

Outcomes of Pulmonary Metastasectomy for Pediatric Sarcoma

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Objective: To evaluate survival outcomes and prognostic factors among pediatric patients with pulmonary metastatic sarcoma who underwent pulmonary metastasectomy at Ramathibodi Hospital.

Materials and Methods: The present study was a retrospective study that included pediatric patients younger than 20 years diagnosed with pulmonary metastatic sarcoma and who underwent surgical resection between January 2007 and December 2019. Demographic, clinical, and operative data were collected from electronic medical records. Survival was analyzed using the Kaplan-Meier method, and prognostic factors were evaluated using the Cox proportional hazards model.

Results: Twenty-seven patients were included, with a mean age of 12.2 ± 4.4 years and with 70.4% male. Osteosarcoma was the most common primary tumor at 66.7%. The majority (77.8%) underwent posterolateral thoracotomy, and 70.4% had wedge resection. Complete resection was achieved in 66.7% of cases. The median overall survival was 13 months, with 3-year and 5-year survival rates of 33.6% and 12.6%, respectively. The median recurrence-free interval was 8.6 months. Disease recurrence occurred in 63% of patients and was the only variable significantly associated with mortality ($p=0.047$). In the Cox regression analysis, older age was the only factor significantly associated with recurrence (HR 1.12, 95% CI 1.00 to 1.30, $p=0.046$). All long-term survivors had osteosarcoma as the primary tumor.

Conclusion: Pulmonary metastasectomy offers a potential survival benefit in pediatric patients with pulmonary metastatic sarcoma. Age at the time of surgery was a significant risk factor of recurrence, whereas surgical approach and extent of resection did not affect outcomes. Osteosarcoma was associated with a trend toward improved survival, though not statistically significant. Further multicenter studies with larger cohorts are warranted to validate these findings and optimize surgical strategies for this challenging patient population.

Keywords: Pediatric sarcoma; Pulmonary metastasis; Pulmonary metastasectomy; Survival; Recurrence-free interval

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Pediatric sarcoma with pulmonary metastases presents a major therapeutic challenge. The lungs are the most common site of distant spread, occurring in 20% to 50% of patients with sarcoma⁽¹⁻³⁾. Moreover, about 70% of these patients exhibit isolated pulmonary metastases without extrapulmonary involvement^(4,5). For such patients, pulmonary metastasectomy remains the mainstay of potentially curative treatment.

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Studies have demonstrated a significant survival advantage for patients who undergo surgical resection of pulmonary metastases compared with those managed non-operatively⁽⁵⁻⁷⁾. In the landmark multicenter analysis by Pastorino et al., which included 5,206 patients who underwent pulmonary metastasectomy for various malignancies, the 5- and 10-year overall survival rates for patients with sarcoma were 31% and 26%, respectively⁽⁸⁾.

Despite these encouraging outcomes, the prognostic factors influencing survival in pediatric patients remain incompletely defined. Variables such as recurrence-free interval, number and size of metastatic nodules, completeness of resection, and patient age have been reported to affect outcomes, but results across studies are inconsistent.

The present study aimed to evaluate the 5-year overall survival and recurrence-free interval of pediatric patients with pulmonary metastatic sarcoma who underwent pulmonary metastasectomy at Ramathibodi Hospital.

Ramathibodi Hospital. Additionally, the authors sought to identify clinical and pathological factors associated with survival and recurrence in this patient population.

MATERIALS AND METHODS

Study design and ethical approval

The present study was a retrospective study conducted at the Faculty of Medicine, Ramathibodi Hospital, Mahidol University, Bangkok, Thailand. The study protocol was reviewed and approved by the Human Research Ethics Committee of the Faculty of Medicine, Ramathibodi Hospital (COA. MURA2020/1561).

Patient selection

All pediatric patients, younger than 20 years, diagnosed with pulmonary metastatic sarcoma and who underwent pulmonary metastasectomy between January 1, 2007, and December 31, 2019, were included. Patients with incomplete medical records or without histopathologic confirmation of metastasis were excluded.

Data collection

Clinical data were retrieved from electronic medical records, including demographic characteristics as age, gender, and underlying disease, primary tumor histology and location, number and size of pulmonary metastases, recurrence-free interval, presence of mediastinal lymph node involvement or pleural effusion, and completeness of resection. Operative details such as surgical approaches as posterolateral thoracotomy or video-assisted thoracoscopic surgery (VATS) and resection type as wedge resection, segmentectomy, or lobectomy, were recorded. Follow-up data regarding recurrence and survival were reviewed from outpatient and inpatient documentation.

Endpoints

The primary endpoint was disease-specific overall survival, defined as the interval from the date of pulmonary metastasectomy to death or last follow-up. The secondary endpoint was recurrence-free interval, defined as the time from surgery to the first documented recurrence.

Statistical analysis

Survival outcomes were analyzed using the Kaplan-Meier method, and survival curves were compared using the log-rank test. A p-value of less

than 0.05 was considered statistically significant. Cox proportional hazards regression was performed to identify potential prognostic factors associated with recurrence or mortality, with results expressed as hazard ratios (HRs) and 95% confidence intervals (CIs). All statistical analyses were performed using Stata, version 14 (StataCorp LP, College Station, TX, USA).

RESULTS

Patient characteristics

Twenty-seven pediatric patients with pulmonary metastatic sarcoma who underwent pulmonary metastasectomy at Ramathibodi Hospital between 2007 and 2019 were included in the present study. The mean age was 12.2 ± 4.4 years, and 70.4% were male. The most common primary diagnosis was osteosarcoma at 66.7%, followed by synovial sarcoma at 11.1%, rhabdomyosarcoma at 7.4%, epithelial cell sarcoma at 3.7%, embryonal cell sarcoma at 3.7%, Ewing sarcoma at 3.7%, and fibrosarcoma at 3.7%. Most primary lesions originated from the extremities in 81.5% (Table 1).

Operative characteristics

The majority of patients (77.8%) underwent posterolateral thoracotomy, while 22.2% were treated via VATS. Wedge resection was the most frequently performed procedure in 70.4%, followed by segmentectomy in 11.1% and lobectomy in 18.5%. Complete resection was achieved in 66.7% of patients. Fifteen patients (55.6%) underwent a single metastasectomy, whereas 12 patients (44.4%) underwent multiple resections (range 2 to 5 operations) (Table 1).

Survival outcomes

The median overall survival was 13 months, with 3-year and 5-year overall survival rates of 33.6% and 12.6%, respectively (Figure 1). The median recurrence-free interval was 8.6 months (Figure 2).

Prognostic factors and recurrence

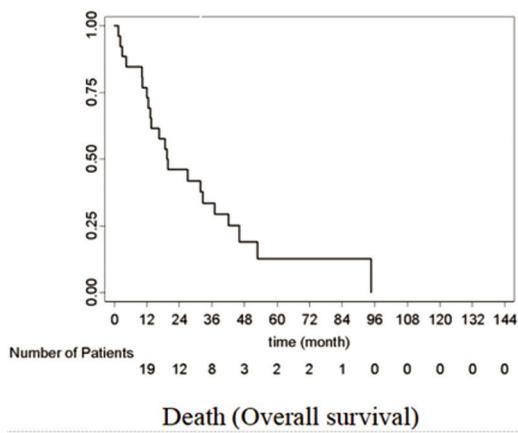
Table 1 summarizes the baseline characteristics according to survival status. Disease recurrence was significantly more frequent among patients who died compared with those who survived at 72.7% versus 20.0% ($p=0.047$). The other variables, including surgical approach, type of resection, and number or size of lesions, were not significantly related to overall survival.

Table 2 compares patients according to recurrence

Table 1. Patient characteristics by survival

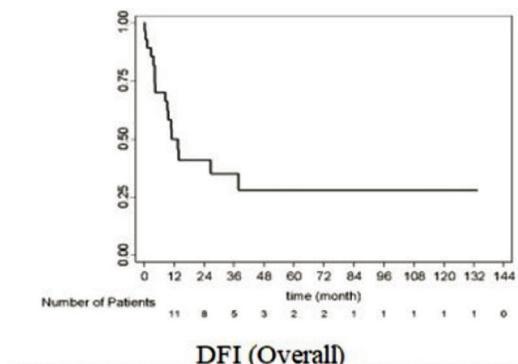
Variable	Total (n=27)	Alive (n=5)	Death (n=22)	p-value
Age (years); mean±SD	12.2±4.4	12.7±5.6	12.1±4.2	0.791
Sex; n (%)				0.999
Male	19 (70.4)	4 (80.0)		
Female	8 (29.6)	1 (20.0)		
Diagnosis; n (%)				0.423
Synovial sarcoma	3 (11.1)	0 (0.0)		
Osteosarcoma	18 (66.7)	5 (100)		
Rhabdomyosarcoma	2 (7.4)	0 (0.0)		
Epithelial cell sarcoma	1 (3.7)	0 (0.0)		
Embryonal cell sarcoma	1 (3.7)	0 (0.0)		
Ewing sarcoma	1 (3.7)	0 (0.0)		
Fibrosarcoma	1 (3.7)	0 (0.0)		
Primary lesion location; n (%)				0.547
Non-extremities	5 (18.5)	0 (0.0)		
Extremities	22 (81.5)	5 (100)		
Size tumor; n (%)				0.547
Small (<3 cm)	22 (81.5)	5 (100)		
Large (>3 cm)	5 (18.5)	0 (0.0)		
Number of lesions; n (%)				0.555
Single lesion	21 (77.8)	5 (100)		
Multiple lesion	6 (22.2)	0 (0.0)		
Lung metastasis location; n (%)				0.493
Right lung	10 (37.0)	2 (40.0)		
Left lung	11 (40.7)	3 (60.0)		
Bilateral lung	6 (22.3)	0 (0.0)		
Pleural effusion; n (%)				0.283
No	20 (74.1)	5 (100)		
Yes	7 (25.9)	0 (0.0)		
Approach; n (%)				0.999
Posterolateral thoracotomy	21 (77.8)	4 (80.0)		
VATS	6 (22.2)	1 (20.0)		
Type of resection; n (%)				0.580
Wedge resection	19 (70.4)	5 (100)		
Segmentectomy	3 (11.1)	0 (0.0)		
Lobectomy	5 (18.5)	0 (0.0)		
Complete; n (%)				0.636
Complete resection	18 (66.7)	4 (80.0)		
Incomplete resection	9 (33.3)	1 (20.0)		
Number of surgeries; n (%)				0.195
1	15 (55.6)	4 (80.0)		
2	7 (25.9)	0 (0.0)		
3	1 (3.7)	1 (20.0)		
4	3 (11.1)	0 (0.0)		
5	1 (3.7)	0 (0.0)		
Recurrence; n (%)				0.047
No	10 (37.0)	4 (80.0)	6 (27.3)	
Yes	17 (63.0)	1 (20.0)	16 (72.7)	

SD=standard deviation; VATS=video-assisted thoracoscopic surgery



Median time (IQR) month

Survival | 13(12, 37)

Figure 1. The overall survival of patients over time (median survival was 13 months with the overall survival rates 33.6% at 3 years and 12.6% at 5 years).

Time Fail Survivor

12	13	0.5001
24	2	0.4091
36	1	0.3507
48	1	0.2806
60	0	0.2806
72	0	0.2806
84	0	0.2806
96	0	0.2806
108	0	0.2806
120	0	0.2806
132	0	0.2806
144	0	.

Median time (IQR)

Recurrence | 8.6(3.8, 11.0)

Figure 2. The recurrence-free interval (DFI) over the time (median time for recurrence-free interval was 8.6 months).

Table 2. Patient characteristics by recurrent

Variable	Total (n=27)	Non- recurrent (n=10)	Recurrent (n=17)	p-value
Age (years); mean±SD	12.2±4.4	9.9±4.6	13.6±3.8	0.037
Sex; n (%)				0.999
Male	19 (70.4)	7 (70.0)	12 (70.6)	
Female	8 (29.6)	3 (30.0)	5 (29.4)	
Size tumor; n (%)				0.621
Small (<3 cm)	22 (81.5)	9 (90.0)	13 (76.5)	
Large (>3 cm)	5 (18.5)	1 (10.0)	4 (23.5)	
Number of lesions; n (%)				0.363
Single lesion	21 (77.8)	9 (90.0)	12 (70.6)	
Multiple lesion	6 (22.2)	1 (10.0)	5 (29.4)	
Lung metastasis location; n (%)				0.351
Right lung	10 (37.0)	3 (30.0)	7 (41.2)	
Left lung	11 (40.7)	6 (60.0)	5 (29.4)	
Bilateral lung	6 (22.3)	1 (10.0)	5 (29.4)	
Pleural effusion; n (%)				0.365
No	20 (74.1)	6 (60.0)	14 (82.4)	
Yes	7 (25.9)	4 (40.0)	3 (17.6)	
Approach; n (%)				0.363
Posterolateral thoracotomy	21 (77.8)	9 (90.0)	12 (70.6)	
VATS	6 (22.2)	1 (10.0)	5 (29.4)	
Type of resection; n (%)				0.999
Wedge resection	19 (70.4)	7 (70.0)	12 (70.6)	
Segmentectomy	3 (11.1)	1 (10.0)	2 (11.8)	
Lobectomy	5 (18.5)	2 (20.0)	3 (17.6)	
Number of surgeries; n (%)				0.370
1	15 (55.6)	8 (80.0)	7 (41.2)	
2	7 (25.9)	1 (10.0)	6 (35.3)	
3	1 (3.7)	0 (0.0)	1 (5.9)	
4	3 (11.1)	1 (10.0)	2 (11.7)	
5	1 (3.7)	0 (0.0)	1 (5.9)	

SD=standard deviation; VATS=video-assisted thoracoscopic surgery

status. Seventeen patients (63%) developed recurrent disease, while 10 (37%) remained disease-free. The mean age of patients with recurrence was significantly higher than those without recurrence at 13.6 ± 3.8 versus 9.9 ± 4.6 years ($p=0.037$). No significant associations were found between recurrence and gender, tumor size, number of lesions, pleural effusion, or surgical variables.

Univariate Cox regression analysis identified patient age as the only variable significantly associated with recurrence (HR 1.12, 95% CI 1.00 to 1.30, $p=0.046$) (Table 3). Other factors including tumor size, number of metastases, laterality, type of resection, and surgical approach showed no significant association with either recurrence or overall survival. In the multivariate analysis, there

Table 3. Univariate Cox regressing analyses of recurrence

Variable	Univariate HR (95% CI)	p-value
Age (years)	1.12 (1.0 to 1.3)	0.046
Sex		
Male	1	
Female	0.75 (0.3 to 2.2)	0.602
Size tumor		
Small (<3 cm)	1	
Large (>3 cm)	1.49 (0.5 to 4.6)	0.490
Number of lesions		
Single lesion	1	
Multiple lesion	1.34 (0.5 to 3.9)	0.563
Lung metastasis location		
Right lung	1	
Left lung	0.61 (0.2 to 1.9)	0.402
Bilateral lung	1.07 (0.3 to 3.5)	0.909
Pleural effusion		
No	1	
Yes	0.57 (0.2 to 2.0)	0.387
Approach		
Posterolateral thoracotomy	1	
VATS	1.36 (0.5 to 3.9)	0.568
Type of resection		
Wedge resection	1	
Segmentectomy	0.86 (0.2 to 3.9)	0.846
Lobectomy	0.99 (0.3 to 3.6)	0.990
Number of surgeries		
1	1	
2	2.21 (0.7 to 6.7)	0.160
3	-	
4	1.7 (0.3 to 8.5)	0.509
5	-	

HR=hazard ratio; CI=confidence interval; VATS=video-assisted thoracoscopic surgery

was no significant association between any variable and either survival or recurrence.

DISCUSSION

Pediatric sarcoma with pulmonary metastases remains a major therapeutic challenge. Surgical resection of metastatic lung lesions continues to represent the cornerstone of management for patients with controlled primary disease and adequate cardiopulmonary reserve. Studies have confirmed that complete pulmonary metastasectomy confers a significant survival advantage compared with non-operative management⁽⁵⁻⁷⁾.

The present study findings support this evidence. Although overall outcomes remain poor, pulmonary metastasectomy offered meaningful survival for a

subset of patients. In this cohort, the 3- and 5-year overall survival rates were 33.6% and 12.6%, respectively, with a median recurrence-free interval of 8.6 months. These results are consistent with previous large-scale studies, such as that of Pastorino et al., who reported 5- and 10-year survival rates of 31% and 26% after lung metastasectomy for sarcoma⁽⁸⁾.

Prognostic factors

In the present study analysis, disease recurrence was the only factor significantly associated with mortality. Furthermore, older age correlated with a higher risk of recurrence. These findings suggest that age may serve as an unfavorable prognostic indicator in pediatric pulmonary metastatic sarcoma. The mechanisms underlying this relationship remain uncertain, but older pediatric patients may have biologically more aggressive tumors or a reduced tolerance to multimodal therapy.

Other commonly proposed prognostic factors, such as number and size of metastatic nodules, laterality, and type of resection, did not significantly influence survival in the present study. This may be attributable to the small sample size or to selection bias, as all included patients were deemed resectable. Roth et al. demonstrated that patients with four or less pulmonary metastases experienced longer post-thoracotomy survival compared with those with more than four nodules ($p<0.02$), whereas the present study limited cohort size precluded detection of such differences⁽³⁾.

Surgical approach and extent of resection

In line with the literature, the surgical approach as thoracotomy versus VATS, and extent of resection as wedge, segmentectomy, or lobectomy, were not significant predictors of outcome. Most metastases were peripheral and could be managed with wedge resection, whereas lobectomy was reserved for lesions near the hilum or multiple nodules within a single lobe. This approach preserved pulmonary parenchyma without compromising oncologic control.

Histological subtype

Interestingly, all long-term survivors in the present series had osteosarcoma as the primary tumor, suggesting a potentially better prognosis compared with soft-tissue sarcomas. However, this observation did not reach statistical significance and may simply reflect the predominance of osteosarcoma within the present study cohort. Previous reports similarly

indicate that histological subtype may influence outcomes, but evidence remains inconclusive^(1,6,7).

Recurrence and long-term outcomes

The high recurrence rate observed in the present study, at 63%, aligns with prior reports, in which 40% to 70% of patients develop new pulmonary metastases after resection⁽¹⁾. The median interval to recurrence of four to six months in other series is comparable to the present study recurrence-free interval of 8.6 months. Although repeated metastasectomy has been advocated in selected patients, the data did not demonstrate a significant survival benefit among those who underwent multiple resections, due to limited sample size and heterogeneity.

LIMITATION

The present study has limitations. First, it was retrospective and single center in nature, with a small sample size that limits statistical power. Second, radiologic data were insufficient to evaluate tumor doubling time or volumetric progression, which may serve as valuable prognostic indicators. Finally, the heterogeneous histologic subtypes and treatment protocols among patients could have introduced confounding factors.

CLINICAL IMPLICATIONS AND FUTURE PERSPECTIVES

Despite these limitations, the present study findings underscore that pulmonary metastasectomy remains an essential component of multimodal therapy for pediatric sarcoma. Complete resection offers the best chance for prolonged survival, and the absence of significant differences among surgical techniques supports the principle of parenchymal preservation whenever feasible. Future multicenter studies with standardized protocols are warranted to refine prognostic models and optimize surgical strategies in this rare but challenging population.

CONCLUSION

Pulmonary metastasectomy remains a key component of multidisciplinary management for pediatric sarcoma with lung metastases. Although the overall prognosis remains poor, complete surgical resection offers the best chance for prolonged survival. In this single-center series, the 5-year survival rate was 12.6%, and the median recurrence-free interval was 8.6 months. Age at the time of surgery was identified as a significant factor associated with recurrence, while surgical approach and resection

type did not influence outcomes. All long-term survivors in the present study had osteosarcoma as the primary tumor.

Given the small cohort and retrospective design, further multicenter studies with larger sample sizes are needed to validate these findings and to better define prognostic factors guiding surgical decision-making in pediatric pulmonary metastatic sarcoma.

WHAT IS ALREADY KNOWN ABOUT THIS TOPIC?

Pulmonary metastasectomy is an established treatment for patients with sarcoma who develop resectable lung metastases and can achieve long-term survival when complete resection is possible. Most available evidence, however, is derived from adult or mixed-age populations, and data focusing exclusively on pediatric patients remain limited. Reported 5-year survival rates after pulmonary metastasectomy for sarcoma range from 25% to 35%, and the prognostic factors influencing survival in children, such as age, number of metastases, and completeness of resection, are still not clearly defined.

WHAT DOES THIS STUDY ADD?

The present study provides single-center data on pulmonary metastasectomy in pediatric patients with metastatic sarcoma in Thailand. The 5-year survival rate in this cohort was 12.6%, with disease recurrence identified as the only factor significantly associated with mortality, and older age as the only variable significantly associated with recurrence. Surgical approach and extent of resection showed no impact on survival outcomes. These findings emphasize the prognostic importance of patient age and recurrence, support the role of complete resection in achieving longer survival, and highlight the need for larger multicenter studies to refine surgical strategies for pediatric sarcoma with pulmonary metastasis.

CONFLICT OF INTEREST STATEMENT

All authors report no conflict of interest.

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