Prognostic implication of *SYT-SSX* fusion type in synovial sarcoma: A multi-institutional retrospective analysis in Japan

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Abstract. The prognostic implication of *SYT-SSX* fusion type in synovial sarcomas is still controversial. The aim of this study is to clarify the prognostic impact of fusion type, in association with other clinical factors, in patients with synovial sarcoma in Japan. Data on 108 *SYT-SSX* fusion transcript-positive patients with synovial sarcoma, treated in 11 tertiary referral cancer centers in Japan, were retrospectively analyzed. The following parameters were examined for their potential prognostic impact: *SYT-SSX* fusion type, patient age at presentation, sex, primary tumor location, tumor size, histological subtype, histological grade, treatment modalities and disease stage at presentation. Among the patients with localized disease at presentation, 5-year overall survival (OS) for *SYT-SSX1* and *-2* subgroups were 84.4 and 74.9%, respectively (P=0.244). Five-year metastasis-free survival (MFS) rates were 67.8% for *SYT-SSX1* and 68.5% for *SYT-SSX2* (P=0.949). Univariate survival analyses for 91 patients with localized disease at presentation showed that tumor size was the only significant prognostic factor for OS (P=0.0033) and MFS (P=0.0029) and the histological grade was marginally significant for MFS (P=0.0785), whereas the *SYT-SSX* fusion type and other variables were not. Multivariate survival analyses further indicated that tumor size was the most significant independent prognostic factor for OS and MFS and the histological grade was also significant for MFS. In conclusion, the *SYT-SSX* fusion type is not a significant prognostic factor unlike tumor size, followed by histological grade for patients with localized synovial sarcoma in Japan.

Introduction

Synovial sarcoma is a relatively aggressive soft-tissue sarcoma that accounts for 5 to 10% of all soft-tissue sarcomas and mainly affects adolescents and young adults (1). Synovial sarcomas are histologically divided into three subtypes: a biphasic subtype containing both epithelial and spindle tumor cells, a monophasic subtype composed solely of spindle tumor cells and a poorly differentiated subtype composed of primitive oval or short-spindle-shaped tumor cells (2). Cytogenetically, however, >95% of synovial sarcomas bear the translocation t(X;18)(p11.2;q11.2), which is a chromosomal re-arrangement specific to this tumor (3). The translocation represents the fusion of the *SYT* gene on the 18q11.2 chromosome with the

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SSX1 or *-2* gene, both of which are closely located on chromosome Xp11.2. The precise function of this chimeric gene still remains unknown, though it has recently been used as a specific diagnostic marker for this tumor (4).

As well as its diagnostic significance, the fusion type has recently been proposed to be a prognostic factor. Kawai *et al* (5) and subsequently Ladanyi *et al* (6) reported that the *SYT-SSX1* form of synovial sarcoma, compared to that of *SYT-SSX2*, has a significantly unfavorable prognosis. Thereafter, several reports with a relatively small number of case series have supported the positive prognostic implication of *SYT-SSX* fusion type in patients with synovial sarcoma (7-9). In contrast, Guillou *et al* most recently showed a trend for tumors bearing *SYT-SSX2* transcripts to behave more aggressively than those of *SYT-SSX1*, but the difference was not statistically significant (10). Thus, the prognostic implication of the *SYT-SSX* fusion type in synovial sarcomas is still controversial. To address this issue, we conducted the present study to investigate the prognostic impact of the fusion type, in association with other clinical factors, in patients with synovial sarcoma in Japan.

Patients and methods

As a multi-institutional retrospective study, 108 patients with SYT-SSX-positive synovial sarcoma treated in 11 tertiary referral cancer centers or university hospitals in Japan from 1978 to 2005 were enrolled. All patients were histologically diagnosed as having synovial sarcoma on routine hematoxylin and eosin stains with appropriate immunohistochemical examinations, including a set of epithelial markers such as cytokeratins and epithelial membrane antigen (EMA) in each center, and were confirmed with the detection of *SYT-SSX* fusion transcripts using the RT-PCR method in frozen tumor samples. We have retrospectively collected patient data from their clinical records including the data on the *SYT-SSX* fusion type, patient age at presentation, sex, primary tumor location, tumor size, histological subtype, histological grade, treatment modalities and disease stage (presence or absence of metastasis) at presentation. Extremity tumors were defined as tumors located in free extremities only, but extremity girdles including the shoulder, axilla, groin or buttock were considered to be trunk locations. Tumor size was defined as the maximum dimension on a magnetic resonance imaging (MRI) or computed tomography (CT) scan. Histological subtyping was carried out on routine hematoxylin and eosin stains using the 2002 WHO classification of tumors (11). Histological grading was based on the criteria of Enzinger and Weiss and assigned to three grades (1, 2 and 3), using several essential histopathological parameters such as cellularity, mitotic activity, tumor necrosis, with or without Ki-67 reactivity as a reliable cell proliferation index (12-16). All patients were treated by the multimodality therapeutic approach, combined with surgery, chemotherapy and/or radiotherapy. Wide local excision for the primary tumors was generally attempted as much as complete re-section was considered possible. Consequently, 63 out of 108 patients underwent wide local excision, 13 patients received marginal excision, 9 intralesional excision, 4 local tumor re-section with an undetermined surgical margin and 15 amputation of the affected limb. The other 4 patients with

metastatic disease did not undergo definitive surgery for the primary tumors. Chemotherapy was performed in 83 out of 108 patients (76.9%), 68 of whom had localized disease and 15 metastatic disease at presentation. The regimens of chemotherapy varied in each center, but mainly included ifosfamide and/or doxorubicin with the exception of 3 cases. Radiotherapy was performed in 23 patients (21.3%) pre- and/ or postoperatively with a mean dose of 43.8 Gy (range: 28-70 Gy). The decision to give adjuvant therapy (chemotherapy and/or radiotherapy) was made independently by each center.

Fusion type analysis. The frozen tumor samples were mostly obtained from the primary site (79 cases), but in some cases from locally recurrent (14 cases) or metastatic sites (3 cases). The other 12 samples were obtained from unspecified tumor sites. Almost all patients were analyzed for the *SYT-SSX* fusion type by reverse transcription-polymerase chain reaction (RT-PCR) using the *SYT* primer: 5'-caacagcaagatgcatacca-3', the *SSX1* specific primers: 5'-ggtgcagttgtttcccatcg-3' and the *SSX2* specific primers: 5'-ggcacagctctttcccatca-3' in most cases, but in some cases using the SSX common primer: 5'-cacttgct atgcacctgatg-3', followed by direct sequencing.

Statistical analysis. For statistical analysis, the following variables were potentially considered for their prognostic factors: patient age at presentation, sex, primary tumor location, tumor size, histological subtype, histological grade, treatment modalities, disease stage at presentation and fusion type. The correlations between these factors were analyzed using the Pearson χ^2 test. Overall survival (OS) was defined as the time from the beginning of treatment to the death of the patient. Metastasis-free survival (MFS) was defined as the first metastasis interval from the beginning of treatment. Patients who died from unrelated causes to sarcoma were censored at the time of death. OS and MFS curves were computed by the Kaplan and Meier method (17). We compared these curves by using the log-rank test (18) for univariate survival analysis. Two-tailed P-values of ≤0.05 were estimated as statistically significant for the prognostic factors. Cox's proportional hazards model was used to identify independent factors predictive of survival for multivariate analysis (19). Patient age at presentation was also evaluated as a continuous variable by Cox's regression model. These statistical analyses were performed using the JMP version 5.01 statistical analysis software package for personal computers (SAS Institute Inc, Cary, NC, USA).

Results

Patient and tumor characteristics. The patient and tumor characteristics are summarized in Table I. *SYT-SSX1* and *-2* fusion transcripts were detected in 68 (63.0%) and 40 (37.0%) cases, respectively. There were 44 men (40.7%) and 64 women. The median age at presentation was 37 (mean, 33 years), ranging from 8 to 74 years. Forty-seven patients (43.5%) were aged ≤30. Seventy-two extremity-based tumors included lower (n=61) and upper extremities (n=11). Thirty-six truncal tumors included lower-extremity (n=17) and upper-extremity girdles (n=5), head and neck (n=2) and abdominal wall (n=12). The data on maximal tumor size were available

Table I. Patient and tumor characteristics.

	All patients (n=108)		Patients with localized disease at presentation (n=91)	
	N	%	N	%
Fusion type				
SYT-SSX1	68	63.0	57	62.6
SYT-SSX2	40	37.0	34	37.4
Age				
≤30	47	43.5	40	44.0
>30	61	56.5	51	56.0
≤35	55	50.9	45	49.5
>35	53	49.1	46	50.5
Sex				
Male	44	40.7	33	36.3
Female	64	59.3	58	63.7
Location				
Extremity	72	66.7	60	65.9
Trunk	36	33.3	31	34.1
Tumor size (9 unspecified)				
≤5 cm	35	35.4	33	39.8
>5 cm	64	64.6	50	60.2
≤7 cm	44	44.4	42	50.6
>7 cm	55	55.6	41	49.4
Histological subtype (1 unspecified)				
Poorly differentiated	8	7.5	4	4.4
Monophasic	67	62.6	58	64.4
Biphasic	32	29.9	28	31.1
Histological grade (22 unspecified)				
Grade 2	48	55.8	44	61.1
Grade 3	38	44.2	28	38.9
Stage				
Localized	91	84.3	91	100
Metastatic	17	15.7		
Surgery (4 unspecified and 4 no surgery)				
Amputation	15	15.0	11	12.8
Wide local excision	63	63.0	56	65.1
Marginal excision	13	13.0	12	14.0
Intralesional excision	9	9.0	7	8.1
Chemotherapy				
No	25	23.1	23	25.3
Yes	83	76.9	68	74.7
Radiotherapy				
No	85	78.7	72	79.1
Yes	23	21.3	19	20.9
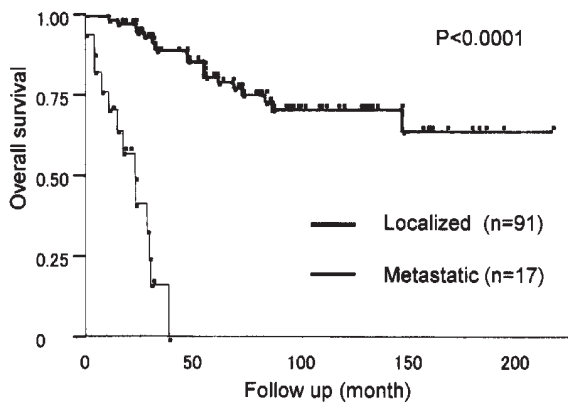
Figure 1. Overall survival according to the disease stage in all patients.

Figure 2. Overall survival according to the fusion type in patients with localized disease at presentation.

in 99 cases. The tumor was <5 cm in 35 patients (35.4%), between 5 and 7 cm in 9 patients (9.0%) and >7 cm in 55 patients (55.6%). The histological subtype was specified in all but one case. The most frequent histological subtype was the monophasic fibrous (n=67, 62.6%), followed by the biphasic (n=32, 29.9%) and poorly differentiated subtype (n=8, 7.5%). The histological grade was determined in 86 cases, grade 2 in 48 and grade 3 in 38 cases. The initial treatment modalities for 108 patients included surgery alone (n=23, 21.3%); a combination of surgery and radiotherapy (n=2, 1.9%); a combination of surgery and chemotherapy (n=59, 54.3%); a combination of surgery, radiotherapy and chemo-therapy (n=20, 18.5%); a combination of radiotherapy and chemotherapy (n=1, 0.9%) and chemotherapy alone (n=3, 2.8%). Ninety-one patients (84.3%) had localized disease and 17 patients (15.7%) had metastasis at presentation. Follow-up periods ranged from 4 to 216 months (median, 54 and mean, 64 months).

Correlations between the various factors. The correlations between the *SYT-SSX* fusion type and other clinical factors are listed in Table II. A significant correlation between the fusion type and primary tumor location was observed (P=0.0166), suggesting a preponderance of truncal (more proximal) tumor location in *SYT-SSX2* fusion type than in *SYT-SSX1*. There was also a trend for patients with *SYT-SSX2* tumors to have a more monophasic fibrous histological subtype, including a poorly differentiated subtype, than those with *SYT-SSX1* tumors. However, the difference did not reach statistical significance in the present series (80 vs 64.2%, P=0.0837). There was no correlation of the fusion type with patient age, sex, tumor size, histological grade, disease stage and treatment modalities including surgery, chemotherapy and radiotherapy.

As for the associations between the disease stage and other factors, the number of patients with metastasis at presentation was significantly smaller in females (P=0.0297), with smaller tumors (<5 vs >5 cm: P=0.0368 or <7 vs >7 cm: P=0.0050), and histological grade 2 tumors (P=0.0249), but the *SYT-SSX* fusion type, patient age, primary tumor location or histological subtype did not significantly associate with the disease stage at presentation.
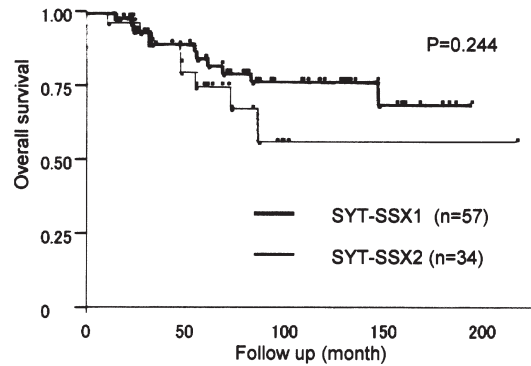
The survival analysis and prognostic factors of all patients. Thirty-two patients (29.6%) died of their tumors, including 13 (76.5%) out of 17 patients with metastasis at presentation. Five-year overall survival (OS) was 69.8% in all patients. The results of the univariate analysis for predictors of OS in all patients are summarized in Table III. Male patients (P=0.0290), with tumor sizes >5 cm (P=0.0051) or >7 cm (P=0.0003), histological grade 3 (P=0.0265) and a presence of metastasis at presentation (P<0.0001) (Fig. 1) were significantly unfavorable predictors of OS in all patients. The fusion type, patient age, primary tumor location and histological subtype showed no prognostic impact on the OS in any of the patients. Then, we performed a multivariate survival analysis including fusion type in 81 patients, whose information about the four prognostic factors in univariate survival analysis (sex, tumor size, histological grade and disease stage) was available (Table IV). It showed that the disease stage at presentation was the most important independent predictor for OS (P<0.001), followed by tumor size (P=0.021). However, fusion type, sex and histological grade were not independent prognostic factors in the multivariate analysis for OS in all patients.

Survival analysis and prognostic factors: patients with localized disease at presentation. Among the 91 patients with localized disease at presentation, 28 patients (30.8%) developed at least one metastasis and 31 patients (34.1%) developed a local recurrence in the course of their disease. Five-year OS and MFS were 81.1 and 67.9%, respectively, in patients with localized disease at presentation. Univariate analyses for predictors of OS and MFS in patients with localized disease at presentation are shown in Table III. *SYT-SSX2* tumors tended to behave in a more aggressive manner than *SYT-SSX1* tumors on OS, but the difference was not statistically significant (P=0.244) (Fig. 2). Tumor size was significantly associated with OS (5 cm, P=0.0233; 7 cm, P=0.0033) (Fig. 3a and b) and MFS (5 cm, P=0.0127; 7 cm, P=0.0029) (Fig. 4a and b). The histological grade also marginally correlated with OS (P=0.156) and MFS (P=0.0785) (Fig. 5), but it did not reach statistical significance in the present series. Patient age, sex, primary tumor location and the histological subtype did not correlate with either OS or MFS.

Table II. Correlations between the *SYT-SSX* fusion type and other factors.

	SYT-SSX1 (n=68)	SYT-SSX2 (n=40)	P
Age			
≤30	27	20	0.297
>30	41	20	
≤35	33	22	0.516
>35	35	18	
Sex			
Male	31	13	0.181
Female	37	27	
Location			
Extremity	51	21	0.0166
Trunk	17	19	
Tumor size			
≤5 cm	24	11	0.363
>5 cm	38	26	
≤7 cm	27	17	0.816
>7 cm	35	20	
Histological subtype			
Poorly differentiated monophasic	43	32	0.0837
Biphasic	24	8	
Historical grade			
Grade 2	32	16	0.280
Grade 3	21	17	
Stage			
Localized	57	34	0.871
Metastatic	11	6	
Surgery			
Amputation and wide local excisions	48	30	0.835[a]
Marginal and intralesional excisions	13	9	
Chemotherapy			
No	15	10	0.726
Yes	53	30	
Radiotherapy			
No	54	31	0.815
Yes	14	9	

[a]The amputation and wide local excisions were categorized as adequate surgery. The marginal and intralesional excisions were categorized as inadequate surgery. The numbers of the two groups were compared using the Pearson χ^2 test.

Multivariate analyses for OS and MFS were then applied to 67 localized patients, whose information on all the factors was available and we took the tumor size, histological grade and fusion type into account. Tumor size (<7 vs >7 cm) was the only independent prognostic factor on both OS (P=0.009) and MFS (P=0.024). Moreover, the histological grade proved to be an independent prognostic factor on MFS (P=0.037) (Table V). The fusion type did not have a prognostic impact on either OS or MFS.

Table III. Survival according to various factors in all of the patients (n=108) and patients with localized disease at presentation (n=91).

	All patients (n=108)			Patients with localized disease at presentation (n=91)				
	N	5-year OS rate	P	N	5-year OS rate	P	5-year MFS rate	P
Fusion type								
SYT-SSX1	68	71.1	0.5320	57	84.4	0.2440	67.8	0.9490
SYT-SSX2	40	66.8		34	74.9		68.5	
Age								
≤30	47	68.7	0.4160	40	77.5	0.5070	70.0	0.7770
>30	61	68.7		51	81.3		65.4	
≤35	55	67.7	0.4320	45	80.6	0.1500	71.2	0.3680
>35	53	68.7		46	78.3		63.4	
Sex								
Male	44	67.7	0.0290	33	79.6	0.6470	68.0	0.8730
Female	64	72.6		58	82.2		67.9	
Location								
Extremity	72	57.4	0.8390	60	82.0	0.5680	72.2	0.1730
Trunk	36	78.1		31	76.6		61.9	
Tumor size								
≤5 cm	35	85.0	0.0051	33	91.3	0.0233	79.4	0.0127
>5 cm	64	57.5		50	70.4		56.9	
≤7 cm	44	82.2	0.0003	42	86.7	0.0033	82.0	0.0029
>7 cm	55	54.5		41	69.9		48.7	
Histological subtype								
Poorly differentiated	8	N/A		4	N/A		N/A	
Monophasic	67	70.4	0.3690	58	81.5	0.3330	66.2	0.2710
Biphasic	32	67.9		28	79.0		71.3	
Histological grade								
Grade 2	48	77.8	0.0265	44	86.5	0.1560	67.4	0.0785
Grade 3	38	52.1		28	68.6		53.4	
Stage								
Localized	91	81.1	<0.00010	91	81.1		67.9	
Metastatic	17	0.00						

N/A, not available.

Discussion

In synovial sarcoma, there are several definite adverse clinical prognostic factors consistently reported in a previous large series: the advanced disease stage, large tumor size and presence of local recurrence (20-29). An adjacent bone and/or neurovascular invasion (24,25,27) and a microscopic positive tumor margin (22,24) also reflect on the failure of the local control associated with a poor prognosis. As for other clinical prognostic factors in patients with localized synovial sarcoma, older age (21,23,26), male sex (25), truncal/proximal tumor location (21,25,29) and a high histological grade (10,25,29) are identified as significant adverse predictors for survival in several of the series. The present study has re-confirmed a strong association of the presence of metastasis at presentation with a worse OS (P<0.0001) in all patients and of a large tumor size with a significantly worse OS (>5 cm, P=0.0233; >7 cm, P=0.0033) and MFS (>5 cm, P=0.0127; >7 cm, P=0.0029) in patients with localized disease at presentation. Primary tumor size is an established prognostic factor in not only synovial sarcoma but also in other soft-tissue sarcomas (30-32) and has been adopted as one of the essential parameters for the AJCC/UICC clinical staging system in soft-tissue sarcomas, together with tumor depth,
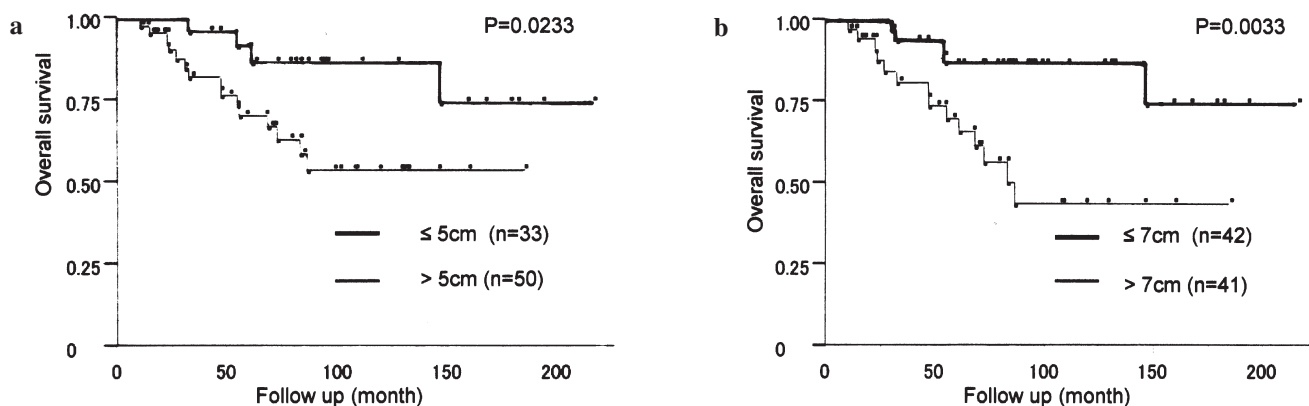
Figure 3. Overall survival according to tumor size (a) >5 or <5 cm, (b) >7 or <7 cm, in patients with localized disease at presentation.
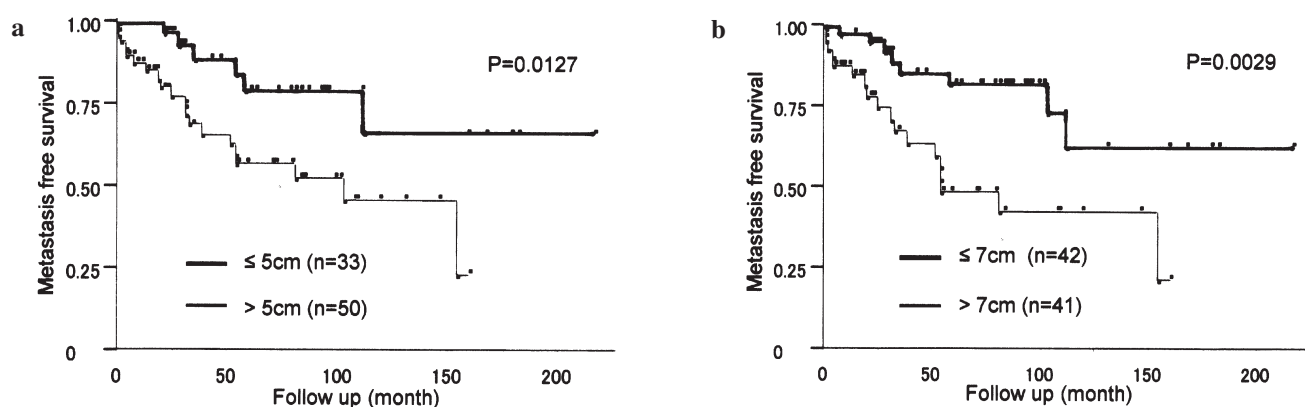

Figure 4. Metastasis-free survival according to tumor size (a) >5 or <5 cm, (b) >7 or <7 cm, in patients with localized disease at presentation.
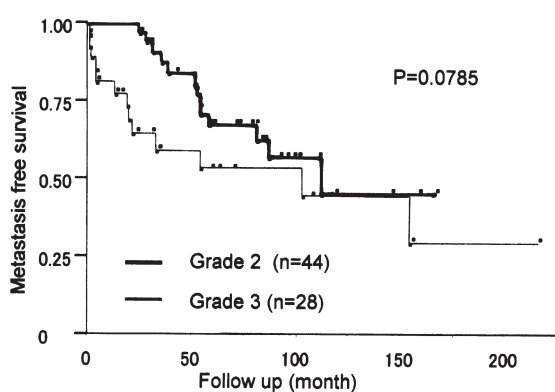

Figure 5. Metastasis-free survival according to the histological grade in patients with localized disease at presentation.

histological grade and the status of regional lymph nodes/ distant metastases (33).

Guillou *et al* (10) recently demonstrated that the French Federation of Cancer Centers (FNCLCC) histological grade (grade 2 vs 3) is the most important prognostic factor for survival in patients with synovial sarcoma. In the present study, the histological grade proved to be an independent prognostic factor for MFS in a multivariate analysis on patients with localized disease at presentation (P=0.037), following tumor

size (P=0.024), though not independently on OS. Among the histopathological factors, a poorly differentiated histology (10,23,34), tumor necrosis (10,21,23,25,34), high mitotic activity (8,10,21,22,25,34) and a high Ki67 (MIB-1) proliferation index (8,34,35) have also been associated with the prognosis of patients with synovial sarcoma and all of these histopathological factors are considered to contribute to the histological grade.

In the present study, female patients showed significantly better OS in the univariate analysis for all patients probably because the number of female patients who had metastasis at presentation was considerably fewer than that of the male ones. This survival difference according to sex lost its prognostic value for patients with localized disease at presentation. From the previous series, Trassard *et al* (25), from the FNCLCC Sarcoma Group, has reported the male sex as an adverse prognostic factor in patients with localized primary synovial sarcoma. The reason why the number of female patients with metastasis at presentation was fewer than the males in the present series could not be explained.

Several studies have reported the clinical difference according to the fusion type (5-10). The association of the fusion type with prognosis in synovial sarcoma patients was first reported by Kawai *et al* (5) in 1998 in a preliminary series of 45 patients. They postulated that patients with *SYT-SSX1* bearing synovial sarcoma showed a poorer prognosis than

Table IV. Multivariate analysis for overall survival according to the various factors in all patients (n=81).

	OS (all patients n=81)		
	Risk ratio	95% Cl	P
Fusion type			
SYT-SSX1	1.46	0.64-3.28	0.36
Sex			
Male	0.54	0.21-1.35	0.19
Tumor size			
≤7 cm	3.01	1.17-8.80	0.021
Histological grade			
Grade 2	1.27	0.55-2.97	0.58
Stage			
Localized	9.77	3.31-32.6	<0.001

those with the *SYT-SSX2* fusion type. This hypothesis was supported by several other series of relatively small numbers of patients (7-9,36) and Ladanyi *et al* (6) confirmed it in 2002 by conducting a multi-institutional retrospective analysis in 243 patients. In contrast, Guillou *et al (*10) reported a large series of 165 patients with synovial sarcoma, in which there was a trend for tumors bearing *SYT-SSX2* to behave more aggressively than *SYT-SSX1*, though the difference was not statistically significant. Our preliminary study, including 10 patients with synovial sarcoma, also showed that all tumors expressing *SYT-SSX2* (n=3) had a recurrence, suggesting that *SYT-SSX2* may correlate with an aggressive character as compared with *SYT-SSX1* (37). Thus, the issue of prognostic implication of the fusion type in synovial sarcoma is still controversial. In our present study, *SYT-SSX2* tumors tended to behave in a more aggressive manner than *SYT-SSX1* (Fig. 2), but the difference did not reach statistical significance

(P=0.244), concordant with the results reported by Guillou *et al* (10). The patient and tumor characteristics in our present series are nearly comparable to other major series (6,10,24-26,28), thus the relative lack of prognostic impact of the fusion type cannot be attributed to these selection biases. The treatment strategy is also basically equivalent, except for the relatively more frequent application of adjuvant chemotherapy in our present series (83/108 patients, 76.9%) compared with other series [38% (24), 41% (28), 44% (38), 53% (26), 57% (10), 62% (6)].

Previous representative large series of adult synovial sarcoma have shown 5-year OS from 57 to 75% (24-26,28). The 5-year OS of the patients with localized disease at presentation in the present series was 81.1%. This relatively better result may be attributed to the high application rate of adjuvant chemotherapy, though we did not show a significant difference in survival between patients treated with and those without adjuvant chemotherapy, probably because of the diversity of chemotherapeutic regimens in each center. Brecht *et al* (39) suggested that the more satisfactory survival in pediatric synovial sarcoma patients (5-year survival: 80-89%) than in adults is attributed not only to age itself but also the therapeutic strategy in which pediatric patients generally receive adjuvant chemotherapy regardless of the risk factors. The role of chemotherapy mainly consisting of ifosfamide with or without doxorubicin in adult patients with synovial sarcoma (at least for high-risk cases) has been recognized (40-42). Thus, a high application rate of adjuvant chemotherapy in the present series may lead to a better survival as compared with other major series. Notably, Guetz *et al* reported at the 2004 ASCO annual meeting that *SYT-SSX2* bearing synovial sarcomas appeared to present a better chemosensitivity than *SYT-SSX1* (n=14, P=0.09), suggesting that chemotherapy overshadows the natural prognosis of patients with synovial sarcoma which is possibly influenced by their fusion type.

In addition to patient prognosis, an association of the fusion type with the histological subtype in synovial sarcoma has already been reported (43,44). We also observed the same trend that tumors bearing *SYT-SSX2* rarely show a biphasic pattern, as previously reported, with marginal significance

Table V. Multivariate analysis for survivals according to the various factors in 67 patients with localized disease at presentation.

	OS (67 patients with localized disease at presentation)			MFS (67 patients with localized disease at presentation)		
	Risk ratio	95% Cl	P	Risk ratio	95% Cl	P
Fusion type						
SYT-SSX1	1.57	0.55-4.24	0.380	0.67	0.25-1.60	0.380
Tumor size						
≤7 cm	1.43	1.41-15.5	0.009	2.73	1.14-7.25	0.024
Histological grade						
Grade 2	0.51	0.61-4.61	0.310	2.44	1.06-5.74	0.037

(P=0.0837). Of note is that we observed a significant association between the fusion type and primary tumor location with a majority of *SYT-SSX1* tumors being in the extremities, whereas *SYT-SSX2* tumors were equally located in the extremities (n=21) and trunk (n=19) (P=0.0166). This trend was also observed in the series of Ladanyi *et al* (6) (P=0.07) and Guillou *et al* (10) (P=0.052). It may be hypothesized that a susceptibility of *SSX1* and -2 fusion to *SYT* may vary in different parts of the body.

In conclusion, our present study demonstrates that the *SYT-SSX* fusion type is not a significant prognostic factor in patients with synovial sarcoma, as Guillou *et al* (10) reported and that the most significant prognostic factor is tumor size followed by the histological grade in patients with localized synovial sarcoma. We also confirm the association between the fusion type and histological subtype and between the fusion type and primary tumor location. A systematic review by a meta-analysis procedure, or prospective large cohort study may be warranted to finally clarify the true prognostic impact of the *SYT-SSX* fusion type on the survival of patients with synovial sarcoma perhaps even with a future international collaboration.

Acknowledgements

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