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Prognostic impact of surgery on thymic malignancies with concurrent or previous extrathymic malignancies: a retrospective analysis from 1998 to 2021

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Abstract

Objective There is limited research on the impact of surgery on the cancer-specific survival (CSS) of patients with malignant thymoma and concurrent or previous extrathymic malignancies (PMTEMs). This retrospective analysis evaluated the prognostic value of surgery in PMTEMs.

Methods Data were sourced from the SEER database, encompassing PMTEMs aged 20–90 with confirmed diagnoses and comprehensive clinical information. Patients were categorized into surgical ($n=105$) and nonsurgical ($n=25$) groups. Propensity score matching (PSM) was employed to mitigate selection bias, resulting in well-balanced baseline characteristics between the groups. Kaplan–Meier curves and the log-rank test were used to investigate the prognostic value of surgery in PMTEMs.

Results Using PSM, the matching of characteristics between the surgical and nonsurgical groups was well-balanced, ensuring the reliability of subsequent analyses. Pre-PSM, the CSS in the surgical group was significantly better than that in the nonsurgical group ($p<.001$). Similarly, according to the post-PSM data, the CSS for PMTEMs in the surgical group remained superior to that in the nonsurgical group, which indicates that the survival advantage of the surgical group persisted after PSM ($p=.030$). Additionally, PMTEMs with smaller thymomas (≤ 5 cm) had a significant advantage in CSS compared to those with larger thymomas ($p=.046$).

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Conclusions In conclusion, this study shows that surgery may significantly improve the survival rate of PMTEMs.

Keywords Malignant thymoma, Extrathymic malignancy, Propensity score matching, Kaplan–Meier curve

Background

Thymoma, a tumor originating from thymic epithelial cells, is one of the most common tumors in the anterior mediastinum. The annual incidence of this disease is approximately 0.2 to 0.5 per million per year, predominantly affecting adult patients [1, 2]. While various treatment options exist, surgery remains the primary treatment for thymoma, especially for localized thymomas, where surgical resection is the preferred approach [3, 4]. Recent studies have shown that patients with recurrent thymoma can achieve significant survival benefits from reoperative surgery, further emphasizing the central role of surgery in the management of thymoma [5].

However, despite the efficacy of surgical treatment in controlling the tumor and extending patient survival in most cases, the management of patients with malignant thymoma and concurrent or previous extrathymic malignancies (PMTEMs) remains a significant clinical challenge [5]. As patients age and accumulate other carcinogenic factors, they are increasingly susceptible to developing a second malignancy, even after receiving radiotherapy or chemotherapy [4, 6]. Adding to this complexity, some patients are diagnosed with extrathymic malignancies (e.g., breast cancer) before their thymoma diagnosis, further complicating treatment decisions [7, 8]. Unfortunately, there is limited research on the impact of surgery on the prognosis of PMTEMs. Therefore, it is essential to investigate the clinical significance of surgery in these complex cases.

This study aimed to evaluate the prognostic value of surgery in PMTEMs using propensity score matching (PSM). PSM is a widely used statistical method that effectively reduces selection bias in retrospective studies, allowing for a more reasonable and credible comparison between different treatment groups [9, 10]. By leveraging sample data from the Surveillance, Epidemiology, and End Results (SEER) database [11], this study will analyze the differences in survival rates between surgical and nonsurgical treatments in these patients and explore other factors that may influence prognosis. Through this research, we hope to provide clinicians with more evidence-based guidance to optimize treatment strategies for these patients.

Materials and methods

Study design

This study is a retrospective analysis aimed at evaluating the prognostic value of surgery in PMTEMs. The data utilized in this study were accessed from the SEER database in 2024. The SEER database is publicly available and contains de-identified patient information. According to SEER database policies, the use of these de-identified data does not require institutional review board approval or informed consent from individual patients [11]. The access to and use of the data in this study adhered to the SEER data use agreement.

Study population

Data for this study were sourced from the SEER database (version 8.4.3). Data on PMTEMs from 1998 to 2021 were collected. The inclusion criteria consisted of the following: (1) patients with a confirmed diagnosis of malignant thymoma and a confirmed concomitant or previous extrathymic malignant tumor with a clearly identified tumor site, (2) adult patients aged 20 years and above but below 90 years, (3) patients with or without a surgical history (including local tumor excision, simple/partial surgical removal of the primary site, or total surgical removal of the primary site), and (4) patients with or without a history of radiotherapy who had complete clinical data and follow-up records. The exclusion criteria were as follows: (1) patients with incomplete clinical data or follow-up information, (2) patients with unspecified extrathymic malignant tumor sites, and (3) patients with more than one type of extrathymic malignant tumor. The collected data included demographic characteristics (gender, age, and race), clinical characteristics (histologic type, tumor size, regional node, Masaoka Koga stage, and extrathymic tumor information), treatment information (surgery and radiotherapy), and follow-up information (cancer-specific survival [CSS] status and follow-up time).

PSM methods

To reduce potential selection bias, a PSM method was performed using the "MatchIt" [12] package for R (version 4.2.2) statistical software [13]. A 1:1 matching approach was employed in which the optimal pair matching algorithm was used to achieve the best balance between groups. The matching process accounted for variables that were significantly unbalanced between the surgical and nonsurgical groups, including key factors, such as radiotherapy status, to reduce confounding and improve the robustness of the subsequent analyses. The effectiveness of the matching was assessed by checking whether the variables were balanced between the two groups post-matching, with p-values from the balance tests (either the chi-squared test or Fisher's exact test) exceeding 0.050.

Statistical analysis

All data analyses were performed using R (version 4.2.2) statistical software and its associated packages [12–18]. The main statistical methods included Kaplan–Meier survival analysis and the log-rank test. The level of statistical significance was set at $p < .050$.

Results

Patient characteristics before PSM

The sample used in this study included 105 patients in the surgical group and 25 patients in the nonsurgical group. Table 1 presents the patient characteristics before PSM for the surgical and nonsurgical groups. There was a significant difference between the groups in terms of histologic type ($p < .001$, Table 1). The surgical group had a higher proportion of patients with indolent forms of histologic type (48.6%) compared to the nonsurgical group (24.0%). A significant difference in regional lymph node status was also observed between the two groups ($p = .003$, Table 1). Moreover, the proportion of patients who received radiotherapy was significantly higher in the surgical group than in the nonsurgical group (37.1% vs. 4.0%, $p = .003$, Table 1).

In the nonsurgical group, males accounted for 60.0% and females for 40.0%, whereas in the surgical group, males accounted for 54.3% and females for 45.7%, with no significant difference in gender distribution between the groups ($p = .770$, Table 1). Regarding age, 60.0% of patients in the nonsurgical group were aged ≥ 65 years old compared to 48.6% in the surgical group, with no statistically significant difference ($p = .421$, Table 1). In terms of racial distribution, white patients were the majority in both groups (64.0% in the nonsurgical group and 70.5% in the surgical group), with no significant differences in the proportions of black patients and other races, including American Indian/Alaska Native and Asian/Pacific Islander ($p = .773$, Table 1).

Concerning tumor size, 72.0% of patients in the nonsurgical group had tumors > 5 cm compared to 53.3% in the surgical group, with no significant difference ($p = .142$, Table 1). Among the PMTEMs included in this study, breast and prostate were the most common sites of extrathymic cancers (> 10 cases), while all other extrathymic tumor sites had no more than 10 cases (Supplementary Material 1). Regarding the types of concomitant or previous extrathymic tumors, other types of tumors (such as bladder and thyroid tumors) accounted for 72.0% in the nonsurgical group and 67.6% in the surgical group, with no statistically significant difference ($p = 1.000$, Table 1).

Impact of surgery on CSS in PMTEMs before PSM

To explore whether surgery impacts CSS in PMTEMs, this study conducted Kaplan–Meier survival curve analyses. As shown in Fig. 1A, before PSM, the CSS for PMTEMs in

Table 1 The characteristics of patients based on the data before propensity score matching (PSM)

Characteristics		Nonsurgical group ($N = 25$)	Surgical group ($N = 105$)	*P*
Gender	Female	10 (40.0%)	48 (45.7%)	0.770
	Male	15 (60.0%)	57 (54.3%)	
Age group	< 65 years	10 (40.0%)	54 (51.4%)	0.421
	≥ 65 years	15 (60.0%)	51 (48.6%)	
Race	Others[a]	6 (24.0%)	22 (21.0%)	0.773
	Black	3 (12.0%)	9 (8.6%)	
	White	16 (64.0%)	74 (70.5%)	
Histologic type	Aggressive forms	5 (20.0%)	35 (33.3%)	< 0.001
	Indolent forms	6 (24.0%)	51 (48.6%)	
	Not specific	14 (56.0%)	19 (18.1%)	
Tumor size	≤ 5 cm	7 (28.0%)	49 (46.7%)	0.142
	> 5 cm	18 (72.0%)	56 (53.3%)	
Regional node	Negative	1 (4.0%)	33 (31.4%)	0.003
	Positive	1 (4.0%)	1 (1.0%)	
	Not examined	23 (92.0%)	71 (67.6%)	
Masaoka Koga stage	I-III	8 (32.0%)	54 (51.4%)	0.127
	IV	17 (68.0%)	51 (48.6%)	
Extrathymic cancer	Other sites	18 (72.0%)	71 (67.6%)	1.000
	Breast	3 (12.0%)	16 (15.2%)	
	Prostate	4 (16.0%)	18 (17.1%)	
Thymoma prior to extrathymic malignancy	No	18 (72.0%)	53 (50.5%)	0.086
	Yes	7 (28.0%)	52 (49.5%)	
Radiotherapy	No	24 (96.0%)	66 (62.9%)	0.003
	Yes	1 (4.0%)	39 (37.1%)	

Notes: [a]American Indian/Alaska Native and Asian/Pacific Islander. The *p*-values were obtained using either the chi-squared test or Fisher's exact test

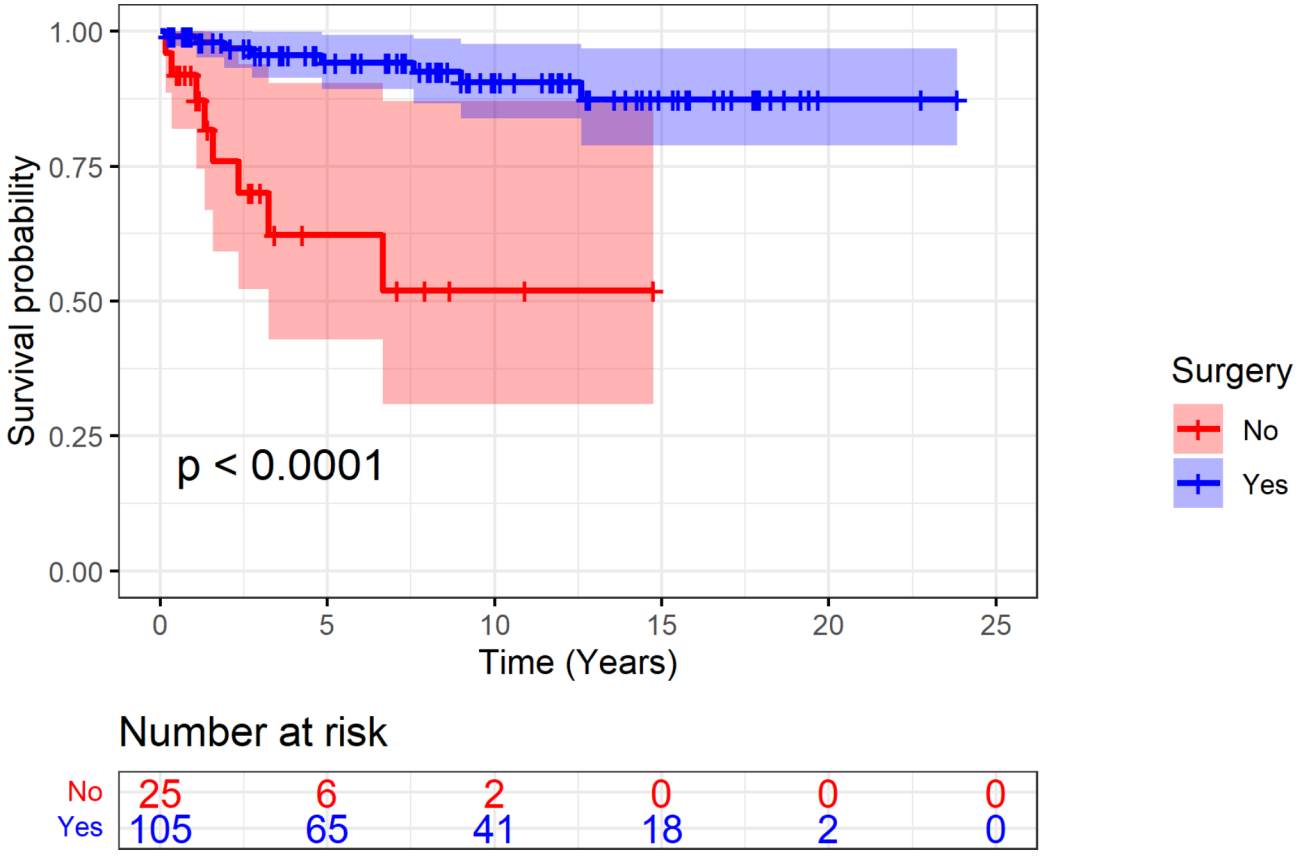

Fig. 1 Kaplan–Meier curve of patients with malignant thymoma and concurrent or previous extrathymic malignancies before propensity score matching. *P*-values were calculated using log-rank tests

the surgical group was longer than that for the nonsurgical group. The CSS rate in the surgical group was significantly higher than that in the nonsurgical group ($p<.001$, Fig. 1A).

Patient characteristics after PSM

As shown in Table 1, characteristic differences were observed between the two groups in the pre-PSM cohort. To address this, PSM was conducted. Initially, three characteristics—histologic type, regional lymph node status, and radiotherapy—were used in the PSM process. However, significant differences remained between the groups regarding tumor size and Masaoka Koga stage ($p<.050$, Supplementary Material 2). As a result, these variables were included in the final PSM analysis. After final PSM, both groups included 25 patients, with no statistically significant differences in all variables ($p>.050$, Table 2). Thus, the matching of characteristics between the surgical and nonsurgical groups was well-balanced, ensuring the reliability of subsequent analyses.

Impact of surgery and other characteristics on CSS in PMTEMs after PSM

According to the post-PSM data, Fig. 2A indicates that the survival advantage of the surgical group persisted after PSM. Specifically, the CSS for PMTEMs in the surgical group was better than in the nonsurgical group, as demonstrated by the Kaplan–Meier curves ($p=.030$; Fig. 2A). Beyond five years, the curves for the surgical group clearly diverged from those of the nonsurgical group (Fig. 2A), indicating a sustained survival benefit.

The study further explored significant prognostic factors, such as gender and age, in PMTEMs. Radiotherapy was not considered in this analysis, as only one PMTEM received radiotherapy in the post-PSM data (Table 2). The Kaplan–Meier curve analysis revealed that PMTEMs with smaller thymomas (≤ 5 cm) had a significant advantage in CSS compared to those with larger thymomas ($p=.046$, Fig. 2B). Additionally, for PMTEMs, no association was found between the site type of the extrathymic tumor and the patients' CSS. Specifically, there was no significant difference in CSS among PMTEM patients with extrathymic tumors of prostate cancer, breast cancer, or tumors other than prostate or breast cancer ($p>.050$, Supplementary Material 3). No significant differences in CSS outcomes based on other characteristics, including gender, age, race, histologic type, regional node status, Masaoka Koga stage, and thymoma prior to extrathymic

Table 2 The characteristics of patients based on data after PSM

Characteristics		Nonsurgical group (*N* = 25)	Surgical group (*N* = 25)	*P*
Gender	Female	10 (40.0%)	10 (40.0%)	1.000
	Male	15 (60.0%)	15 (60.0%)	
Age group	< 65 years	10 (40.0%)	13 (52.0%)	0.570
	≥ 65 years	15 (60.0%)	12 (48.0%)	
Race	Others[a]	6 (24.0%)	4 (16.0%)	0.658
	Black	3 (12.0%)	5 (20.0%)	
	White	16 (64.0%)	16 (64.0%)	
Histologic type	Aggressive forms	5 (20.0%)	8 (32.0%)	0.488
	Indolent forms	6 (24.0%)	7 (28.0%)	
	Not specific	14 (56.0%)	10 (40.0%)	
Tumor size	≤ 5 cm	7 (28.0%)	12 (48.0%)	0.244
	> 5 cm	18 (72.0%)	13 (52.0%)	
Regional node	Negative	1 (4.0%)	1 (4.0%)	1.000
	Positive	1 (4.0%)	1 (4.0%)	
	Not examined	23 (92.0%)	23 (92.0%)	
Masaoka Koga stage	I-III	8 (32.0%)	12 (48.0%)	0.386
	IV	17 (68.0%)	13 (52.0%)	
Extrathymic cancer	Other sites	18 (72.0%)	20 (80.0%)	0.888
	Breast	3 (12.0%)	3 (12.0%)	
	Prostate	4 (16.0%)	2 (8.0%)	
Thymoma prior to extrathymic malignancy	No	18 (72.0%)	13 (52.0%)	0.244
	Yes	7 (28.0%)	12 (48.0%)	
Radiotherapy	No	24 (96.0%)	25 (100.0%)	1.000
	Yes	1 (4.0%)	0 (0.0%)	

Notes: [a]American Indian/Alaska Native and Asian/Pacific Islander. The *p*-values were obtained using either the chi-squared test or Fisher's exact test

malignancy, were observed among PMTEMs with varying statuses (Supplementary Material 3).

Discussion

Surgery is one of the main treatments for malignant thymoma [19]. However, there is limited understanding of its prognostic impact on PMTEMs. This study is the first to use PSM to evaluate the prognostic value of surgery in PMTEMs. The results consistently show that the CSS rate of the surgical group is significantly higher than that of the nonsurgical group, emphasizing the importance of surgical intervention in improving the prognosis of PMTEMs.

Surgery could be a potential treatment option for PMTEMs. Previous studies indicate that PMTEMs account for over 20% of patients with thymoma and suggest a possible association between thymoma and extrathymic malignancies [6, 20]. On the one hand, patients with thymoma are prone to developing extrathymic malignancies, most commonly lung cancer [6]. Thymomas predominantly composed of cortical components may be associated with a loss of normal function in cortical thymic epithelial cells [21]. This dysfunction hampers the maturation of T lymphocytes, resulting in immunodeficiency and an elevated risk of developing extrathymic malignancies [21, 22]. On the other hand, for patients with thymoma who have undergone surgery, the coexistence of extrathymic malignancies is an important prognostic risk factor [7, 20]. Clinically, the presence of tumors in other locations might be a contraindication for surgery in specific cancer patients [23, 24]. However, to our knowledge, no prior study has clarified whether surgery benefits PMTEMs in terms of CSS, although previous research has revealed the significant prognostic value of reoperation for recurrent patients with thymoma [5, 25]. Through the PSM method used, our study is the first to confirm that surgical treatment can benefit the prognosis of PMTEMs. Therefore, surgical treatment should be considered an option for PMTEMs without obvious contraindications to improve CSS rates.

Several parameters may be related to the prognosis of PMTEMs. Demographic characteristics (e.g., gender), disease conditions (e.g., tumor size), and treatment methods (e.g., chemotherapy) have been identified as prognostic factors in certain tumors [26, 27]. In our study, we found that the size of the thymoma plays an important role in PMTEMs, with smaller thymomas (≤ 5 cm) being associated with a lower CSS risk compared to larger thymomas. However, the association between tumor diameter and the prognosis of thymoma remains controversial [28–30], which may be due to a variety of factors. Tumor diameter may, to some extent, reflect tumor aggressiveness: larger thymomas are more likely to invade adjacent tissues

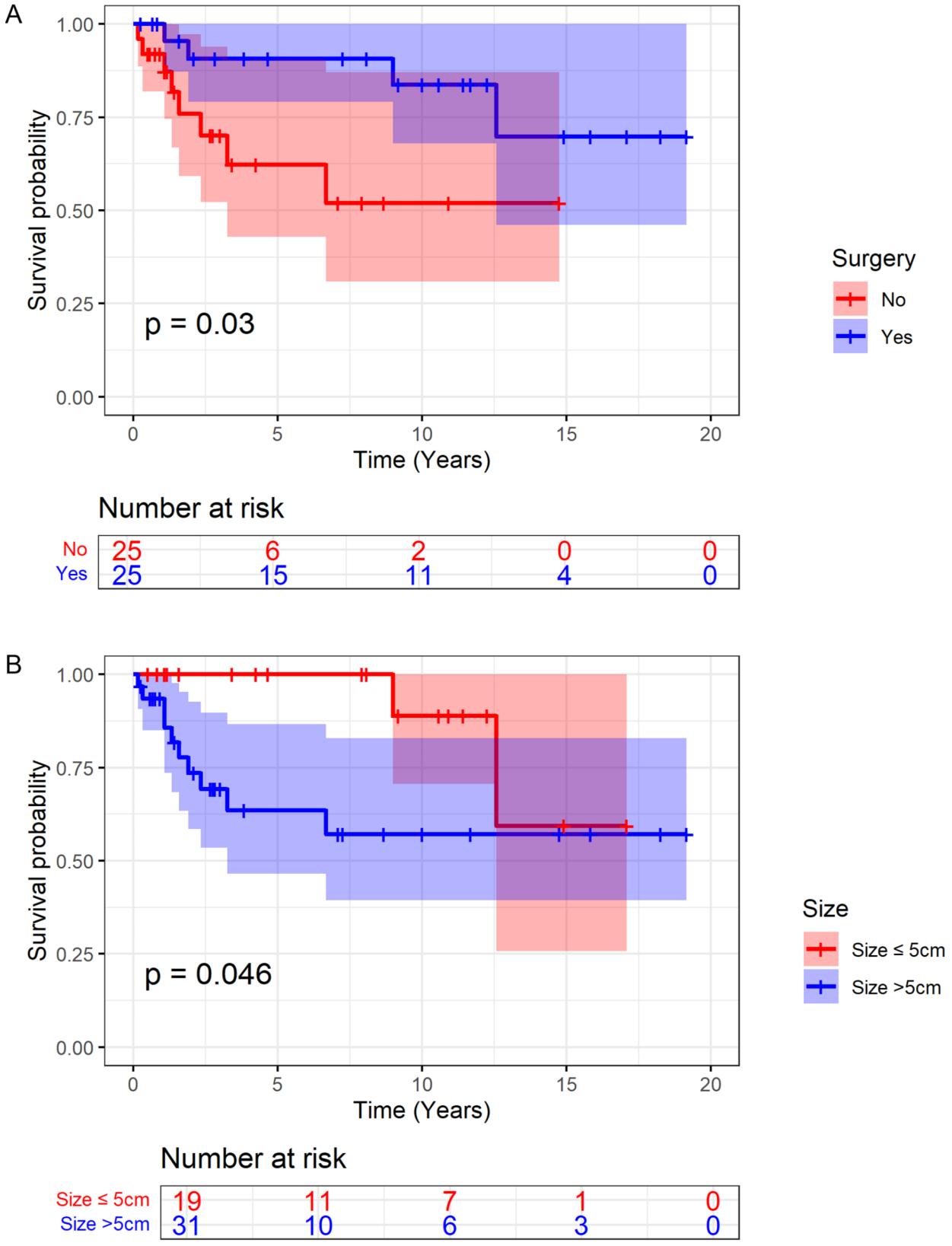

Fig. 2 Kaplan–Meier curve of patients with malignant thymoma and concurrent or previous extrathymic malignancies after propensity score matching. This figure displays Kaplan–Meier curves stratified by two characteristics: (**A**) surgery and (**B**) thymoma size. *P*-values were calculated using log-rank tests

[31], thereby leading to a worse prognosis. However, for thymoma, when tumor size is used as a categorical variable, differences in the selection of grouping thresholds may yield different outcomes [32]. In addition, variations in cohort characteristics (e.g., treatment modalities), differences in follow-up duration, and the selection of confounding factors may all contribute to bias in evaluating the relationship between thymoma diameter and prognosis [28, 30, 33]. In our study, we used PSM to balance the differences in characteristics between the surgical and nonsurgical groups in PMTEMs, thereby mitigating the influence of confounding factors. Furthermore, the follow-up duration of the PMTEM cohort spans approximately 20 years. These measures facilitate a more reliable understanding of the prognostic value of thymoma size in PMTEMs. However, it is necessary to ultimately validate this finding in a larger prospective cohort using additional statistical methods (e.g., restricted cubic spline). Other characteristics, such as histologic type, did not significantly affect CSS outcomes among PMTEMs based on the current results of our study.

Despite this study's encouraging findings, it has some limitations. First, although we employed PSM to balance differences in key characteristics (such as Masaoka Koga staging) between the surgical and nonsurgical groups—thereby better approximating the independent impact of surgery on CSS—the limitations of the SEER data prevented us from evaluating the effect of surgical indications on this outcome. This issue should be addressed in future studies. Second, limited by the data available, this study could not explore whether there were prognostic differences in PMTEMs who received treatments for different extrathymic cancers. Third, another key limitation of the SEER database is the lack of recurrence data, which is particularly critical for patients with thymoma, as recurrence often signifies treatment failure in long-surviving individuals. Future studies incorporating recurrence information are essential to better evaluate treatment efficacy and long-term outcomes. Finally, the relatively small sample size may affect the stability of the statistical analyses. The difference in patient numbers between the surgical and nonsurgical groups could lead to biased results. These limitations highlight the need for multicenter studies to validate our findings.

Conclusion

Through PSM, this study shows that surgery significantly improves the CSS of PMTEMs. The research provides a reference for clinical decision-making and underscores the importance of surgical intervention in the management of PMTEMs.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s13019-025-03442-6.

Supplementary Material 1

Supplementary Material 2

Supplementary Material 3

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Author contributions

GSL, GYF, and JL: resources, data curation, formal analysis, investigation, methodology, software, validation, visualization, writing - original draft, and writing - review & editing. HFZ, GBL, and NY: conceptualization, project administration, funding acquisition, writing - review & editing. ZYX and TH: writing - review & editing. JJG: funding acquisition and writing - review & editing.

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Data availability

Data used in this study were obtained from the Surveillance, Epidemiology, and End Results database (https://seer.cancer.gov). More detailed data would be available from the corresponding authors.

Declarations

Ethics approval and consent to participate

All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008. This study was exempt from Institutional Review Board approval because all data were derived from the SEER database and did not include any personally identifying information.

Consent for publication

Not Applicable.

Competing interests

The authors declare no competing interests.

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