sarcoma: a multicenter, retrospective study. Radiat Oncol 2023;18(1):68.
[31] Lodeweges JE, et al. Long-term outcome of surgery or stereotactic radiotherapy for lung oligometastases. J Thorac Oncol 2017;12(9):1442–5.
[32] Bartels S, et al. Real-world data on malignant and borderline phyllodes tumors of the breast: a population-based study of all 921 cases in The Netherlands (1989 -2020). Eur J Cancer 2024;201:113924.