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Factors associated with actual long-term survival following soft tissue sarcoma pulmonary metastasectomy

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Abstract

Aims: To identify clinicopathologic and treatment variables associated with long-term overall survival (OS) in soft tissue sarcoma (STS) patients with lung metastases undergoing pulmonary metastasectomy (PM).
Methods: Retrospective review of 94 STS PM patients with an actual follow-up ≥5 years. Data were collected on demographics, tumor features, treatment, and outcome.
Results: Most primary tumors were intermediate/high grade and the common histopathologies were evenly distributed. Half of the primary tumors were located on the extremities. The mean disease-free interval (DFI) from time of original diagnosis until metastases was 25 months (median 15 months). Eighteen patients had synchronous metastatic disease. Bilateral pulmonary metastases and >1 metastasis were common. The median number of metastases resected was 2.5. Thirty-four patients had extrapulmonary tumor at the time of PM; all extrapulmonary disease was resected. Negative margin resection (R0) PM was performed in 74 patients. Actual 5-year disease-free survival (DFS) and OS for all patients were 5% and 15%, respectively. For the R0 group, actual 5-year DFS and OS were 7% and 18%, respectively. R0 resection and a prolonged DFI were associated with improved OS. Patient characteristics, tumor features, local recurrence, and adjuvant therapy did not affect OS.
Conclusions: Less than 20% of STS PM patients will survive 5 years. Complete resection and DFI are the most predictive factors for prolonged survival.

Keywords: Sarcoma, soft tissue; Neoplasm metastasis; Pulmonary surgical procedures; Thoracic surgery; Disease-free survival; Survival analysis

Introduction

Approximately 20–25% of all soft tissue sarcoma (STS) patients will develop pulmonary metastases (40–60% for high grade tumors) and 70% of these patients will have disease limited only to the lungs.[1–3] The majority of the lung metastases will manifest clinically in the first 2 years following diagnosis.[4]

Due to the high rate of isolated lung metastases, pulmonary metastasectomy (PM) has developed as a potentially curative therapy with a 3-year overall survival (OS) of 30–42%.[5–8] Factors associated with improved survival include complete resection, number of metastases, tumor doubling time, and the disease-free interval (DFI) from diagnosis of the primary tumor until metastases.[5,6,9–11] The relative importance of these variables has been mixed except for incomplete resection, which has a dismal prognosis in all series. Even with complete resection of all metastases, pulmonary recurrence occurs in 45–83% of patients.[5,12–14] Re-resection remains the only salvage therapy with a 5-year disease-specific survival of up to 36%.[15]

Given the limited follow-up of some previous STS PM series and the high rate of pulmonary recurrence, we have examined a group of STS patients undergoing potentially curative PM with an actual follow-up ≥5 years to identify clinicopathologic and treatment variables associated with long-term OS. Due to the lack of other effective therapies, patients were treated aggressively with PM, including

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re-resection of recurrent disease, when technically and medically feasible.

Methods

Patient population

All patients at Roswell Park Cancer Institute undergoing STS PM from January 1976 through December 2000 were retrospectively identified through a computerized coding search of the tumor registry and the medical records. A total of 99 patients were identified for the given time period and 94 patients had complete follow-up information for a minimum of 5 years.

Data collection

The hospital and outpatient records for each patient were reviewed. For portions of care received away from the institute, records and correspondence were obtained from outside sources, when possible. All data collection and analysis were performed under an institutional review board (IRB) approved protocol. Patient demographics, tumor characteristics, therapy, and outcome were recorded for all patients. In the case of grade of the primary tumor, if the grade was not expressly recorded, then it was considered high grade if there were $\geq$20 mitoses per 10 high powered fields or necrosis was seen. The other variables were recorded directly from the charts.

Statistical methods

Five year actual disease-free survival (DFS) and OS were calculated for all patients from the time of PM. For patients undergoing re-resection of recurrent pulmonary metastatic disease, survival was determined from the time of the initial complete resection. However, multiple resections were included on multivariate analysis to determine its effect on survival as a whole. For patients undergoing staged thoracotomies for bilateral disease, survival was calculated from the date of the second resection. The completeness of resection margin or R groups (R0 microscopic negative; R1 grossly negative but microscopic positive; R2 gross residual) was also analyzed for DFS and OS.

The data analysis was performed by software package SAS, version 9.1. Fisher's exact test, χ^2 test, and Cochran–Armitage trend test were used to assess the statistical significance of associations between expressions of resection margin (R) and other clinicopathologic variables. Univariate survival analysis was done using Kaplan–Meier method; difference in survival curves was assessed with the log-rank test. Multivariate survival analysis was done via Cox's proportional hazard model.[16] A backward selection was performed to find a model of best linear combination of variables. Hazard Ratios (HR) and 95% Confidence Interval were calculated based upon parameters estimates from the finally fitted Cox's proportional hazard model. Proportional hazard assumption was checked in a visual evaluation of log (−log (survival)) plots. *P*-values less than 0.05 were considered to be significant.

Results

Patient groups

The clinicopathologic variables of the STS PM patients are summarized in Table 1. Median age was 49 years (range 9–75 years). Seventy-seven primary tumors were intermediate/high grade and the common histopathologies were fairly evenly distributed. Half of the primary tumors were located on the extremities. "Other" primary tumor sites included 10 buttock/pelvis, seven chest wall/trunk, four head and neck, two breast, one small bowel, one prostate, and one vagina. The mean disease-free interval (DFI) from the original diagnosis until metastases was 25 months

Table 1
Clinicopathologic features of soft tissue sarcoma patients undergoing pulmonary metastasectomy

Characteristic	*n*
Sex	
Male	47
Female	47
Tumor histology	
Malignant fibrous histiocytoma	16
Synovial sarcoma	18
Leiomyosarcoma	22
Liposarcoma	12
Other	26
Grade	
High	64
Intermediate	13
Low	11
Unknown	6
Primary tumor site	
Extremity	47
Retroperitoneum	6
Uterus	12
Other	29
Local recurrence	
Yes	44
No	50
Synchronous metastases	
Yes	18
No	76
Bilateral pulmonary metastases	
Yes	60
No	34
Number of pulmonary metastases	
1	34
>1	60
Extrapulmonary disease at time of surgery	
Yes	34
No	60