ORIGINAL ARTICLE

Clinicopathologic characteristics, treatment outcomes, and prognostic factors of primary thoracic soft tissue sarcoma: A multicenter study of the Anatolian Society of Medical Oncology (ASMO)

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Abstract

Background: Soft tissue sarcomas (STSs) are rare malignant tumors of embryogenic mesoderm origin. Primary thoracic STSs account for a small percentage of all STSs and limited published information is available. This study aimed to identify the prognostic factors for thoracic STSs and evaluate the disease's clinical outcomes.

Methods: The medical records of 109 patients with thoracic STSs who were treated between 2003 and 2013 were retrospectively reviewed. Patients' survival rates were analyzed and potential prognostic factors evaluated.

Results: The median follow-up period was 29 months (range: 1–121 months). STSs were most frequently localized on the chest wall ($n = 42$; 38.5%) and lungs ($n = 42$; 38.5%). The most common histological types were malignant fibrous histiocytoma ($n = 23$; 21.1%), liposarcoma ($n = 17$; 15.6%), and leiomyosarcoma ($n = 16$; 14.7%). The median survival time of all patients was 40.3 months (95% confidence interval, 14.22–66.37 months), with one and five-year survival rates of 93.4% and 63.5%, respectively. Univariate analysis of all groups revealed that metastatic stage, unresectability, tumor diameter of >10 cm, tumor location other than the chest wall, and grade 3 diseases were predictable of poor survival. However, only grade 3 diseases and tumor location other than the chest wall were confirmed by multivariate analysis as poor prognostic factors.

Conclusions: Primary thoracic STSs are rarely seen malignant tumors. Our results indicated that patients with low-grade tumors and those localized on the chest wall often experienced better survival outcomes.

Introduction

Soft tissue sarcomas (STSs) are rare malignant tumors of embryogenic mesoderm origin.[1] They account for less than 1% of all human malignancies.[1] Approximately 60% of STSs are localized on the extremities with the remaining commonly found in the gastrointestinal, retroperitoneal, head, and neck regions.[2] Thoracic STSs account for a small percentage (3–8%) of STSs[3,4] with tumors often found in the lungs, mediastinum, pleura, pericardium, heart, and chest walls.[5]

STS is a heterogenous disease with more than 60 histological types.[6] Malignant fibrous histiocytomas and liposarcomas are the most commonly observed STSs of the extremities, whereas the frequency of thoracic STS histological types varies depending on tumor location,[2] such as fibrosarcomas and leiomyosarcomas in the lungs, angiosarcomas in the heart, and malignant fibrous histiocytomas on the chest wall.[7–10]

Multimodality therapy, including surgery, radiotherapy, and chemotherapy, is commonly used for the treatment of STSs.[2,11–13] Of these, surgery is the most important component. Clinical parameters such as patients' age, Eastern Cooperative Oncology Group (ECOG) performance status, tumor histology, and tumor grade are often considered when other treatment modalities are elected. Although the surgical treatment outcomes of thoracic STSs have been analyzed in several published studies, such analyses are not available for any other treatment modalities.

Furthermore, although the prognostic factors for overall STS patient survival have been thoroughly analyzed,[11,14] only one study thus far has specifically examined those in primary thoracic STSs.[15] Otherwise, most published reports have focused on surgical or radiological studies of thoracic STS retrospective case series or case reports.[16–18]

The present study aimed to determine the clinicopathological features, survival rates, and prognostic factors of patients with primary thoracic STSs treated at major hospitals in Turkey.

Materials and methods

Study design

The present study was designed as a retrospective analysis of a primary thoracic STS patient cohort.

Methods

The Executive Committee of Anatolian Society of Medical Oncology approved this study. We collected data from patients with primary STSs treated at 15 different medical oncology centers in Turkey. Data collection began in February 2012. Information on patients' age, gender, tumor size, location, and the presence of primary tumor and metastatic site were retrieved from their medical records. The 2002 World Health Organization criteria were used for histopathological diagnosis of all patients,[19] and the Fédération Nationale des Centres de Lutte Contre le Cancer system was used for tumor grading.[20] In addition, treatment modalities (cytotoxic agents, chemotherapy regimen, surgery, and radiotherapy), clinical outcomes, time to disease progression, mortality rates, and the length of follow-up periods were recorded until the last visit in October 2013.

The inclusion criteria were as follows: (i) STS histology; (ii) the primary tumor site being within the thoracic region, including the chest wall, lungs, pleura, mediastinum, pericardium, and heart; and (iii) patient's age of >18 years. The exclusion criteria included: (i) skeletal sarcoma (excluding extra-skeletal Ewing sarcoma and extra-skeletal chondrosarcoma); (ii) desmoid tumor; and (iii) dermatofibrosarcoma protuberans.

Statistical analysis

Data were analyzed using the Statistical Package for the Social Sciences (SPSS) version 15.0 for Windows (SPSS Inc., Chicago, IL). Overall survival (OS) was calculated from the surgery time or the time of diagnosis to death or the last day of the follow-up period. The Kaplan-Meier method was used for OS analysis. For the comparison of survival rate differences, a log-rank (Mantel-Cox) test was used for univariate analysis and Cox-proportional hazards model for multivariate analysis. A P-value of <0.05 was considered statistically significant. The following factors were evaluated in the prognostic factor analysis: gender (male or female); age (<50 and ≥50 years), stage (local, locally advanced, and metastatic), tumor diameter (0–5 cm, 5–10 cm, or ≥10 cm), grade (1 and 3), resection (complete, incomplete resection, and unresectable), ECOG performance status (0, 1, and 2), tumor location (the chest wall, lungs, or other), adjuvant radiotherapy (applied or not), and adjuvant chemotherapy (applied or not).

Results

Global patient characteristics and treatment alternatives

This study enrolled 109 patients with a male/female ratio of 1:3. Patient characteristics are summarized in Table 1. The primary tumor was commonly located in the mediastinum ($n = 16$; 14.7%), pleura ($n = 5$; 4.6%), intracardiac region ($n = 3$; 2.8%), and pericardium ($n = 1$; 0.9%). Malignant fibrous histiocytoma was the most frequently observed histological type. When separate groups were considered, malignant fibrous histiocytoma was often found on the chest wall

Table 1 Patient characteristics

		All patients (n = 109)	Surgery group (n = 75)
Median age		46 (18–85)	46 (19–85)
Gender	Male	62 (56.9%)	43 (57.3%)
	Female	47 (43.1%)	32 (42.7%)
Primary tumor site	Chest wall	42 (38.5%)	36 (48%)
	Lung	42 (38.5%)	25 (33.3%)
	Others†	25 (23%)	14 (18.7%)
Histological type	Malignant fibrous histiocytoma	23 (21.2%)	20 (26.7%)
	Liposarcoma	17 (15.6%)	12 (16%)
	Leiomyosarcoma	16 (14.7%)	10 (13.3%)
	Unclassified	14 (12.8%)	10 (13.3%)
	Ewing sarcoma	11 (10.1%)	6 (8%)
	Synovial sarcoma	10 (9.1%)	6 (8%)
	Fibrosarcoma	6 (5.5%)	4 (5.3%)
	Rare types	12 (11%)‡	7 (9.4%)
Tumor diameter	<5 cm	20 (18.3%)	17 (22.7%)
	5–10 cm	45 (41.3%)	37 (49.3%)
	≥10 cm	19 (17.4%)	18 (24%)
	Unknown	25 (23%)	3 (4%)
Grade	1	33 (30.3%)	26 (34.7%)
	2	4 (3.7%)	1 (1.3%)
	3	54 (49.5%)	37 (49.3%)
	Unknown	18 (16.5%)	11 (14.7%)
Stage at diagnosis	Local	57 (56.1%)	54 (72%)
	Locally advanced	29 (22.8%)	21 (28%)
	Metastatic	23 (21.1%)	
Surgery	Complete resection	63 (57.8%)	63 (84%)
	Incomplete resection§	12 (11%)	12 (16%)
	Unresectable	34 (31.2%)	
ECOG	0	27 (24.8%)	23 (30.6%)
	1	58 (53.2%)	41 (53.3%)
	2	24 (22%)	11 (16.1%)

ECOG, Eastern Cooperative Oncology Group performance status. †Other, mediastinal, pleural, pericardial, or cardiac locations; ‡Rhabdomyosarcoma (3), angiosarcoma (2), hemangiopericytoma (2), chondrosarcoma (2), spindle cell (2), alveolar soft sarcoma (1), epiteloid sarcoma (1), giant cell sarcoma (1); §R1 resection.

(n = 16; 38%), leiomyosarcoma in the lungs (n = 12; 28.5%), liposarcoma in the mediastinum (n = 4; 25%), unclassified sarcoma in the pleura (n = 2; 40%), and angiosarcoma in the intracardiac region (n = 2; 66.6%). Synovial sarcoma was detected in the pericardium of one patient. Ewing sarcomas were observed in the lungs (n = 9) and mediastinum (n = 2). Additionally, chondrosarcomas were detected in the lungs of two patients.

Seventy-five patients underwent tumor resection, mostly complete resection with only 11% incomplete resection (R1 resection). The characteristics of these surgical patients are listed in Table 1. Adjuvant chemotherapy (n = 46) or radiotherapy (n = 39) was provided to all surgical patients. The adjuvant chemotherapy regimens included ifosfamide-doxorubicin (n = 32), vincristine-adriamycin-cyclophosphamide (VAC) and ifosfamide-etoposide (IE) combination (n = 7), cisplatin and doxorubicin combination (n = 4), and VAC (n = 3).

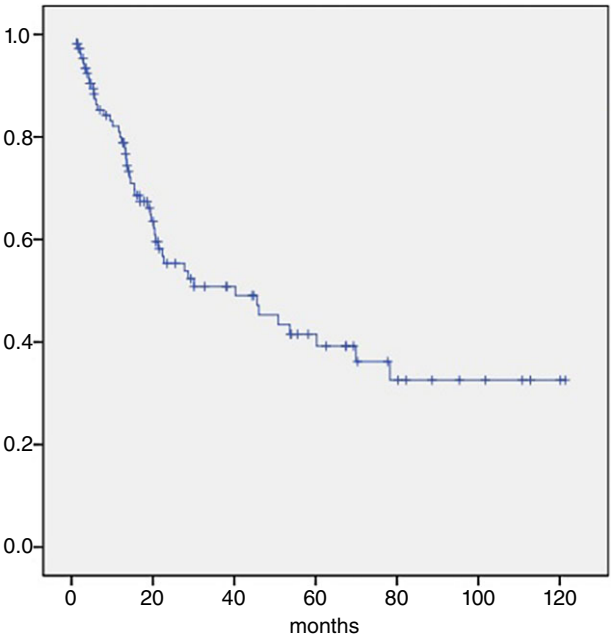

Figure 1 Mean survival of all groups. ⌐¬, Survival Function; +, Censored.

Palliative chemotherapy was provided to 58 patients with metastatic diseases at baseline or progression. The administered regimens included IE combination, gemcitabine-docetaxel combination, cisplatin-etoposide combination, cyclophosphamide, vincristine, doxorubicin, and dacarbazine (CYVADIC), and paclitaxel.

Survival outcomes

The median follow-up period was 29 months (range, 1–121 months). At the time of the present analysis, 51 patients had died. The median OS of all patients was 40.3 months (95% confidence interval [CI], 14.2–66.3 months) (Fig 1) with one and five-year survival rates of 93.4% and 63.5%, respectively. The median OS of patients undergoing resection was 53.6 months (95% CI, 16–91.3 months) with one and five-year survival rates of 91.5% and 46.5%, respectively (Fig 2). Patients with tumors located on the chest wall tended to experience a better OS (median, 78.2 months) than those with diseases in the lungs (median, 20.6 months) and other locations (median, 15.4 months) (P = 0.022) (Fig 3).

Analysis of potential prognostics

The factors included in the univariate and multivariate analyses of surgical patients' survival rates are listed in Table 2.

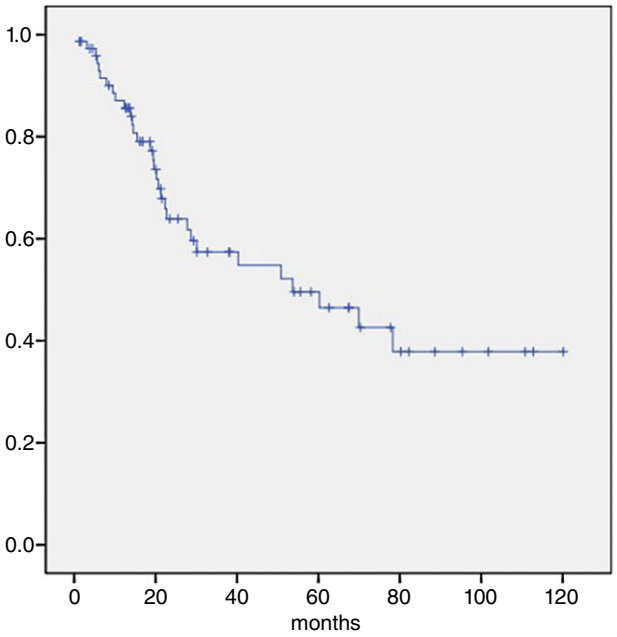

Figure 2 Mean survival of resected patients. ⌐¬, Survival Function; +, Censored.

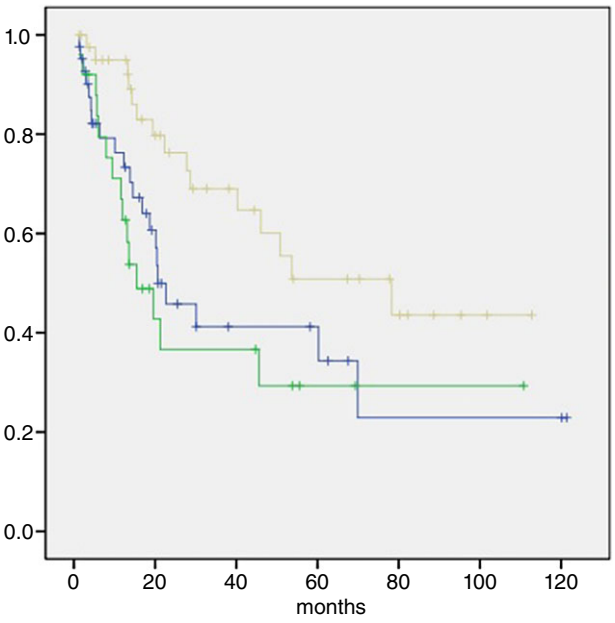

Figure 3 Mean survival of primary site. ⌐¬, Lung; ⌐¬, Other; ⌐¬, Chest Wall; +, Lung-censored; +, Other-censored; +, Chest Wall-censored.

Univariate analysis revealed that the absence of adjuvant chemotherapy, tumor diameter of >10 cm, tumor location other than the chest wall, and the presence of a grade 3 tumor were poor prognostic factors. These four factors were included in the subsequent multivariate analysis, which confirmed grade 3 tumors and tumor location other than the chest wall as poor prognostic factors. Similarly, the univariate and multivariate analyses of all patients' survival rates are summarized in Table 3. The univariate analysis identified metastatic stage, unresectability, tumor diameter of >10 cm, tumor location other than the chest wall, and the presence of a grade 3 tumor as poor prognostic factors, whereas the multivariate analysis subsequently confirmed the prognostic value of grade 3 tumors and tumor locations other than the chest wall.

Discussion

The present study aimed to define the clinical characteristics, treatment alternatives, and prognostic factors for thoracic STSs using data from multiple institutes in Turkey. The incidences of both STSs and thoracic STSs peaked at 50 years of age with a male dominancy. In our series, the median patient age was 46 years, and there were slightly more male than female patients, which is comparable to other published STS and thoracic STS series.[2,15,21]

Malignant fibrous histiocytoma is the most common STS[21] and thoracic STS type, but other histological types can also be observed at other thoracic locations.[10] In our series, angiosarcomas were frequently detected in the cardiac region, whereas

Table 2 Univariate and multivariate analyses of surgical patients' survival rates ($n = 75$)

	Univariate analysis	Multivariate analysis	
Variable	*P*-value	HR (95% CI)	*P*-value
Gender (male vs. female)	0.98		
Age (<50 years, ≥50 years)	0.39		
Stage (local, locally advanced)	0.67		
Tumor diameter (0–5 cm, 5–10 cm, ≥10 cm)	0.003		
Grade (1 vs. 3)	<0.001	27.6 (6.8–112.2)	<0.001
Resection (complete, incomplete)	0.09		
Tumor location (chest wall, lung, other)	0.02	4.63 (1.57–13.7)	0.006
Adjuvant radiotherapy (present, absent)	0.38		
Adjuvant chemotherapy (present, absent)	0.01		

CI, confidence interval; HR, hazard ratio.

Table 3 Univariate and multivariate analysis of all patients' survival rates ($n = 109$)

	Univariate analysis	Multivariate analysis	
Variable	*P*-value	HR (95% CI)	*P*-value
Gender (male vs. female)	0.47		
Age (<50 years, ≥50 years)	0.16		
Stage (local, locally advanced)	<0.001		
Tumor diameter (0–5 cm, 5–10 cm, ≥10 cm)	0.006		
Grade (1 vs. 3)	<0.001	36.9 (8.9–152.7)	<0.001
Resection (complete, incomplete, unresectable)	0.002		
ECOG performance status (0, 1, 2)	0.13		
Tumor location (chest wall, lung, other)	0.022	4.47 (1.63–12.3)	0.004

CI, confidence interval; ECOG, Eastern Cooperative Oncology Group; HR, hazard ratio.

liposarcomas were observed more often in the mediastinum. Our findings are in agreement with those previously reported on these two locations.[9,22] Leiomyosarcoma and fibrosarcoma are commonly reported for lung STSs,[7,8] which was also the case in our study. However Pieper *et al*. reported Ewing sarcoma as the most commonly detected STS in the lungs with extra-osseous tumors found in the broncho-pulmonary region.[23]

The survival rates in primary thoracic STS patients are lower than those with STSs of the extremities with reported five-year survival rates for the two diseases being 56–79% and >75%, respectively.[15,16,24–27] In our study, the five-year survival rate and median survival time were 65% and 57 months, respectively, which was similar to the results of previously published thoracic STS series.

Similar prognostic factors have been assumed to affect both patients with resected thoracic STS and those with diseases of the extremities. However, such an assumption is of limited value owing to the lower incidence of primary thoracic STS. Pisters *et al*. studied 1041 patients with STS of the extremities and found positive histological tumor margins, larger tumor size, and higher tumor grade to be associated with higher mortality rates.[26] On the other hand, Duranti *et al*. evaluated 337 patients with resected thoracic STSs and reported that grade 3 tumors, pulmonary and mediastinal STS, and R1 resection were more risky than grade 1 tumors (1.89 fold), thoracic wall STS (1.6 and 1.9 fold), and R0 resection (1.9 fold), respectively.[15] Furthermore, McMillan *et al*. reported that tumor grade was the most important determinant of survival and recurrence pattern in patients with thoracic wall STSs,[10] whereas Gross *et al*. identified tumor grade and diameter as the most important prognostic factors for survival in patients with chest wall STSs. In our study, among all patients with resected thoracic STSs, the best prognosis was noted in those with grade 1 chest wall STSs, which is comparable to the results published by Duranti *et al*. that had the largest patient cohort to date.

Additionally, we also evaluated adjuvant treatment modalities in patients with resected thoracic STS. Adjuvant chemotherapy, but not radiotherapy, was found to significantly increase survival rates. Alkis *et al*. also obtained similar outcomes in their study.[2] Radiotherapy has been shown to decrease local recurrence rate without contributing to improved survival in STS patients, as confirmed in our study.[12]

However, to our knowledge, no study on the prognostic factors for STS patient survival is available. Meanwhile, resectability has emerged as an important prognostic factor in thoracic STS, as well as all other types of STS.[28] Other prognostic factors, such as tumor grade, diameter, and stage were similar to those detected in previous large STS series.[2,4,20,21,26] However, among patients with resectable tumors, thoracic STS patients might have better prognostic characteristics.

This retrospective study has many inevitable limitations. Selection bias might have existed and patients from certain major medical centers were enrolled. Additionally, treatment modalities might differ with time and among clinics.

Conclusion

In conclusion, thoracic STS is a rare malignancy with diverse histological types according to the primary tumor location. The survival time of thoracic STS patients is apparently shorter than that of extremity STS patients. Adjuvant chemotherapy might be useful for patients with resectable tumors, whereas adjuvant radiotherapy was found to have no effect on survival. Although the prognostic factors for thoracic STS patient survival were similar to those of extremity STS, thoracic tumor location appeared to be another important factor affecting survival.

Disclosure

No authors report any conflict of interest.

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