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ORIGINAL ARTICLE – SARCOMA

Clinical Outcomes of Patients with Metastatic Solitary Fibrous Tumors: A Japanese Musculoskeletal Oncology Group (JMOG) Multiinstitutional Study

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ABSTRACT

Background. Although the unpredictable malignant behavior of solitary fibrous tumors (SFTs) has been recognized, the clinical features and prognosis of metastatic SFTs have not been well documented due to the extreme rarity of these cases. The aim of this study is to investigate the clinical features, prognostic factors, and optimal management of patients with metastatic SFTs.

Patients and Methods. Sixty patients with metastatic SFT were retrospectively reviewed. Univariate and multivariate analyses were performed to identify the factors associated with survival. Time to next treatment (TNT) was used to evaluate the effects of various chemotherapy regimens.

Results. A total of 34 male and 26 female patients (median age 55 years, range, 23–87 years) were included in the study. The median follow-up period after metastasis was 32 months (range 1–126 months). Tumor location and local recurrence were correlated with late metastasis. The 3- and 5-year overall survival rates were 72.7% and 49.2%, respectively. Primary tumor location, number of metastases, and metastasectomy were significantly associated with survival. Metastasectomy was the only significant variable on multivariate analysis. The TNT was significantly different among the various regimens.

Conclusions. Patients with metastatic SFTs had relatively longer survival periods compared with those with other metastatic soft-tissue sarcomas. Tumor location and number of metastases was associated with survival. Surgical resection of the metastatic lesions offers the best chance of survival, however further studies are warranted to define patients who would benefit from metastasectomy, and the most effective chemotherapeutic regimen for patients with metastatic SFTs remains unknown.

Solitary fibrous tumor (SFT), a rare subtype of mesenchymal tumor, is generally considered as a potential intermediate malignant tumor that can arise in any part of the body and affect both sexes equally. Histologically, a

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high mitotic rate (> 4/10 high-power fields), necrosis, hemorrhage, cellular atypia, and hypercellularity have been considered as significant features of malignancy.[1,2] However, SFTs that do not present with any of these features can develop distant metastases. Although several risk stratification models have been proposed,[3–5] accurate prediction of the metastatic potential of SFTs remains challenging.[6] Surgical complete resection is the standard treatment for localized SFT. Whereas distant metastases have been reported in 5–41% of SFTs,[2,3,5,7–10] the roles of chemotherapy and radiotherapy in patients with metastatic SFT remain unclear. In addition, due to its extreme rarity, little is known about the clinical features of this condition. Therefore, we conducted a multiinstitutional retrospective study in Japan to evaluate the clinical features of metastatic SFTs, the survivorship and factors associated with survival in patients with metastatic SFTs, and the optimal treatment of these patients.

PATIENTS AND METHODS

Patients and Treatment

Sixty metastatic SFT patients who were diagnosed and treated at 22 tertiary referral centers for musculoskeletal tumors affiliated with the Japanese Musculoskeletal Oncology Group (JMOG) were retrospectively reviewed between September 2000 and October 2018. This study was approved by the institutional review board of each institution and conducted in accordance with the Declaration of Helsinki. The following data were collected and analyzed: patient and tumor demographics (age at diagnosis of metastasis, gender, time to metastasis, primary tumor location, and primary tumor size), histopathological features (malignant/borderline/not otherwise specified (NOS) and mitotic count), status of metastasis at first presentation (location and number of metastasis), treatment procedures (surgery, radiotherapy, and chemotherapy), and oncological outcomes at last follow-up. Time to metastasis was defined as the period from the date of first diagnosis of SFT to the date the metastasis was detected. The pathological diagnosis was performed by an experienced soft-tissue tumor pathologist from each institution. Overall survival (OS) was defined as the period from the date of metastasis detection to the date of last follow-up or death. The chemotherapeutic regimens were classified into seven groups: anthracycline-based, eribulin mesylate, gemcitabine plus docetaxel (GD), ifosfamide-based, pazopanib, trabectedin, and others. Doxorubicin plus ifosfamide was included in the anthracycline-based regimen. Time to next treatment (TNT), defined as the period from the date of onset of a chemotherapeutic regimen to the date of onset of the next regimen or death, whichever came first, was utilized to evaluate the effect of each regimen.

Statistical Analysis

Fisher's exact test was used to assess the correlation between time to metastasis and each variable, and the Bonferroni method was used as a post hoc test. The OS was calculated using the Kaplan–Meier method with a 95% confidence interval (CI). The log-rank test was used for univariate analysis to identify the factors associated with OS, whereas the backward stepwise Cox proportional hazards model was used for multivariate analysis. Variables with P-value < 0.2 on univariate analysis were included in the multivariate analysis. Differences in TNT among the regimens were assessed using the Kruskal–Wallis test, while the Steel–Dwass test was used for post hoc analysis. All statistical analyses were performed using the EZR software.[11] P-value < 0.05 was considered statistically significant.

RESULTS

Patient and Tumor Characteristics

A total of 34 males and 26 females with median age of 55 years (range 23–87 years) were included in the study. The median follow-up period after metastasis was 32 months (range 1–126 months). The clinical characteristics of the patients are summarized in Table 1. The most common site of the primary tumor was the trunk (28%), followed by the head and neck (25%), extremities (22%), abdomen or retroperitoneum (18%), and thorax (7%). The primary tumor size was obtained from 49 patients with a median of 10 cm; 21 tumors (35%) were < 10 cm, and 28 (47%) were ≥ 10 cm in size. The mean tumor size of head and neck, trunk, extremities, abdomen or retroperitoneum, and thorax was 6, 14, 11, 13, and 10 cm, respectively. The median time to metastasis was 12 months (range 0–312 months), and in 29 patients (48%) the time to metastasis was < 12 months. Nineteen patients (32%) presented with metastases at first diagnosis of SFT. Furthermore, the time to metastasis was > 5 years in 19 patients (32%) and > 10 years in 8 (13%) patients. Primary tumor location and local recurrence were significantly correlated with time to metastasis ($P = 0.015$ and < 0.01, respectively; Table 2). The post hoc analysis revealed that tumors in the head and neck tended to take a longer time to develop metastasis compared with those in the trunk ($P = 0.055$; data not shown). Thirty-five primary tumors (58%) were diagnosed as malignant, 7 (12%) as borderline, and 18 (30%) as NOS. Twenty-two patients (37%) developed local recurrence

TABLE 1 Patient demographics and factors associated with overall survival

	Number	Univariate		Multivariate		
		3-Year OS (%)	*P*-value	HR	95% CI	*P*-value
Age (years)			0.459			
< 60	34	80.1				
≥ 60	26	61.3				
Gender			0.299			
Male	34	69.4				
Female	26	75.6				
Primary tumor location			< 0.01	0.756	0.463–1.237	0.266
Head and neck	15	100				
Trunk	17	66.1				
Extremity	13	47.5				
Abdomen or retroperitoneum	11	59.7				
Thorax	4	100				
Primary tumor size (cm)			0.152	1.459	0.519–4.095	0.473
< 10	21	86.2				
≥ 10	28	57				
NA	11					
Time to metastasis (month)			0.235			
< 12	29	67.4				
≥ 12	31	77.5				
Metastasis at first diagnosis			0.976			
M0	41	68.1				
M1	19	82				
Tumor type			0.22			
Malignant	35	62.5				
Borderline	7	71.4				
NOS	18	94.4				
Local recurrence			0.183	0.694	0.217–2.220	0.538
Yes	22	68.6				
No	38	79.3				
Metastatic site at first occurrence			0.527			
Lung	26	72.6				
Other	28	73.1				
Multiorgan	6	66.7				
Number of metastases at first occurrence			0.013	1.690	0.308–9.273	0.546
Single	17	94.1				
Multiple	40	67				
NA	3					
Metastasectomy			< 0.001	0.105	0.024–0.460	< 0.01
Yes	30	95.8				
No	30	51.3				
Radiotherapy			0.115	1.347	0.488–3.721	0.565
Yes	23	72.8				
No	37	71.7				
Palliative chemotherapy			0.339			
Yes	31	62.2				
No	29	85.8				

NA data not available

postoperatively. The most common metastatic site at first occurrence was the lung (43%) followed by the bone (15%) and liver (15%). The number of metastases at first occurrence was documented in 57 patients, and 17 patients (30%) presented with solitary metastasis and 40 (70%) with multiple metastases.

Treatment After Metastases

The treatment patterns after a diagnosis of metastasis are described in Table 3. Thirty (50%) patients underwent metastasectomy, 23 (38%) received radiotherapy with a median dose of 40 Gy (range, 20–62 Gy), 12 received both metastasectomy and radiotherapy, and 19 did not receive any locoregional treatment. Of the 11 patients who received radiotherapy, only 4 (36%) had regrowth of the metastatic tumor. Thirty-one patients (52%) received at least one regimen of palliative chemotherapy; among them, 11 were administrated with anthracycline-based regimens, 4 with eribulin mesylate, 10 with GD, 7 with ifosfamide-based regimens, 22 with pazopanib, 6 with trabectedin, 13 with other regimens, and 21 with multi-regimens.

Overall Survival and Prognostic Factors

At time of last follow-up, 28 patients were alive with the disease, 5 were free from disease, and 27 died of the disease. Median OS was 55 months (95% CI 40–86 months), and OS rate was 72.7% (95% CI 58–83%) at 3 years and 49.2% (95% CI 32.6–63.7%) at 5 years (Fig. 1). The univariate analysis revealed significant correlations between the OS and primary tumor location ($P < 0.01$), number of metastasis at first occurrence ($P = 0.013$), and metastasectomy ($P < 0.001$; Table 1; Fig. 2). The post hoc analysis revealed that tumors located in the extremities ($P = 0.05$) and the abdomen or retroperitoneum ($P = 0.011$) were significantly associated with poor survival compared with those in the head and neck region. Neither histological classification of the primary tumor nor chemotherapy was associated with OS. On multivariate analysis, only metastasectomy remained statistically significant (hazard ratio 0.105; 95% CI 0.024–0.460, $P < 0.01$; Table 1). The mitotic counts of the primary tumors obtained from 42 patients were not correlated with OS ($P = 0.522$, data not shown). Likewise, the mitotic counts of the metastatic tumors obtained from 16 out of the 30 patients who underwent metastasectomy were not correlated with OS ($P = 0.857$, data not shown).

Time to Next Treatment

The median TNT of each chemotherapeutic regimen is described in Table 3. TNT was significantly different among the regimens ($P = 0.028$; Fig. 3). The post hoc analysis revealed that the TNT of the ifosfamide-based regimens were significantly shorter than those of eribulin mesylate, GD, pazopanib, and others ($P = 0.033$, 0.015, $<$ 0.01, and 0.014, respectively).

DISCUSSION

The histological classification of malignant or benign SFT does not accurately reflect its clinical behaivor.[8,12] As a result, each case of SFT has the potential to metastasize. However, there are very few studies on metastatic SFTs, and the optimal management of the patients with this condition has not been well documented. In this study, the 3- and 5- year OS rates after metastasis were 72.7% and 49.2%, respectively, and the median survival was 55 months. Metastasectomy was the most important prognostic factor for improvement of OS in patients with metastatic SFT. Chemotherapy did not favorably affect survival, but the response appeared to differ among the

TABLE 2 Factors associated with late metastasis

	TM < 5 years	TM ≥ 5 years	*P*-value	TM < 10 years	TM ≥ 10 years	*P*-value
Primary tumor location			0.017			0.015
Head and neck	5	10		9	6	
Trunk	15	2		17	0	
Extremity	10	3		12	1	
Abdomen or retroperitoneum	8	3		10	1	
Thorax	3	1		4	0	
Local recurrence			< 0.01			< 0.01
Yes	10	12		15	7	
No	31	7		37	1	

TM time to metastasis

TABLE 3 Treatment procedures and regimens for patients with metastatic SFT

	Number	3-year OS (%)	TNT (median, months)
Local treatment			
Metastasectomy	18	100	
Radiotherapy	11	53	
Metastasectomy + radiotherapy	12	90.9	
None	19	49.1	
Chemotherapy			
Anthracycline-based	11		3
Eribulin mesylate	4		8
Gemcitabine + docetaxel	10		8
Ifosfamide-based	7		2
Pazopanib	22		6.5
Trabectedin	6		3.5
Others	13		8
None	29		

OS overall survival, *TNT* time to next treatment

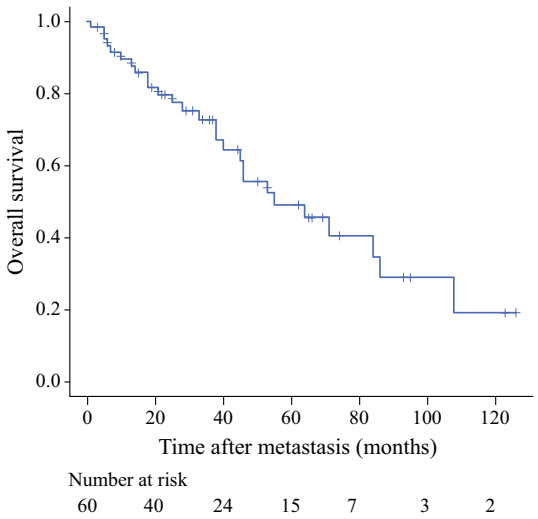

FIG. 1 Kaplan–Meier curve showing the overall survival of patients with metastatic SFTs

chemotherapeutic regimens. To the best of our knowledge, this is the largest study to report clinical outcomes of metastatic SFTs.

There is a lack of comprehensive data on the clinical outcomes of metastatic soft-tissue sarcoma. Italiano et al. analyzed 1024 patients from the French Sarcoma Group database and reported a median OS of 14 months and a 2-year OS rate of 33.2%.[13] A randomized phase 3 trial of the first-line treatment for metastatic soft-tissue sarcoma demonstrated a median OS of 14.3 months in the doxorubicin plus ifosfamide treatment group.[14] A randomized clinical trial exploring the effect of olaratumab in patients with advanced soft-tissue sarcoma demonstrated a median OS of 20.4 months in the doxorubicin plus olaratumab treatment group.[15] Based on these studies, the median survival of metastatic soft-tissue sarcomas was approximately 1–2 years. Considering the median OS of 55 months and a 3-year OS rate of 72.7% in the current study, the survival of patients with metastatic SFTs appeared to be better than that of those with other metastatic sarcomas, probably due to the slowly spreading nature of this tumor. Late relapse of SFTs, often after more than 10 years, has been described in literature,[5,16] but the risk factors for this phenomenon have not been well elucidated so far. This is the first study to show that the location of the primary tumor and local recurrence are correlated with late metastases.

Age, tumor size, high mitotic counts, cellular atypia, cellularity, primary tumor location, the margin of surgical resection, and dedifferentiation have been reported as prognostic factors for the OS of patients with SFT (Table 4).[2,3,5,7,8,17] In the present study, primary tumor location, number of metastases, and metastasectomy were found to be associated with OS on univariate analysis. The size of tumor at head and neck location tended to be smaller than those at other sites, and this may affect favorable outcomes. However, in this cohort, tumor size did not have a significant impact on survival even after considering 5-cm size as a cut-off for analysis (data not shown). Therefore, head and neck location itself appears to have some positive impact on survival. Gholami et al demonstrated that thoracic and abdominal or retroperitoneum locations were associated with poorer survival in patients who had resected SFTs.[8] Interestingly, this finding was confirmed in the current study, wherein abdominal or retroperitoneum location was significantly associated with

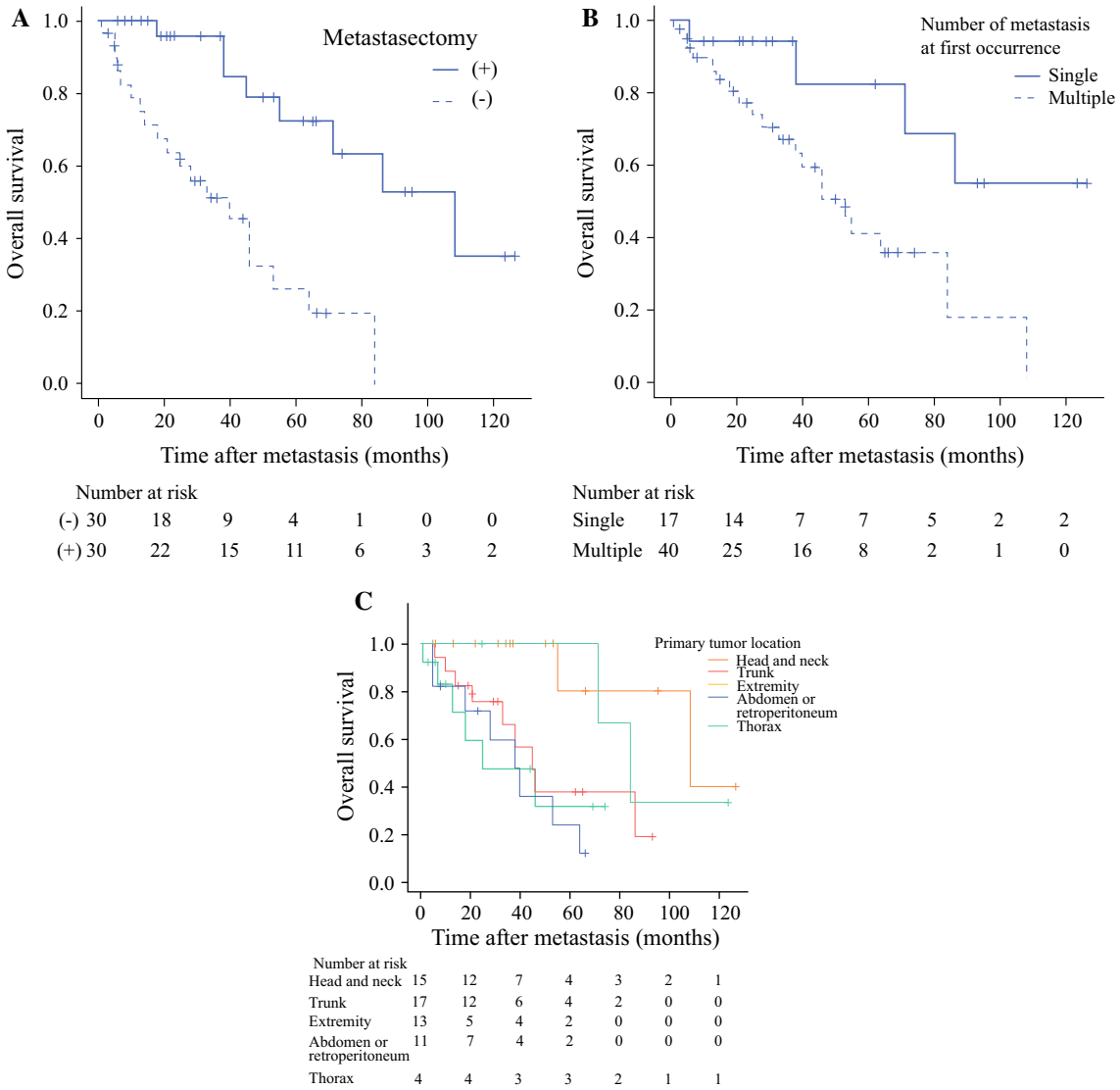

FIG. 2 Kaplan–Meier curves showing the overall survival of patients (**a**) with or without metastasectomy, (**b**) based on the number of metastasis at first occurrence, and (**c**) the location of the primary tumor

poorer survival compared with head and neck tumors. However, intrathoracic tumors appeared to have a favorable prognosis, which might be partially due to the small number of patients with this disease. A high mitotic count is considered as the strongest prognosticator of malignant behavior[12] and has been reported as an unfavorable prognostic factor of OS.[3,7] In addition, according to Martin-Broto et al, it has a prognostic significance in a metastatic setting.[18] However, we observed no significant correlation between high mitotic count and OS, even after using the data of resected metastatic tumor specimens for the analysis. Thus, the predictability of high mitotic count for poorer OS among the clinically malignant populations compared with the whole SFT populations might not be considerable. The number of metastases has been reported to be a prognostic factor for metastatic sarcoma patients who underwent metastasectomy.[19,20] A similar finding was observed in the metastatic SFT patients in the current study, regardless of metastasectomy.

Metastasectomy was the only significant prognostic factor after the multivariate analysis in this study. The role of metastasectomy in metastatic soft-tissue sarcoma remains unclear. Although several studies assessed the impact of surgery among patients who underwent metastasectomy,[21–24] little has been reported on the role of metastasectomy in the whole population, including patients

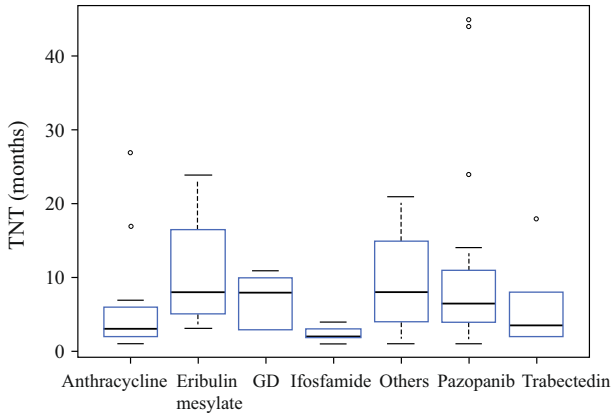

FIG. 3 Box plot showing time to next treatment for each regimen. *GD*, gemcitabine and docetaxel

who did not undergo metastasectomy. In the current study, we demonstrated that the survival period was significantly longer in the SFT patients who underwent metastasectomy compared with those who did not. However, we need to interpret this result with caution owing to the selection bias that less aggressive tumors are likely to be managed by surgical resection. Indeed, in this study, patients whose primary tumors were diagnosed as malignant and those with multiple metastases had significantly less chance to undergo metastasectomy (data not shown). Besides, the optimal candidate for metastasectomy is not well elucidated. Patients with primary head and neck tumors and single metastasis appear to be suitable candidates for metastasectomy among those with metastatic SFT. However, further studies are needed to define the optimal candidates for metastasectomy. That being said, owing to the presence of patient selection bias, the resection of metastases seems to be the treatment of choice for metastatic SFTs. Krengli et al. reported that the inclusion of radiotherapy at a median dose of 60 Gy with surgery could improve the local control in SFT patients with extremity/superficial trunk tumors.[25] Hass et al. reported that the local control rate of palliative radiotherapy with a median dose of 39 Gy was 62.5% at 5 years and suggested that radiation therapy had a clinical benefit for patients with SFT.[26] In the current study, the local control rate by radiotherapy alone with a median dose of 40 Gy was 64% and comparable to those reported in the study,[26] which indicated the usefulness of the local treatment with palliative intent despite no survival benefit.

The role of palliative chemotherapy in SFT remains unclear due to a lack of comparatives studies in the literature. Several case series and a single-arm phase 2 study have demonstrated the efficacy of palliative chemotherapy in SFT.[18,27–31] The role of conventional chemotherapy, which mainly consists of doxorubicin and/or ifosfamide, in advanced SFTs was limited, and the median progression-free survival has been reported to be 4–5 months.[27,28] Moreover, the study by Stacchiotti et al. indicated lower activity of ifosfamide monotherapy.[27] On the other hand, Khalifa et al. reported a promising outcome with the use of trabectedin in 11 malignant SFT patients. In the study, one patient (9%) showed partial response and the median PFS was 11.6 months.[29] Park et al. evaluated the activity of temozolomide and bevacizumab in 14 advanced SFT patients and reported two (14%) partial responses and a median PFS of 10.8 months.[30] Furthermore, 6–9% of patients with advanced SFT demonstrated partial responses with a median PFS of 4.7–5.6 months when treated with pazopanib.[18,31] TNT is considered as a weak surrogate for

TABLE 4 Summary of risk factors associated with outcomes of patients with SFT in published series

Previous study	*N*	Risk factors		
		Local recurrence	Distant metastasis	Overall survival
Gold et al.[9]	79	Extrathoracic location, margin, mitosis	Margin, tumor size, mitosis, pleomorphism, cellularity	
Demicco et al.[3]	110		Age, tumor size, mitosis	Age, tumor size, mitosis
Wilky et al.[15]	83	Malignant histology		
van Houdt et al.[7]	81	Margin	Tumor size, mitosis	Tumor size, mitosis
Pasquali et al.[2]	243	Mitosis, atypia, cellularity		Atypia, cellularity, tumor size
Gholami et al.[8]	219	Location, size	Tumor size	Tumor size, location, margin
Salas et al.[5]	162	Age, location, radiotherapy	Location, mitosis	Age
Demicco et al.[6]	79		Age, tumor size, mitosis, necrosis	
Yamada et al.[16]	145		Hypoglycemia, dedifferentiation	Dedifferentiation
This study (metastatic series)	60			Metastasectomy, location, number of metastasis

PFS,[32] and has been suggested as a useful surrogate for OS in metastatic soft-tissue sarcomas.[33] When compared with previous studies, the efficacy of conventional chemotherapy in the present study was limited, and the TNTs with the ifosfamide-based regimens were shorter than those with other regimens. The TNT of pazopanib appeared to be longer than that of the conventional chemotherapy; however, contrary to the previous report, the TNT of trabectedin was limited. Eribulin mesylate, GD, and others showed relatively longer TNTs, which may be explained by the fact that these regimens are often used in the later lines. The TNT of the last line tended to be prolonged because it denoted the TNT or death.

This study has several limitations. First, we did not conduct a central pathology review, therefore the potential risk of diagnostic problems exists. Furthermore, the criteria for histological classification might be different between institutions, which may have resulted in inaccurate estimations of the prognostic significance of the histological classification. However, the institutions that participated in this study were tertiary referral centers of sarcoma in each region, and the pathological diagnosis was expected to be correct in most cases. Second, due to its retrospective nature, this study had a patient and treatment selection bias which might have affected the prognostic significance of chemotherapy, radiotherapy, and metastasectomy. Additionally, we could not obtain accurate data concerning the PFS for various regimens, due to which we had to use TNT as a weak surrogate for PFS. Third, the number of patients was small and the analyzed variables were limited, thus hindering the identification of statistically significant prognostic factors. Despite these limitations, this study is one of the largest series of metastatic SFTs and the findings may contribute to the clinical management of patients with this disease.

CONCLUSIONS

A relatively longer survival period for metastatic SFT patients was observed in the current study, with a median survival of 55 months even after metastasis. Patients with head and neck tumors or local recurrence were associated with late metastasis. The location of the primary tumor and the number of metastases significantly affected the survival of the patient. Surgical resection of the metastatic lesions offers the best chance of survival, however further studies are warranted to define patients who would have improved survival after metastasectomy, and the most effective chemotherapeutic regimen for patients with metastatic SFTs remains unknown. This study provides fundamental data for further clinical study for this extremely rare disease.

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REFERENCES

1. Enzinger FM, Smith BH. Hemangiopericytoma An analysis of 106 cases. *Hum Path.* 1976;7(1):61–82.
2. Pasquali S, Gronchi A, Strauss D, et al. Resectable extra-pleural and extra-meningeal solitary fibrous tumours: A multi-centre prognostic study. *Eur J Surg Ooncol.* 2016;42(7):1064–1070.
3. Demicco EG, Park MS, Araujo DM, et al. Solitary fibrous tumor: a clinicopathological study of 110 cases and proposed risk assessment model. *ModPathol.* 2012;25(9):1298–1306.
4. Demicco EG, Wagner MJ, Maki RG, et al. Risk assessment in solitary fibrous tumors: validation and refinement of a risk stratification model. *Mod Pathol.* 2017;30(10):1433–1442.
5. Salas S, Resseguier N, Blay JY, et al. Prediction of local and metastatic recurrence in solitary fibrous tumor: construction of a risk calculator in a multicenter cohort from the French Sarcoma Group (FSG) database. *Ann Oncol.* 2017;28(8):1979–1987.
6. Demicco EG, Griffin AM, Gladdy RA, et al. Comparison of published risk models for prediction of outcome in patients with extrameningeal solitary fibrous tumour. *Histopathology.* 2019;75(5):723–737.
7. van Houdt WJ, Westerveld CM, Vrijenhoek JE, et al. Prognosis of solitary fibrous tumors: a multicenter study. *Annals of surgical oncology.* 2013;20(13):4090–4095.
8. Gholami S, Cassidy MR, Kirane A, et al. Size and location are the most important risk factors for malignant behavior in resected solitary fibrous tumors. *Ann Surg Oncol.* 2017;24(13):3865–3871.
9. Gold JS, Antonescu CR, Hajdu C, et al. Clinicopathologic correlates of solitary fibrous tumors. *Cancer.* 2002;94(4):1057–1068.
10. Tan MC, Brennan MF, Kuk D, et al. Histology-based classification predicts pattern of recurrence and improves risk stratification in primary retroperitoneal sarcoma. *Ann Surg.* 2016;263(3):593–600.
11. Kanda Y. Investigation of the freely available easy-to-use software 'EZR' for medical statistics. *Bone Marrow Transplant.* 2013;48(3):452–458.
12. Machado I, Nieto-Morales G, Cruz J, et al. Controversial issues in soft tissue solitary fibrous tumors: A pathological and molecular review. *Pathol Intl.* 2020;70(3):129–139.
13. Italiano A, Mathoulin-Pelissier S, Cesne AL, et al. Trends in survival for patients with metastatic soft-tissue sarcoma. *Cancer.* 2011;117(5):1049–1054.
14. Judson I, Verweij J, Gelderblom H, et al. Doxorubicin alone versus intensified doxorubicin plus ifosfamide for first-line treatment of advanced or metastatic soft-tissue sarcoma: a randomised controlled phase 3 trial. *Lancet. Oncol.* 2014;15(4):415–423.

15. Tap WD, Wagner AJ, Schöffski P, et al. Effect of doxorubicin plus olaratumab vs doxorubicin plus placebo on survival in patients with advanced soft tissue sarcomas: The ANNOUNCE randomized clinical trial. *JAMA*. 2020;323(13):1266–1276.
16. Wilky BA, Montgomery EA, Guzzetta AA, Ahuja N, Meyer CF. Extrathoracic location and "borderline" histology are associated with recurrence of solitary fibrous tumors after surgical resection. *Ann Surg Oncol.* 2013;20(13):4080–4089.
17. Yamada Y, Kohashi K, Kinoshita I, et al. Clinicopathological review of solitary fibrous tumors: dedifferentiation is a major cause of patient death. *Virchows Arch.* 2019;475(4):467–477.
18. Martin-Broto J, Stacchiotti S, Lopez-Pousa A, et al. Pazopanib for treatment of advanced malignant and dedifferentiated solitary fibrous tumour: a multicentre, single-arm, phase 2 trial. *Lancet Oncol.* 2019;20(1):134–144.
19. Casson AG, Putnam JB, Natarajan G, et al. Five-year survival after pulmonary metastasectomy for adult soft tissue sarcoma. *Cancer.* 1992;69(3):662–668.
20. Kim S, Ott HC, Wright CD, et al. Pulmonary resection of metastatic sarcoma: prognostic factors associated with improved outcomes. *Ann ThoracSurg.* 2011;92(5):1780–1786; discussion 1786–1787.
21. Ueda T, Uchida A, Kodama K, et al. Aggressive pulmonary metastasectomy for soft tissue sarcomas. *Cancer.* 1993;72(6):1919–1925.
22. Wigge S, Heissner K, Steger V, et al. Impact of surgery in patients with metastatic soft tissue sarcoma: A monocentric retrospective analysis. *J Surg Oncol.* 2018;118(1):167-176.
23. Mizuno T, Taniguchi T, Ishikawa Y, et al. Pulmonary metastasectomy for osteogenic and soft tissue sarcoma: who really benefits from surgical treatment? *Eur J Cardiothoracic Surg.* 2013;43(4):795–799.
24. Yamamoto Y, Kanzaki R, Kanou T, et al. Long-term outcomes and prognostic factors of pulmonary metastasectomy for osteosarcoma and soft tissue sarcoma. *Int J Clin Oncol.* 2019;24(7):863–870.
25. Krengli M, Cena T, Zilli T, et al. Radiotherapy in the treatment of extracranial hemangiopericytoma/solitary fibrous tumor: Study from the Rare Cancer Network. *Radiother Oncol.* 2020;144:114–120.
26. Haas RL, Walraven I, Lecointe-Artzner E, et al. Radiation therapy as sole management for solitary fibrous tumors (SFT): A retrospective study from the global sft initiative in collaboration with the sarcoma patients EuroNet. *Int J Radiat Oncol Biol Phys 1.* 2018;101(5):1226–1233.
27. Stacchiotti S, Libertini M, Negri T, et al. Response to chemotherapy of solitary fibrous tumour: a retrospective study. *Eur J Cancer (Oxford, England : 1990)* 2013;49(10):2376–2383.
28. Park MS, Ravi V, Conley A, et al. The role of chemotherapy in advanced solitary fibrous tumors: a retrospective analysis. *Clin Sarcoma Res.* 2013;3(1):7.
29. Khalifa J, Ouali M, Chaltiel L, et al. Efficacy of trabected in malignant solitary fibrous tumors: a retrospective analysis from the French Sarcoma Group. *BMC Cancer.* 2015;15:700.
30. Park MS, Patel SR, Ludwig JA, et al. Activity of temozolomide and bevacizumab in the treatment of locally advanced, recurrent, and metastatic hemangiopericytoma and malignant solitary fibrous tumor. *Cancer.* 2011;117(21):4939–4947.
31. Maruzzo M, Martin-Liberal J, Messiou C, et al. Pazopanib as first line treatment for solitary fibrous tumours: the Royal Marsden Hospital experience. *Clin Sarcoma Res.* 2015;5:5.
32. Liang C, Li L, Fraser CD, et al. The treatment patterns, efficacy, and safety of nab ((R))-paclitaxel for the treatment of metastatic breast cancer in the United States: results from health insurance claims analysis. *BMC Cancer.* 2015;15:1019.
33. Savina M, Le Cesne A, Blay JY, et al. Patterns of care and outcomes of patients with METAstatic soft tissue SARComa in a real-life setting: the METASARC observational study. *BMC Med.* 2017;15(1):78.