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Superficial soft tissue sarcomas (S-STS): A study of 367 patients from the French Sarcoma Group (FSG) database ☆

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ABSTRACT

Aim: The specific natural history of superficial soft tissue sarcomas (S-STS) has been rarely considered. We describe the clinical characteristics of a large series of S-STS ($N = 367$) from the French Sarcoma Group (GSF-GETO) database and analyse the prognostic factors affecting outcome.

Methods: We performed univariate and multivariate analyses for overall survival (OS), metastasis-free survival (MFS) and local recurrence-free survival (LRFS).

Results: The median age was 59 years. Fifty-eight percent patients were female. Tumour locations were as follows: extremities, 55%; trunk wall, 35.4%; head and neck, 8% and unknown, 1.6%. Median tumour size was 3.0 cm. The most frequent tumour types were unclassified sarcoma (24.3%) and leiomyosarcoma (22.3%). Thirty-three percent of cases were grade 3. Median follow-up was 6.18 years. The 5-year OS, MFS and LRFS rates were 80.9%, 80.7% and 74.7%, respectively. Multivariate analysis retained histological type and wide resection for predicting LRFS and histological type and grade as prognostic factors of MFS. The factors influencing OS were age, histological type, grade and wide resection.

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STS with early invasion into but not through the underlying fascia had a significantly poorer MFS than with strict S-STS.

Conclusion: S-STS represent a separate category characterised by a better outcome. Adequate surgery, i.e. wide resection, is essential in the management of S-STS.

1. Introduction

Superficial soft tissue sarcomas (S-STS) are defined by a localisation exclusively above the superficial fascia without invasion of the fascia. (AJCC Cancer Staging Manual, 6th ed.). The importance of tumour depth has been stressed in several studies.[1–5] Tumour depth has been previously shown to be an independent prognostic factor for metastasis-free survival[1,3] and superficial location has also been shown to be equal to size in predictive strength on multivariate analysis.[1] However, the specific natural history of S-STS has been rarely considered. Prognostic information remains limited to a small series or to those including only superficial extremity soft tissue sarcomas.[6,7] Cany et al. demonstrated that among soft tissue sarcomas, superficial tumours represent a peculiar category with a behavioural difference mainly characterised by a reduced metastatic risk.[7] In this study, we describe the clinical characteristics of a large series of superficial STS from the French Sarcoma Group (GSF-GETO) database and analyse prognostic factors affecting outcome with the principal aim of studying the prognostic factors for overall survival.

2. Patients and methods

2.1. Patient selection

From January 1, 1980 to December 31, 2007, 3095 consecutive adult patients with an STS were treated for their first tumoural event in 22 participating cancer centres and were entered into the French Sarcoma Group database. Among these patients, 371 (12%) had a histologically proven S-STS. Atypical fibroxanthoma and Kaposi's sarcomas were not selected. Four out of 371 patients who had evidence of metastatic spread at the time of diagnosis were excluded from the study. We restricted our analysis to patients with local disease to obtain a more homogeneous patient population. S-STS are defined as being exclusively above the superficial fascia, with no infiltration into it. The superficial nature may have been suspected during the clinical examination, radiological examination and during the surgical procedure but always needed to be confirmed by histological analysis (Fig. 1). Superficial sarcomas reaching the superficial fascia are characterised as penetration of the fascia by the tumour cells but without perforation and overshooting. In the case of extension of the tumour along the fascia, the latter was considered affected only if it was penetrated by tumour cells. In the case of a tumour pseudocapsule extending into the fascia, we considered that in this case there was indeed invasion. This criterion of damage to the superficial fascia was exclusively histological (Fig. 2). Deep sarcomas were defined as sarcomas situated entirely below the superficial fascia and as sarcomas situated both below and above the superficial fascia. The deep nature of a sarcoma was often suspected at clinical examination and confirmed by radiological examination, during surgery or in pathology (macroscopic and/or histological).

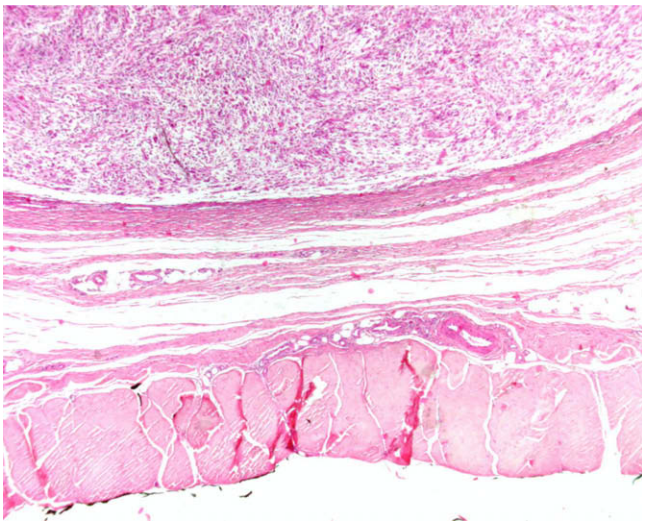


Fig. 1 – The tumour is located above the fascia and does not invade it.

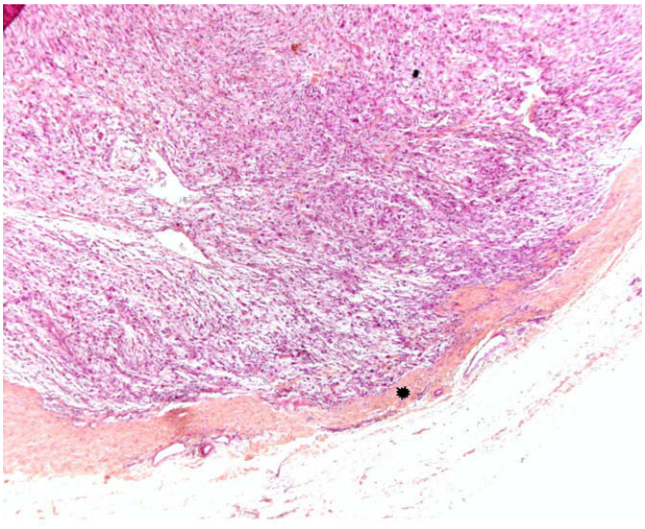


Fig. 2 – The tumour invades the fascia but does not penetrate it.

The diagnosis of STS was confirmed by histological analysis. Therefore, a complementary analysis was performed to compare strict S-STS with STS with early invasion into but not through the underlying fascia, treated and registered at the same period ($n = 81$).

2.2. Pathology review

Histological slides of all patients entered were reviewed by the pathology subcommittee of the French Sarcoma Group (GSF). This subcommittee included 20 pathologists, and a monthly slide review session was performed. For each tumour, one to eight slides were collegially reviewed. Immunohistochemistry was used for confirmation of the diagnosis of sarcoma or for tumour typing. Histological typing was based on the World Health Organisation (WHO) histological typing of soft tissue tumours.[8] Tumour grade was evaluated according to the previously established FNCLCC system based on tumour differentiation, mitotic count and necrosis.[9,10]

2.3. Data collection

Data concerning patients, clinical tumour characteristics, treatment modalities and their results and outcome were obtained from a retrospective review of medical records. These and histological data were entered into a centralised computerised database (www.conticabase.org). The following nine variables were analysed for their potential prognostic value: age at presentation, sex, previous medical history of radiotherapy (PHR), presence of chronic lymphoedema in the area of the primary tumour, tumour size, tumour site (extremity, trunk wall and head and neck), histological type, tumour grade and surgical procedures (wide resection (3–5 cm of normal tissue on all sides) versus simple local excision).

2.4. Statistical analysis

Overall survival (OS) was computed from the date of diagnosis to the date of death (whatever the cause) or to the date of last follow-up. Metastasis-free survival (MFS) was calculated from the date of initial diagnosis to the date of initial diagnosis of metastases or to the date of last follow-up and local recurrence-free survival (LRFS) was defined from the date of initial diagnosis to the date of local recurrence or to the date of last follow-up. Because superficial dermatofibrosarcoma protuberans tumours do not metastasize, patients with this histological subtype ($n = 64$) were excluded from the analyses for MFS. Follow-up times were described as medians by use of the inverse Kaplan–Meier estimator.[11] Continuous variables were expressed as median (range) and categorical variables were expressed as percentage. Survival curves were obtained by the Kaplan–Meier method and compared with the log-rank test. The Cox proportional hazards model was used to calculate adjusted hazard ratios (HRs) and their 95% confidence intervals (95% CIs). All statistical tests were two sided and the threshold for statistical significance was $p = 0.05$. Variables with a p-value inferior to 0.20 in the univariate analysis were tested in the multivariate analysis. Analyses were performed with SAS software (version 9.1).

3. Results

3.1. Patient and disease characteristics

Patient characteristics are presented in Table 1. Tumour size was known in 357 cases (97.3%) and with a median of 3.0 cm (range: 1–20). The most frequent tumour types were unclassified (undifferentiated) sarcoma (24.3%) and leiomyosarcoma (22.3%). Dermatofibrosarcoma protuberans and angiosarcoma represented 17.4% and 14.4% of the tumours, respectively. The sarcomas listed in the group called "others" were: epithelioid sarcoma ($n = 2$), well-differentiated liposarcoma ($n = 12$), myxoid liposarcoma ($n = 9$), dedifferentiated liposarcoma ($n = 1$), epithelioid leiomyosarcoma ($n = 1$), pleomorphic rhabdomyosarcoma ($n = 2$), synovial sarcoma ($n = 6$), osteosarcoma ($n = 3$), ewing sarcoma ($n = 4$), malignant peripheral nerve sheath tumour ($n = 3$), neurilemoma and malignant ($n = 3$). Both dermal (cutaneous) and hypodermal (subcutaneous) involvements were present in 225 (61.3%) cases.

3.2. Treatment characteristics

The treatment of patients with local S-STS is presented in Table 2.

3.2.1. Local treatment

Surgical procedures were simple local excision for 78 patients (21.2%), wide resection of the tumour and biopsy scars (margins being several centimetres of macroscopically healthy tissue) for 280 patients (76.3%) and unknown for 9 patients (2.5%). A histological evaluation of surgical margins was available in only 125 (45%) cases. Radiotherapy generally included photons or electrons with a median dose of 50 Gy. The field included the tumour bed and all tissues handled during intervention such as scars and drain courses; to this volume was added 5-cm margins on all sides. Thirteen (3.5%) patients received preoperative radiotherapy to reduce tumour bulk.

3.2.2. Chemotherapy

All patients who received chemotherapy were treated with an anthracycline-containing regimen using a median of three drugs, which were administered for a median of six cycles. Chemotherapy was given only to 74 patients (20%), as adjuvant or/and neoadjuvant treatment in 67 (18.2%) patients or as palliative treatment in 7 (2%) patients.

3.3. Outcome

Median follow-up was 6.18 years (95% CI: 5.50–7.45).

3.3.1. Response to treatment

Complete remission was obtained in 350 (95.4%) patients.

3.3.2. Recurrence

At the end of the follow-up, metastatic recurrence was observed in 53 (14.4%) patients and local recurrence in 86 (23.4%) patients.

Table 1 – Patient and disease characteristics at baseline.

		Overall patients (N = 367)
Age at diagnosis, years	Median (range)	59 (16, 97)
Sex, N (%)	Male	154 (42)
	Female	213 (58)
Tumour localisation, N (%)	Extremity	202 (55)
	Trunk wall	130 (35.4)
	Head and neck	29 (8)
	Unknown	6 (1.6)
Tumour size (cm)	⩽5	280 (76.3)
	>5	77 (21)
	Unknown	10 (2.7)
Histological diagnosis and subtype, N	Leiomyosarcoma	82 (22.3)
	Myxofibrosarcoma	33 (9)
	Dermatofibrosarcoma protuberans	64 (17.4)
	Angiosarcoma	53(14.4)
	Unclassified sarcoma	89 (24.2)
	Others	46 (12.5)
Tumour grade (FNCLCC), N (%)	Grade 1	104 (28.3)
	Grade 2	128 (34.9)
	Grade 3	121 (33)
	Unknown	14 (3.8)
PHR, N (%)	No	316 (86)
	Yes	51 (14)
Chronic lymphoedema, N (%)	No	347 (94.5)
	Yes	20 (5.5)
Cutaneous and subcutaneous involvement, N (%)	Dermal	18 (4.9)
	Hypodermal	117 (31.9)
	Dermal and hypodermal	225 (61.3)
	Unknown	7 (1.9)

3.3.3. *Survival analysis*

The overall survival rates at 5 and 10 years were 80.9% and 69.1%, respectively. The metastasis-free survival rates at 5 and 10 years were 80.7% and 77.8%, respectively. The local recurrence-free survival rates at 5 and 10 years were 74.7% and 71.3%, respectively. Median metastasis-free survival and median local recurrence-free survival were not reached. At the last follow-up visit, 229 (62.4%) patients were alive and tumour-free; 11 (3%) were alive with metastatic sarcoma and 5 (1.3%) were alive with another cancer. Ninety patients (24.5%) were deceased at the time of analysis, with a median overall survival of 17.1 years. Twenty-three (6.2%) patients died from a cause unrelated to the treated sarcoma and 67 (18.2%) deaths were related to sarcoma. Thirty-two (8.7%) patients were lost to follow-up.

3.4. *Prognostic factors*

3.4.1. *Prognostic factors of overall survival*

The factors influencing overall survival in univariate analysis were age ($p < 0.0001$), sex ($p = 0.04$), PHR ($p < 0.0001$), chronic lymphoedema ($p < 0.0001$), cutaneous and subcutaneous involvements ($p = 0.02$), size ($p = 0.026$), grade ($p = 0.0002$), histological type ($p < 0.0001$) (Fig. 3) and surgical procedure ($p = 0.05$) (Table 3). In multivariate analysis, age ⩾ 55 (HR = 2.7, 95% IC = 1.53–4.87, $p = 0.0006$), histological type (angiosarcoma: HR = 1; dermatofibrosarcoma: HR = 0.07, 95% IC = 0.02–0.36; $p < 0.0001$), grade 3 (HR = 2.1, 95% IC = 1.02–4.39, $p = 0.04$) and wide resection (HR = 0.59, 95% IC = 0.35–0.99, $p = 0.04$) remained statistically significant (Table 4).

3.4.2. *Prognostic factors of metastasis-free survival*

Univariate analysis (Table 3) showed that seven variables were statistically correlated with the MFS: sex ($p = 0.05$), PHR ($p = 0.008$), chronic lymphoedema ($p < 0.0001$), cutaneous and subcutaneous involvements ($p = 0.005$), size ($p = 0.007$), grade ($p = 0.003$) and histological type (<0.0001) (Fig. 4). Multivariate analysis retained histological type (angiosaroma: HR = 1; myxofibrosarcoma: HR = 0.16, 95% IC = 0.05–0.55; unclassified sarcoma: HR = 0.16, 95% IC = 0.07–0.35; $p < 0.0001$) and grade 3 (HR = 3.2, 95% IC = 1.23–8.28, $p = 0.004$) as prognostic factors of MFS (Table 5).

3.4.3. *Prognostic factors of local recurrence-free survival*

In univariate analysis (Table 3), age ($p = 0.002$), sex ($p = 0.009$), PHR ($p < 0.0001$), chronic lymphoedema ($p < 0.0001$), cutaneous and subcutaneous involvements ($p = 0.005$), size ($p = 0.03$), histological type ($p < 0.0001$) (Fig. 5) and surgical procedures ($p = 0.0006$) (Fig. 6) had a significant impact on LRFS. In multivariate analysis, histological type (angiosarcoma: HR = 1; dermatofibrosarcoma protuberans: HR = 0.06, 95% IC = 0.02–0.16, $p < 0.0001$) and wide resection (HR = 0.42, 95% IC = 0.27–0.67, $p = 0.0003$) remained statistically significant (Table 6).

Table 2 – Treatment characteristics and outcome.

		Overall patients (N = 367)
Surgical procedures, N (%)	Simple local excision	78 (21.2)
	Wide resection	280 (76.3)
	Unknown	9 (2.5)
Surgical margins, N (%)	Microscopically complete tumour resection (R0)	142 (38.7)
	Microscopically incomplete tumour resection (R1)	21 (5.7)
	Macroscopically incomplete resection (R2)	2 (0.6)
	Unknown	202 (55)
Radiotherapy, N (%)	No radiotherapy	232 (63.2)
	Preoperative radiotherapy	13 (3.5)
	Postoperative radiotherapy	117 (31.9)
	Unknown	5 (1.4)
Chemotherapy, N (%)	No chemotherapy	288 (78.4)
	Preoperative chemotherapy	5 (1.3)
	Postoperative chemotherapy	55 (14)
	Preoperative and postoperative chemotherapy	7 (2)
	Palliative chemotherapy	7 (2)
	Unknown	5 (1.3)
Follow-up	Follow-up, years, median, 95% CI	6.18 (5.50–7.45)
	Overall survival, years, median	17.1
	Metastasis-free survival, months, median	NR
	Complete response	350 (95.4)
	Incomplete response	17 (4.6)
	Local recurrence-free survival, months, median	NR
	Metastatic recurrence, N (%)	53 (14.4)
	Local recurrence, N (%)	86 (23.4)
	Death	90 (24.5)

NR: not reached.

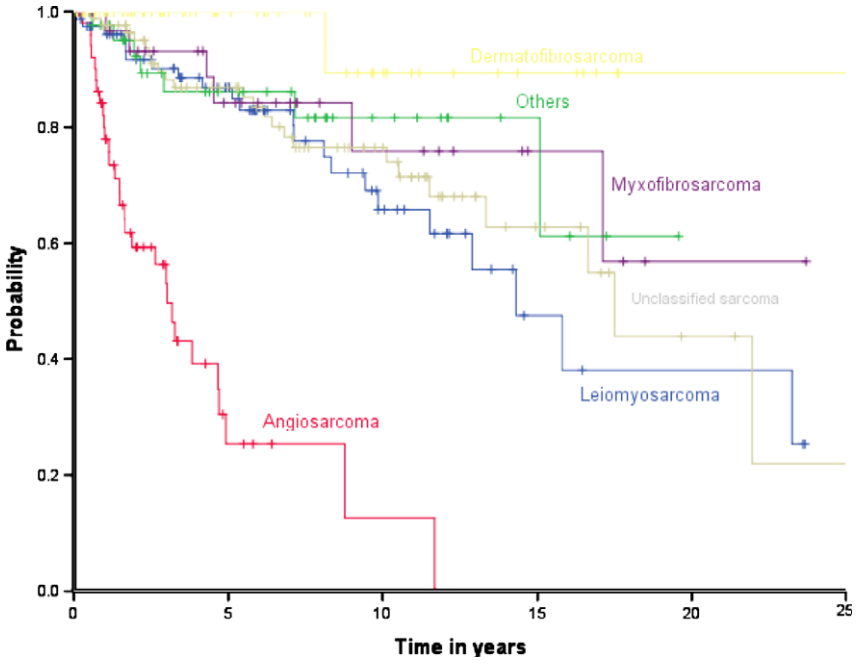
3.5. *Comparison of patients with strict S-STS to those with STS with an invasion of the underlying fascia but not penetrating it (Table 7)*

Patients with STS with invasion of the underlying fascia but not penetrating it had a significantly poorer MFS than those with strict S-STS ($p = 0.03$).

4. Discussion

S-STS are usually analysed together with deep STS. The specific natural history of superficial sarcomas has been rarely considered, whereas in several large studies, tumour depth is an independent prognostic factor for tumour mortality and metastasis-free survival.[3,5] Few studies have addressed the prognosis of patients with primary S-STS. Published studies reported limited patient populations ($n = 105$)[7] or included only superficial extremity soft tissue sarcoma.[6] Our study includes a large series of adult patients treated for their first diagnosis of S-STS whatever their location and with a long-term outcome. The main aim was to identify significant prognostic variables in a large group of localised adult S-STS. We studied the prognostic factors without taking into account the competitive risks, which for overall survival (our main objective) does not result in skewing because the event studied was death, whatever the cause. However, by not taking into account competitive risks we were able to overestimate the risk of occurrence of metastases and of local relapse. It would be of interest to study the cumulated incidence of these events taking into account the competitive risks[12] or, for multivariate analysis, to use Gray's model.[13]

In our patient cohort, 11.8% of the 3095 adult patients of the whole French Sarcoma Group (GSF) database had S-STS with no evidence of metastatic spread at the time of diagnosis. Earlier studies have shown that S-STS are rare (20%).[6,7] In our series, the number of patients with S-STS is probably underestimated because recruitment was derived exclusively from Cancer Centres. Only four patients (1%) had metastatic disease at the time of presentation while the metastasis rate at diagnosis was 7.8% in the whole population of STS.[14] Other important differences among the characteristics of superficial sarcomas are the lower incidence of high-grade disease and the smaller size of tumours. In this series 33% were grade 3 and median tumour size was 3 cm as compared to 43.5% and 8 cm in all STS patients taken together.[14] Cany et al. have already reported these results and have suggested that these data could explain the better prognosis of S-STS.[7] On the other hand, Rydholm et al. reported that multivariate analysis showed no major prognostic effect of tumour depth when grade and size were taken into account. Therefore, most of the prognostic values of tumour depth in soft tissue sarcomas of the extremity or trunk wall can be explained by the association between tumour size and depth.[15] Deep tumours were bigger than superficial tumors because they were probably discovered later. In our series, we were able to note an over-representation of angiosarcomas (14.4%) and of LMS (22%) in comparison with the series previously published on all sarcomas.[14] DFSP are sarcomas which have not been taken



	Follow-up (Years)	0	5	10	15	20	25
Leiomyosarcoma	Number of patients at risk	80	47	18	4	3	0
	Number of events	0	9	17	21	21	22
	Probability	100.0	86.9	65.8	38.1	38.1	--
Others	Number of patients at risk	43	24	10	4	0	0
	Number of events	0	5	6	6	7	7
	Probability	100.0	86.2	81.7	81.7	--	--
Unclassified	Number of patients at risk	86	55	32	10	3	1
	Number of events	0	10	16	20	22	23
	Probability	100.0	86.9	76.5	62.8	44.0	22.0
Myxofibrosarcoma	Number of patients at risk	30	18	9	4	1	0
	Number of events	0	4	5	5	6	6
	Probability	100.0	84.3	75.9	75.9	56.9	--
Dermatofibrosarcoma	Number of patients at risk	19	19	13	6	1	1
	Number of events	0	0	2	2	2	2
	Probability	100.0	100.0	89.5	89.5	89.5	89.5
Angiosarcoma	Number of patients at risk	51	5	1	0	0	0
	Number of events	0	28	29	30	30	30
	Probability	100.0	25,4	12.7	--	--	--

Fig. 3 – Effect of histological type on overall survival (OS). Patients with angiosarcoma had a significantly poorer outcome ($p < 0.001$).

into account in the other series because their malignancy is intermediate (Enzinger's classification 2008). In our series, they represented 17% of superficial sarcomas. We reported only 13 well-differentiated and dedifferentiated liposarcomas, or 3.5% of all S-STS. Coindre et al. reported 15.2% in a large series comprising a majority of deep sarcomas. Likewise, synovial sarcoma, malignant peripheral nerve sheath tumours and rhabdomyosarcoma were rare in our series. In this study including sarcomas of the trunk wall, angiosarcomas were over represented as a histological subtype in S-STS (14.4%). Brooks et al. reported only 3% of angiosarcomas in a population of 215 adult patients with superficial extremity STS.[6] In contrast, an analysis of whole S-STS allowed the recognition of a significant subgroup of patients with angiosarcoma located in the trunk wall and were linked to a previous medical history of radiotherapy and chronic lymphoedema. Consequently, the poor prognostic value of dermal infiltration was correlated to the angiosarcoma histological subtype, which often shows extensive involvement of the dermis.

Superficial tumours had an improved survival at 5 years compared to deep tumours. The reports of Ravaud et al.[1] and Coindre et al.[3] confirmed this survival advantage. In our report from this database, the 5-year overall survival in superficial tumours was 80.9%, whereas the 5-year overall survival for deep tumours was 61.4% in the series of Coindre et al.[3] Therefore, this study confirms that among soft tissue sarcomas, S-STS represent a peculiar category with a behavioural difference mainly characterised by a better MFS. However, we reported a high local recurrence rate (23.4%), even though it was lower to the local recurrence rate of the whole population of STS (29%).[3] These data suggest that local control should be enhanced by adequate local treatment and in particular by a wide resection.

In our cohort population, FNCLCC histological grade was an independent predictive factor for metastasis development as in other series in which deep sarcomas were included.[14] A previous study on superficial extremity soft tissue sarcoma also reported that high grade was equally predictive of an increased incidence of metastasis.[6] These data suggest that

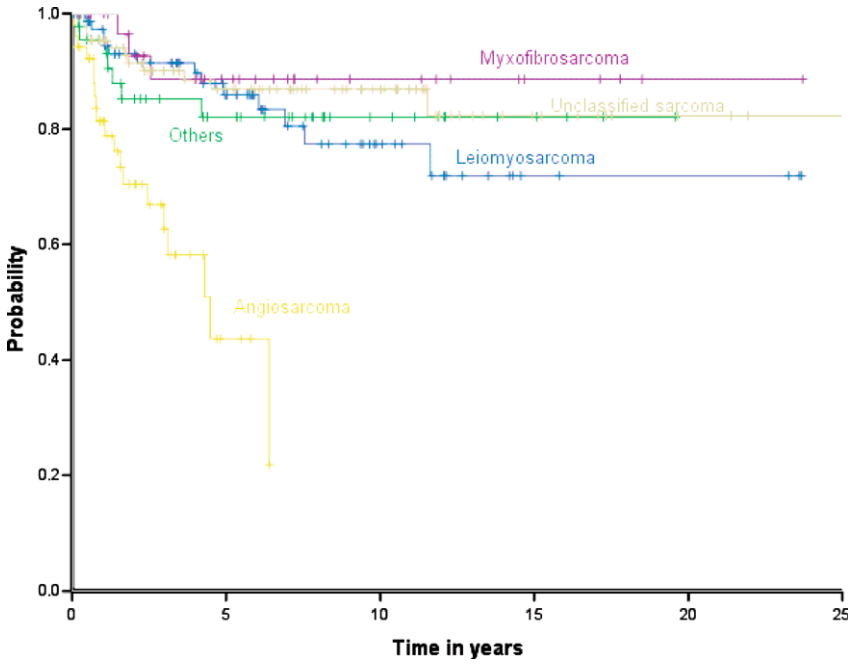
Table 3 – Univariate analysis for prognostic factors in OS, MFS and local recurrence-free survival.

Factors	No. of patients	Overall 5-year survival rate	Overall 10-year survival rate	Log-rank	Metastasis-free 5-year survival rate	Metastasis-free 10-year survival rate	Log-rank	5-Year local recurrence-free survival rate	10-Year local recurrence-free survival rate	Log-rank
Age (year)										
<55	157	93.6	85.1	**<0.0001**	88.6	82.9	0.10	82.7	81.6	**0.002**
⩾55	207	72.2	58.0		76	74.8		68.6	63.0	
Sex										
M	154	88.5	74.1	**0.04**	86	82.6	**0.05**	80.5	79.1	**0.009**
F	213	75.3	65.4		76.6	73.9		70.6	65.9	
PHR										
No	316	86.5	74.6	**<0.0001**	83.7	81.2	**0.008**	80.3	77.1	**<0.0001**
Yes	51	45.7	34.3		61.6	52.8		38.9	34.6	
Chronic lymphoedema										
No	347	84.6	72.9	**<0.0001**	82.5	80.2	**<0.0001**	80.3	77.1	**<0.0001**
Yes	20	15.3	–		51.6	–		38.9	34.6	
Cutaneous and subcutaneous involvements										
Dermal	18	49.7	33.2	**0.02**	64.3	64.3	**0.005**	43.6	32.7	**0.0005**
Hypodermal	117	89.5	77.3		88.2	86.6		85.1	82.9	
Dermal and hypodermal	225	77.5	66.7		74.6	69.4		69.9	66.3	
Tumour size (cm)										
⩽5	280	84.8	73.9	**0.026**	84.9	80.8	**0.007**	78	74.1	**0.03**
>5	77	67.8	55.1		67.6	67.6		64.1	64.1	
FNCLCC grade										
1	104	86.7	74.6	**0.0002**	86.1	86.1	**0.003**	80.4	74.9	0.12
2	128	82.1	74.6		87.4	84		76.2	71.2	
3	121	74.2	57.1		72.4	68.4		67.1	67.7	
Histological type										
Leiomyosarcoma	82	86.9	65.8	**<0.0001**	86.0	77.4	**<0.0001**	88.8	88.8	**<0.0001**
Myxofibrosarcoma	33	84.3	75.9		88.7	88.7		75.4	75.4	
Dermatofibrosarcoma	64	100.0	89.5		NE	NE		93.1	82.9	
Angiosarcoma	53	25.4	12.7		43.7	–		24.9	–	
Unclassified sarcoma	89	86.9	76.5		86.9	86.9		71.2	66.7	
Others	46	86.2	81.7		82.1	82.1		84.6	84.6	
Location										
Extremity	202	81.9	71.9		83.1	78.7		72.4	68.1	
Wall trunk	130	80.9	69	0.38	75.7	75.7	0.72	79.8	77.5	0.35
Head and neck	29	78.5	39.2		71.5	71.5		78.6	78.6	
Surgical resection										
Simple local excision	78	79.3	59.9	**0.05**	74.7	71.6	0.31	61.5	57	**0.0006**
Wide resection	280	83.1	73.6		83.1	80.1		79.9	77	

NE: Not estimated.

Table 4 – Multivariate overall survival analysis.

	Crude hazards ratio	95% Confidence interval	*p*-Value
Age			
< 55	1		0.0006
⩾55	2.73	1.53–4.87	
Histological type			
Angiosarcoma	1		<0.0001
Leiomyosarcoma	0.21	0.11–0.40	
Myxofibrosarcoma	0.16	0.04–0.27	
Dermatofibrosarcoma	0.07	0.02–0.36	
Others	0.17	0.07–0.40	
Unclassified sarcoma	0.14	0.07–0.26	
FNCLCC grade			
1	1	0.59–2.66	0.04
2	1.26	1.02–4.39	
3	1.77	1.14–2.75	
Surgical resection			
Simple local excision	1		0.04
Wide resection	0.59	0.35–0.99	

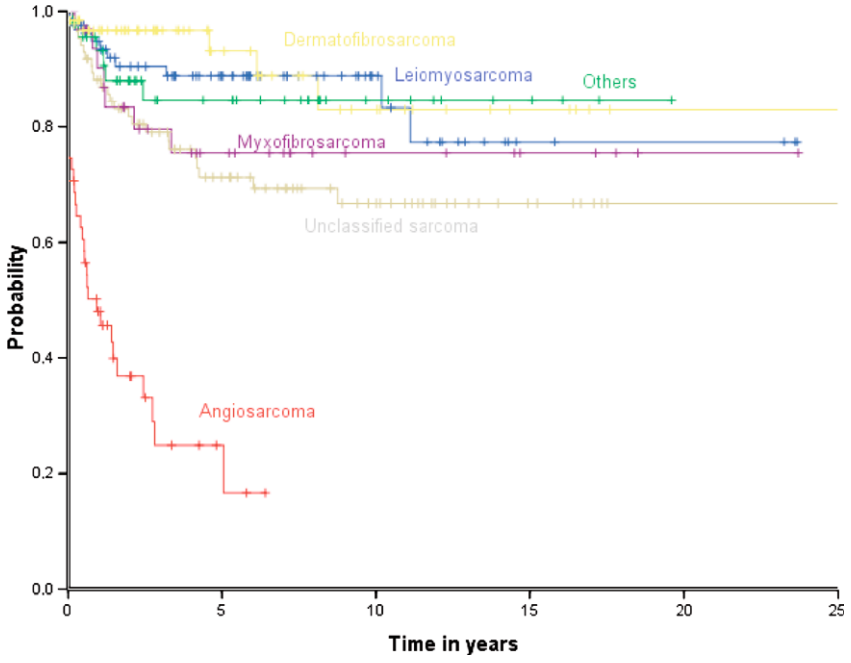


	Follow-up (Years)	0	5	10	15	20	25
Leiomyosarcoma	Number of patients at risk	76	44	17	4	3	0
	Number of events	0	9	12	13	13	13
	Probability	100.0	86.0	77.4	71.9	71.9	71.9
Others	Number of patients at risk	45	24	10	4	0	0
	Number of events	0	7	7	7	7	7
	Probability	100.0	82.1	82.1	82.1	82.1	82.1
Unclassified	Number of patients at risk	86	51	31	9	3	1
	Number of events	0	10	10	11	11	11
	Probability	100.0	86.9	86.9	82.4	82.4	82.4
Myxofibrosarcoma	Number of patients at risk	28	18	9	4	1	0
	Number of events	0	3	3	3	3	3
	Probability	100.0	88.7	88.7	88.7	88.7	--
Angiosarcoma	Number of patients at risk	52	4	0	0	0	0
	Number of events	0	18	19	19	19	19
	Probability	100.0	43.7	--	--	--	--

Fig. 4 – Effect of histological type on metastasis-free survival (MFS). Patients with angiosarcoma had a significantly poorer outcome ($p < 0.001$).

Table 5 – Multivariate metastasis-free survival analysis.

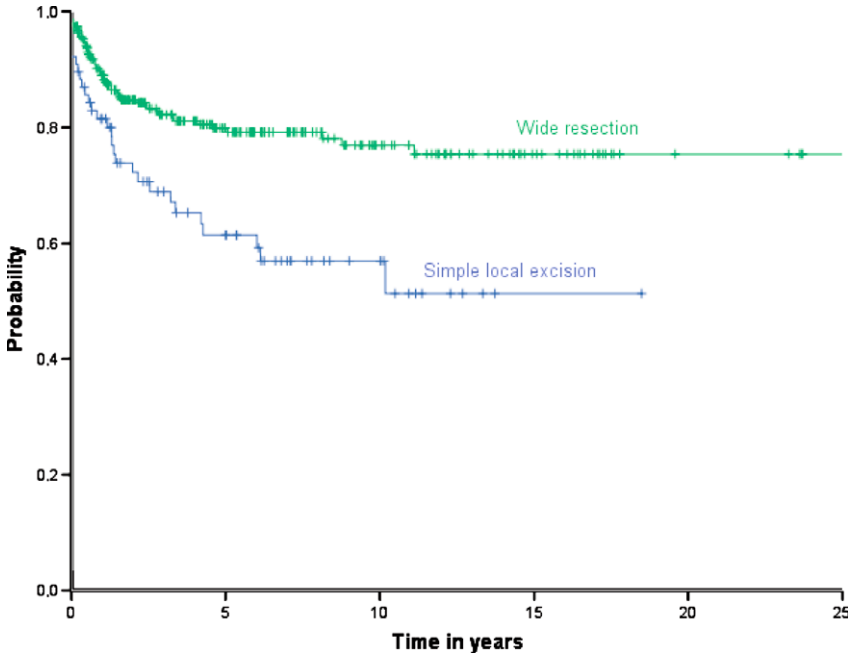
	Crude hazards ratio	95% Confidence interval	*p*-Value
Histological type			
Angiosarcoma	1		<0.0001
Leiomyosarcoma	0.27	0.13–0.58	
Myxofibrosarcoma	0.16	0.05–0.55	
Others	0.24	0.10–0.58	
Unclassified sarcoma	0.16	0.07–0.35	
FNCLCC grade			
1	1		0.004
2	1.33	0.48–3.7	
3	2.6	1.47–4.58	



	Follow-up (Years)	0	5	10	15	20	25
Leiomyosarcoma	Number of patients at risk	80	43	8	4	3	0
	Number of events	1	8	17	10	10	13
	Probability	98.8	88.8	88.8	77.3	77.3	--
Others	Number of patients at risk	46	22	9	4	0	0
	Number of events	0	6	6	6	6	6
	Probability	100.0	84.6	84.6	84.6	--	--
Unclassified	Number of patients at risk	84	41	23	7	1	1
	Number of events	2	22	24	24	24	24
	Probability	97.7	71.2	66.7	66.7	66.7	66.7
Myxofibrosarcoma	Number of patients at risk	32	15	7	5	1	0
	Number of events	0	7	7	7	7	7
	Probability	100.0	75.4	75.4	75.4	75.4	--
Dermatofibrosarcoma	Number of patients at risk	62	24	12	5	1	0
	Number of events	1	3	5	5	5	5
	Probability	98.4	93.1	82.9	82.9	82.9	--
Angiosarcoma	Number of patients at risk	38	3	0	0	0	0
	Number of events	13	33	34	34	34	34
	Probability	74.5	24.9	--	--	--	--

Fig. 5 – Effect of histological type on local recurrence-free survival (LRFS). Patients with angiosarcoma had a significantly poorer outcome ($p < 0.001$).

grade 3 S-STS sarcomas should be considered for future adjuvant systemic treatment using new drugs because adjuvant chemotherapy is still controversial for sarcomas.[16] In multivariate analysis, grade was not statistically correlated with LRFS, which suggests that grade is not a factor to be considered for the indication of radiotherapy. The confidence interval of grade 2 was 0.48–3.7. Consequently, the clinical behaviour of grade 2 S-STS was similar to that of grade 1 S-STS. The therapeutic strategy might therefore be the same as for low grade S-STS.



	Follow-up (Years)	0	5	10	15	20	25
Wide resection	Number of patients at risk	265	116	55	23	6	2
	Number of events	6	48	51	52	52	52
	Probability	97.8	79.9	77.0	75.4	75.4	75.4
Simple Local Excision	Number of patients at risk	65	32	13	1	0	0
	Number of events	6	26	28	29	29	29
	Probability	92.2	61.5	57.0	51.3	--	--

Fig. 6 – Effect of surgical procedure on local recurrence-free survival (LRFS). Patients with simple local excision had a significantly poorer outcome than patients with wide resection ($p = 0.0006$).

Table 6 – Multivariate local recurrence-free survival analysis.

	Crude hazards ratio	95% Confidence interval	*p*-Value
Histological type			
Angiosarcoma	1		<0.0001
Leiomyosarcoma	0.09	0.04–0.19	
Myxofibrosarcoma	0.17	0.07–0.39	
Dermatofibrosarcoma	0.06	0.02–0.16	
Others	0.10	0.04–0.25	
Unclassified sarcoma	0.20	0.11–0.34	
Surgical resection			
Simple local excision	1		0.0003
Wide resection	0.42	0.27–0.67	

Multivariate analysis showed that histological type was correlated with LRFS, MFS and OS. Superficial angiosarcoma subtype had an overall poor outcome. Angiosarcoma behaves more aggressively and progresses more rapidly.[17] Patients with superficial angiosarcoma of the trunk wall generally had a previous medical history of radiotherapy, which is an unfavourable prognostic factor. Since angiosarcomas are often multifocal, which complicates therapeutic options and surgical treatment, they should be treated specifically. So, this subtype of sarcoma could benefit from antiangiogenic systemic treatment. Sorafenib is currently under evaluation for treatment of locally advanced or metastatic angiosarcomas, which are not accessible to curative surgery in a French Sarcoma Group phase II trial (Angio-Next protocol).

In contrast with a previous study,[7] the quality of initial resection was found to be an important prognostic factor for LRFS in multivariate analysis. Consequently, adequate surgery should be considered as essential in the treatment of S-STS, this means wide resection encompassing the superficial aponeurosis and 3–5 cm of normal tissue on all sides.[18] Wide resection is the key to success in the management of STS whatever be their depth. For this reason, referral to a special centre adopting a multidisciplinary approach to sarcomas is usually of paramount importance. In our series, the high rate of local recurrence (23.4%) was probably related to the type of surgical procedure. However, it is a retrospective study and impact of R1-resection on the outcomes had not been analysed.

Table 7 – Comparison of patients with STS without invasion of the fascia and patients with STS with invasion of the fascia.

	No. of patients	Overall 5-year survival rate	Overall 10-year survival rate	Log-rank	5-Year metastasis-free survival rate	10-Year metastasis-free survival rate	Log-rank	5-Year local recurrence-free survival rate	10-Year local recurrence-free survival rate	Log-rank
Superficial STS	367	80.9	69.1	0.06	80.5	77.8	**0.03**	74.8	71.4	0.85
STS with invasion of the fascia	81	71.4	56.4		70	67.3		74.4	71.4	

When we compared S-STS and STS with invasion of the underlying fascia but not trespassing it, we found that strict S-STS had a better prognosis. The metastasis-free survival rates at 5 and 10 years were 80.5% and 77.8%, respectively for S-STS, whereas they were 70% and 67.3%, respectively, for STS with an invasion of the underlying fascia but not trespassing it. These results are consistent with the AJCC cancer staging that considers superficial tumours with invasion of the fascia as deep tumours (AJCC Cancer Staging Manual, 6th ed.). However, we cannot exclude the possibility of a bias such as tumour size or other important factors in this subgroup of patients with invasion of the fascia.

Conflict of interest statement

None declared.

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