

Pulmonary Metastasectomy in Adult Patients with Synovial Sarcoma: A Single-Center Experience

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Background: This study assessed the efficacy of pulmonary metastasectomy for synovial sarcoma in adult patients. **Methods:** Fifty patients, diagnosed with pulmonary metastasis from June 1990 to August 2010, were reviewed retrospectively. Twenty-eight patients underwent complete pulmonary metastasectomy, and their survival was evaluated. Age, sex, time to metastatic progression, laterality, number of tumors, size of largest nodule, and number of metastasectomies were analyzed as potential prognostic factors. **Results:** In all, 29 patients underwent at least one pulmonary metastasectomy, and 51 resections were performed. One intra-operative mortality occurred, and the 5-year survival rate was 58.4%. Bilateral metastases and early metastatic progression were associated with poor survival in multivariate analyses. **Conclusion:** Surgical resection can be a good option for treating pulmonary metastasis in patients with synovial sarcoma. Repeated resection was feasible with low mortality and morbidity.

Key words: 1. Metastasectomy
2. Synovial sarcoma
3. Sarcoma
4. Neoplasm metastasis
5. Tumor, malignant

Introduction

Synovial sarcoma (SS) is a very rare but highly malignant neoplasm of soft tissue that accounts for 5%–10% of malignant soft-tissue sarcomas and is the most common non-rhabdomyosarcoma in pediatric patients [1-3]. According to reports from Western countries, the majority of patients are 15 to 30 years of age [1] and 30% of SSs are diagnosed in patients

less than 20 years old [4]. The most commonly affected site is the popliteal fossa of the knee. About 80%–95% of SSs occur in the extremities, more commonly in lower (60%–71%) than in upper extremities (16%–25%) [5].

The lungs are the most common site for distant metastasis, and a pulmonary metastasis occurs in 50%–70% of patients [6]. Most studies on SS have regarded pulmonary metastasectomy as a good prog-

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nostic factor [7-12], whereas other studies have reported no significant differences in survival [13]. Only one study focused on pulmonary metastasectomy and evaluated the prognostic factors in pediatric patients [7].

In this study, we focused on adult patients who underwent complete resection of a pulmonary metastasis, to help define the long-term survival and prognostic factors for such patients.

Methods

A total of 145 patients who were diagnosed with SS and had undergone complete resection of the primary site at Korea Cancer Center Hospital between June 1990 and August 2010 were enrolled in our study. Among them, 50 patients had developed pulmonary metastasis, and 29 had undergone a pulmonary metastasectomy.

Pulmonary metastasectomy was attempted in all cases whenever complete resection was feasible, but the size and number of nodules were not considered. A median sternotomy was performed preferentially when bilateral metastases were suspected, a thoracotomy was done when unilateral metastasis was obvious, and video-assisted surgery (VATS) was conducted in selected cases. Digital palpation and manual resection were the principle operative procedures to preserve normal lung parenchyma. Repeated resection was done for recurrent pulmonary metastases. Computed tomography scans were taken every 3 months during follow-up for the first 2 years after metastasectomy and every 6 months thereafter. Regular magnetic resonance imaging follow-up was performed at the primary tumor site, and ultrasonography was used if needed.

Survival was defined as the time interval from first pulmonary metastasectomy until death (or the last recorded follow-up). Early progression was defined when pulmonary metastases were diagnosed within 1 year from the operation for primary disease. Survival was analyzed using the Kaplan-Meier method, and survival between groups was compared to the log-rank test. The Cox proportional hazards model was used for multivariate analyses. A p -value <0.05 was considered significant.

Table 1. Patient characteristics

Characteristic	Study group (n=29)
Age (yr)	32 (17-63)
Sex	
Male	14
Female	15
Time to progression	
Early progression (≤ 1 yr)	15
Late progression (> 1 yr)	14
Laterality	
Unilateral	20
Bilateral	9
Histologic subtype	
Monophasic	18
Biphasic	7
Others	4
No. of nodules detected by CT	3.7 \pm 4.4
Mass size on CT (cm)	1.5 \pm 1.06

Values are presented as median (range), number, or mean \pm standard deviation.

CT, computed tomography.

Results

Median patient age was 32 years (range, 17 to 63 years) at diagnosis, and 14 males and 15 females were included. Nine patients presented with early progression, and 9 patients presented with bilateral metastases (Table 1). Median follow-up was 67.9 months (range, 10.4 to 216.5 months). In all, 51 resections were performed in 29 patients, complete resection was achieved in 50 cases. A median sternotomy was done in 14 cases, thoracotomy in 32 cases, and VATS in 5. There was 1 segmentectomy, 1 lobectomy, and 1 pneumonectomy. Twelve patients underwent a second operation, and 5 received a third metastasectomy. A female patient who was diagnosed at 26 years received 7 pulmonary resections, survived for 11 years from the first metastasectomy, and has been living for 3 years without any signs of recurrence. One operative mortality occurred: a 57-year-old female received a pneumonectomy as a fourth metastasectomy and died on postoperative day 1 due to sudden cardiac arrest (Fig. 1). The median length of survival was 79.5 months (95% confidence interval, 51.7 to 107.2), and the 5-year survival rate was 58.4%. Multivariate analyses of patients who underwent metastasectomy showed that bilateral disease ($p < 0.01$) and early progression ($p = 0.004$) were sig-

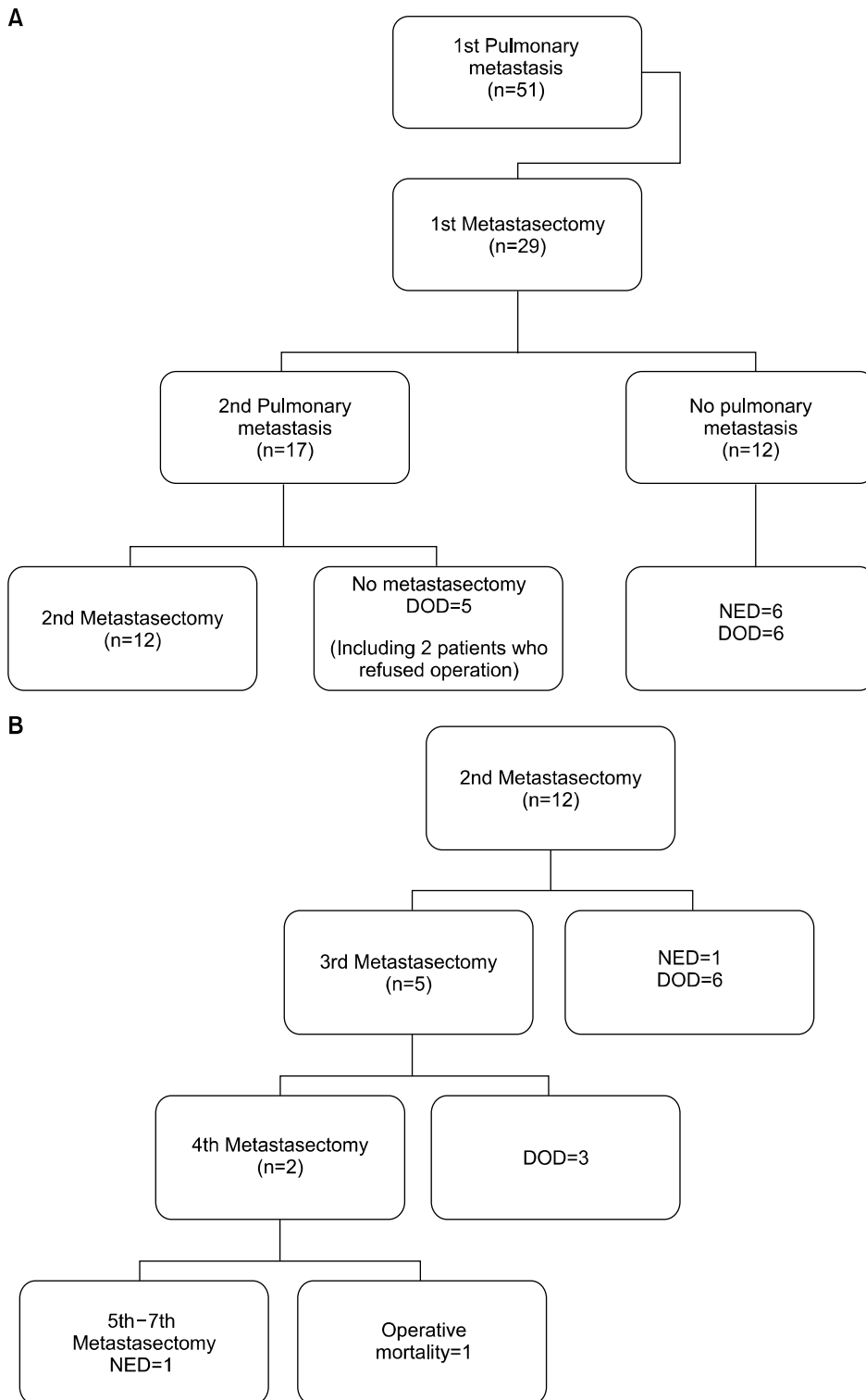


Fig. 1. (A, B) Repeated pulmonary metastasectomy. NED, no evidence of disease; DOD, dead of disease.

nificant prognostic factors. The number of metastasectomies was not a significant risk factor for survival (Table 2).

Discussion

Synovial sarcoma is a rare but highly malignant

Table 2. Multivariate Cox proportional hazard analysis of patients who underwent pulmonary metastasectomy

Variable	Hazard ratio (95% confidence interval)	p-value
Male gender	3.00 (1.06–8.45)	0.038
Bilateral metastasis	12.24 (3.21–46.67)	<0.001
Early progression ^{a)}	5.12 (1.68–15.64)	0.004

^{a)}Metastases diagnosed within 1 year from the operation for primary disease.

disease; thus, most hospitals have limited clinical experience with it. A few clinical studies have been conducted, but most have reported a small number of cases. The mean patient age in Western studies is 15–30 years, whereas East Asian studies have reported a mean age of >34 years [14–16], suggesting that the patient populations in these studies may not have been fully representative or that some ethnic or epidemiological differences were undetected.

The lungs are the most common site of distant metastasis in patients with SS, but treatment of pulmonary metastasis is controversial. Although SSs are chemosensitive, patients who undergo chemotherapy for a pulmonary metastasis of a soft-tissue sarcoma generally gain no survival benefit [11,12]. Lanza et al. [11] reported that preoperative chemotherapy in patients with soft-tissue sarcomas does not affect survival after pulmonary metastasectomies.

Pulmonary metastasectomy is not a well-established treatment for SS. Spurrell et al. [13] reported no survival gain in patients who underwent pulmonary metastasectomy. In contrast, Stanelle et al. [7] published positive outcomes of pulmonary metastasectomy in patients with SS. They retrospectively reviewed 72 pulmonary resections in 41 pediatric patients (<22 years), and reported a 2-year survival of 65% and a 5-year survival of 24% in the metastasectomy group. No patient survived more than 2 years in their control group; therefore, they concluded that pulmonary metastasectomy is a good prognostic factor. They also reported that complete resectability has prognostic value, but that size, number of tumors, and bilateral metastasis were not significant prognostic factors. Spillane et al. [8] examined 61 patients with pulmonary metastasis; 21 had undergone pulmonary resection, which improved the median survival and 5-year survival rates (38 months vs. 11 months and 6% vs. 23%).

Because the possibility of a cure is often emphasized after complete resection of pulmonary metastases, repeated resections are often performed regardless of other factors. We observed one operative mortality, but no major morbidities. Two of 5 patients who underwent more than 3 pulmonary resections were alive for more than 5 years, and 1 patient survived after 7 repeated resections and experienced a 3-year disease-free interval. No significant survival difference was observed between patients who underwent 1 and more than 1 metastasectomy. In this regard, repeated pulmonary resection is possible and can be performed safely.

In our study, patients who had undergone at least 1 metastasectomy had a higher survival rate. Bilateral metastases and early progression were significant poor prognostic factors in multivariate analyses. These outcomes somewhat differ from those of Stanalle et al. [7], who reported that only complete resectability has prognostic value, but this may be due to a lower number of incomplete resections. Despite the limitations of a small sample size, our study provides more detailed prognostic factors.

In conclusion, pulmonary metastasectomy is a good treatment option to extend survival in patients with SS, and repeated resection is feasible in selected cases. Bilateral metastases and early progression are significant factors for a poor prognosis in SS. A larger study is needed to confirm our findings.

Conflict of interest

No potential conflicts of interest relevant to this article are reported.

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References

1. Fisher C. *Synovial sarcoma*. Ann Diagn Pathol 1998;2:401-21.
2. Kransdorf MJ. *Malignant soft-tissue tumors in a large referral population: distribution of diagnoses by age, sex, and location*. AJR Am J Roentgenol 1995;164:129-34.
3. Ferrari A, Gronchi A, Casanova M, et al. *Synovial sarcoma: a retrospective analysis of 271 patients of all ages treated*

- at a single institution. *Cancer* 2004;101:627-34.
4. Okcu MF, Munsell M, Treuner J, et al. *Synovial sarcoma of childhood and adolescence: a multicenter, multivariate analysis of outcome*. *J Clin Oncol* 2003;21:1602-11.
 5. Murphey MD, Gibson MS, Jennings BT, Crespo-Rodriguez AM, Fanburg-Smith J, Gajewski DA. *From the archives of the AFIP: imaging of synovial sarcoma with radiologic-athologic correlation*. *Radiographics* 2006;26:1543-65.
 6. Singer S, Baldini EH, Demetri GD, Fletcher JA, Corson JM. *Synovial sarcoma: prognostic significance of tumor size, margin of resection, and mitotic activity for survival*. *J Clin Oncol* 1996;14:1201-8.
 7. Stanelle EJ, Christison-Lagay ER, Wolden SL, Meyers PA, La Quaglia MP. *Pulmonary metastasectomy in pediatric/adolescent patients with synovial sarcoma: an institutional review*. *J Pediatr Surg* 2013;48:757-63.
 8. Spillane AJ, A'Hern R, Judson IR, Fisher C, Thomas JM. *Synovial sarcoma: a clinicopathologic, staging, and prognostic assessment*. *J Clin Oncol* 2000;18:3794-803.
 9. Gadd MA, Casper ES, Woodruff JM, McCormack PM, Brennan MF. *Development and treatment of pulmonary metastases in adult patients with extremity soft tissue sarcoma*. *Ann Surg* 1993;218:705-12.
 10. Billingsley KG, Burt ME, Jara E, et al. *Pulmonary metastases from soft tissue sarcoma: analysis of patterns of diseases and postmetastasis survival*. *Ann Surg* 1999;229:2-10.
 11. Lanza LA, Putnam JB Jr, Benjamin RS, Roth JA. *Response to chemotherapy does not predict survival after resection of sarcomatous pulmonary metastases*. *Ann Thorac Surg* 1991;51:219-24.
 12. Predina JD, Puc MM, Bergey MR, et al. *Improved survival after pulmonary metastasectomy for soft tissue sarcoma*. *J Thorac Oncol* 2011;6:913-9.
 13. Spurrell EL, Fisher C, Thomas JM, Judson IR. *Prognostic factors in advanced synovial sarcoma: an analysis of 104 patients treated at the Royal Marsden Hospital*. *Ann Oncol* 2005;16:437-44.
 14. Song WS, Jeon DG, Park JH, et al. *Long term survival of synovial sarcoma and treatment strategy*. *J Korean Orthop Assoc* 2004;39:329-34.
 15. Koh KH, Cho EY, Kim DW, Seo SW. *Multivariate analysis of prognostic factors in synovial sarcoma*. *Orthopedics* 2009;32:824.
 16. Hasegawa T, Yokoyama R, Matsuno Y, Shimoda T, Hirohashi S. *Prognostic significance of histologic grade and nuclear expression of beta-catenin in synovial sarcoma*. *Hum Pathol* 2001;32:257-63.