original article

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Primary extremity soft tissue sarcomas: outcome improvement over time at a single institution

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Background: To assess changes in survival over time of extremity soft tissue sarcoma (ESTS) patients treated at a single reference institution.

Patients and methods: Patients with primary localized adult-type ESTS surgically treated at our institution between 1987 and 2007 were retrospectively reviewed. Patients were categorized into four 5-year groups according to the timing of their first operation. Crude cumulative incidence (CCI) of sarcoma-specific mortality (SSM), local recurrence (LR), and distant metastases (DMs) were calculated for each time period.

Results: A total of 1094 patients were identified. Median follow-up was 81 months. CCI of SSM and LR were significantly better in period 4 in comparison to periods 1–3 ($P < 0.001$ for both end points), dropping, respectively, from 15% to 6% and from 23% to 9%. An overall improvement of DMs-free survival at 5 years could be detected in the latter period, as well as a better postmetastasis survival.

Conclusions: Reference institutions for sarcomas may have improved their outcome in the last years. Although biases of retrospective analyses as well as the effect of institutional learning curves need to be discounted, it is possible that optimal exploitation of a series of subtle improvements in sarcoma treatment may make a difference in results currently achievable.

Key words: chemotherapy, prognosis, radiotherapy, sarcoma, surgery, treatment outcome

introduction

Extremity soft tissue sarcomas (ESTS) are a heterogenous group of rare diseases, whose prognosis has been extensively studied over the past years. The availability of large institutional prospective databases has helped to identify clinical predictors of outcome, related to either the tumor biology (size, histological grade of aggressiveness, histolgical subtype, and depth) or the treatment (surgical margins, delivery of radiotherapy, and chemotherapy) [1–6]. The notion that tumor biology prevails over the extent of local treatment as the primary determinant of patient outcome has led to the acceptance of limb- and function-sparing procedures [7–10]. If the appropriateness of local treatment was first viewed as determined by radical surgery alone, it is now seen as the product of surgical resection and complementary treatments. A multimodal approach, including radiation therapy and chemotherapy, has been increasingly used in the management of high-risk ESTS in the last years [11, 12]. In addition to a better understanding of prognostic factors and an evolution in the clinical management of patients with STS, insights from molecular studies promise to allow an even better risk stratification in the future, at a time when molecular-targeted agents are entering the armamentarium of sarcoma medical oncologists, and even chemotherapy is refined, through its tailoring to the histological variety of STS [12–14].

In light of all this, we decided to retrospectively evaluate whether there have been any major change in survival over time of ESTS patients treated at our institute in a 20-year time span.

patients and methods

Between January 1987 and December 2007, 1094 consecutive adult patients affected by primary adult-type ESTSs were operated on with a curative intent at the Istituto Nazionale Tumori, Milan, Italy, within a dedicated surgical unit. Clinical data were extracted from a prospective database of all adult patients with soft tissue sarcoma. Well-differentiated liposarcoma, dermatofibrosarcoma protuberans, and desmoid-type fibromatosis were excluded from the present analysis, since they virtually never metastasize.

For the purpose of the present analysis, patients were grouped according to the calendar time of first operation at our Institution, taking into account the following periods: 1987–1992, 1993–1997, 1998–2002, and 2003–2007.

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Data retrieved included gender, age at diagnosis, site, size, depth, histotype, grade and margin status, adjuvant treatments, dates of neoplastic events, death, or last follow-up.

Tumors were characterized as superficial or deep according to the involvement of the investing fascia. Pathologically, all tumors were diagnosed by two experienced pathologists at our institution. The Fédération Nationale des Centers de Lutte Contre le Cancer (FNCLCC) [15] grading system was applied to the untreated primary tumors.

Surgical excisions were considered as macroscopically complete in the absence of gross residual disease. The surgical specimen was examined in the presence of the operating surgeon; margins were inked and separately sampled. All macroscopically complete resections were classified according to the closest surgical margin, which was microscopically categorized as positive (tumor within 1 mm from the inked surface, R1) or negative (absence of tumor within 1 mm from the inked surface, R0).

The indication to radiation therapy (RT) was given by both the operating surgeon and the radiation oncologist when a higher risk of relapse was supposed to exist on clinical grounds. However, no prospectively selected criteria were used to this end. External beam radiation was used in all such cases, and doses ranged from 45 to 70 Gy (median 60 Gy).

Chemotherapy (CT) was given at the discretion of the multidisciplinary institutional sarcoma board or as part of ongoing clinical trials. Anthracycline-based regimens were used, in most of the cases combined with ifosfamide.

In the absence of any event after treatment, all patients were regularly followed up, generally at least every 4 months for the first 2 years, then every 6 months for the following 3 years, and then yearly.

statistical methods

The prognostic analyses mainly focused on investigating the prognostic effect of first calendar time on the following end points: sarcoma-specific mortality (SSM), local recurrence (LR), and distant metastases (DMs). Concomitant local relapses and DMs were included in the computations as DMs. The analyses were carried out in a competing risks framework [16]; in the analysis of cause-specific mortality, deaths due to conditions unrelated with sarcoma were regarded as competing events. For LR and DMs analyses, deaths without evidence of disease and DMs, or LR, respectively, whichever occurred first, were regarded as competing events. Time to events was computed from the date of surgery at our institution, or censored at the date of last follow-up assessment for event-free subjects.

Crude cumulative incidence (CCI) curves were estimated in the four time periods and compared by means of the Gray test [17].

Multivariable analyses of the effect of calendar time were based on cause-specific hazards and were therefore carried out using Cox regression models. The following covariates, chosen on the ground of literature information and our past experience [1, 4, 6, 18], were included in the models for the purpose of adjustment: patient age, tumor size, depth, grading, histotype, surgical margins, pre- and postoperative chemotherapy, and radiotherapy. The models also included interaction terms suitable to take into account possible synergism between preoperative CT and RT [19] and the temporal trends in the adoption of their combination. Patient age and tumor size were modeled as continuous variables by using four-knot restricted cubic splines [20] to obtain flexible fits, by allowing their prognostic effect not to be the same in every part of the range, whereas the other covariates were modeled as categorical by using dummy variables.

An additional analysis was carried out by including (first) local relapse and DMs as time-dependent variables in the multivariable Cox model on SSM, so as to verify their relative impact on sarcoma mortality.

Additional descriptive analyses of times to events were based on Kaplan–Meier method for the estimation of survival curves.

We considered as significant two-sided P values below the 5% conventional threshold.

All statistical analyses were carried out using the SAS (SAS Institute Inc., Cary, NC) and the R software [R Development Core Team. R: A Language and Environment for Statistical Computing. R Foundation for Statistical Computing, Vienna, Austria, 2006; http://www.r-project.org/ (24 November 2009, date last accessed)].

results

Main patient characteristics are listed in Table 1.

Median follow-up (interquartile range) was 81 months (40–121 months) in the whole series [127 (106–168), 123 (114–141), 95 (77–115), and 38 (26–54) in the first to fourth period, respectively].

disease-specific mortality

Out of 1094 patients investigated, 247 deaths were recorded. Of these, 199 (81%) were related to ESTS and were thus considered in our analyses. The number of deaths related to STS and the 5- and 10-year crude cumulative mortality estimates according to period are reported in Table 2.

Crude cumulative mortality curves (Figure 1, panel A) differed significantly according to period ($P = 0.001$).

The cause of death was mainly related to DMs in all four periods; nine patients overall (four in the first period, one in the second, three in the third, and one in the fourth) died of exclusive locoregional disease without having developed any DMs.

Table 3 shows the results from the multivariable Cox regression model for the whole case series. Significant prognostic factors were size, histological grade, histological subtype, surgical margins, and neoadjuvant CT-RT interaction, along with the period.

The period of the first treatment was no longer significant when including LR and DMs as additional (time-dependent) variables into the Cox model ($P = 0.136$).

local recurrence

One-hundred and sixty-five patients developed LR (Table 2). Overall, 76 patients had only LR, while 89 had LR and DMs (LR anticipating DMs in 49 patients, being concurrent in 23 and posterior in 17). In the first, second, third, and fourth period, respectively, 26, 21, 17, and 12 patients had a LR alone, while 30, 25, 22, and 12 had a LR and DMs (LR anticipating DMs in 15, 17, 11, and 6 patients, being concurrent in 8, 8, 5, and 6 and posterior in 7, 4, 6, and 0 patients).

One-hundred and twenty-five recurrences occurred as first event; the 5- and 10-year CCI estimates according to period are reported in Table 2. CCI curves (Figure 1, panel B) differed significantly according to period ($P < 0.001$).

Table 3 shows the results from the multivariable Cox regression model. Significant prognostic factors were age and surgical margins along with the period of the first treatment.

distant metastases

Two-hundred and ninety-six patients developed DMs (Table 2). Overall, 207 patients had only DMs, while 89 had a LR and DMs, as reported above. In the first, second, third,

Table 1. Main patients and disease characteristics according to the calendar time of operation

	1987–1992	1993–1997	1998–2002	2003–2007	Overall
N	250	194	274	376	1094
Median age, years (IQ)	47 (32–59)	49 (34–61)	54 (36–66)	51 (37–65)	50 (36–64)
Gender					
Female	117 (46.8%)	102 (52.6%)	122 (44.5%)	175 (46.5%)	516 (47.2%)
Male	133 (53.2%)	92 (47.4%)	152 (55.5%)	201 (53.5%)	578 (52.8%)
Median tumor size, cm (IQ)	7 (3.3–12)	6 (4–10)	6 (3–10)	6 (3–10)	6 (3–10)
Tumor site					
Upper extremity	46 (18.4%)	37 (19.1%)	60 (21.9%)	79 (21.0%)	222 (20.3%)
Lower extremity	189 (75.6%)	142 (73.2%)	185 (67.5%)	270 (71.8%)	786 (71.8%)
Girdle	15 (6.0%)	15 (7.7%)	29 (10.6%)	27 (7.2%)	86 (7.9%)
Depth					
Superficial	22 (8.8%)	16 (8.3%)	88 (32.1%)	138 (36.7%)	264 (24.1%)
Deep	228 (91.2%)	178 (91.7%)	186 (67.9%)	238 (63.3%)	830 (75.9%)
Grade					
GI	39 (15.6%)	49 (25.3%)	75 (27.4%)	87 (23.2%)	250 (22.9%)
GII	44 (17.6%)	59 (30.4%)	96 (35.0%)	102 (27.1%)	301 (27.5%)
GIII	167 (66.8%)	86 (44.3%)	103 (37.6%)	187 (49.7%)	543 (49.6%)
Histological subtype					
Myxoid/round cell liposarcoma	38 (15.2%)	42 (21.5%)	42 (15.3%)	52 (13.8%)	174 (15.9%)
Dedifferentiated liposarcoma	16 (6.4%)	10 (5.2%)	12 (4.4%)	17 (4.5%)	55 (5.0%)
Synovial sarcoma	37 (14.8%)	29 (15.0%)	27 (9.9%)	35 (9.3%)	128 (11.7%)
Leiomiosarcoma	31 (12.4%)	24 (12.3%)	53 (19.3%)	79 (21.0%)	187 (17.1%)
MPNST	22 (8.8%)	15 (7.7%)	20 (7.3%)	29 (7.7%)	86 (7.9%)
MFH	59 (23.6%)	38 (19.6%)	61 (22.3%)	82 (21.8%)	240 (21.9%)
Vascular sarcoma	7 (2.8%)	3 (1.6%)	9 (3.3%)	3 (0.8%)	22 (2.0%)
Other	40 (16.0%)	33 (17.1%)	50 (18.2%)	79 (21.0%)	202 (18.5%)
Surgical procedure					
Conservative	229 (91.6%)	190 (97.9%)	271 (98.9%)	373 (99.2%)	1063 (97.2%)
Amputation	21 (8.4%)	4 (2.1%)	3 (1.1%)	3 (0.8%)	31 (2.8%)
Reconstructive procedures					
Yes	24 (9.6%)	12 (6.2%)	37 (13.5%)	76 (20.2%)	149 (13.6%)
No	226 (90.4%)	182 (93.8%)	237 (86.5%)	300 (79.8%)	945 (86.4%)
Surgical margins					
R0	215 (86.0%)	164 (84.5%)	250 (91.2%)	333 (88.6%)	962 (87.9%)
R1	35 (14.0%)	30 (15.5%)	24 (8.8%)	43 (11.4%)	132 (12.1%)
CT					
Not carried out	200 (80.0%)	166 (85.6%)	219 (79.9%)	259 (68.8%)	844 (77.1%)
Preoperative/pre- and postoperative	44 (17.6%)	14 (7.2%)	25 (9.1%)	87 (23.1%)	170 (15.5%)
Combined with RT	1 (0.4%)	0 (0%)	6 (2.2%)	45 (12.0%)	52 (4.8%)
Postoperative	6 (2.4%)	14 (7.2%)	30 (11.0%)	30 (8.0%)	80 (7.3%)
Combined with RT	3 (1.2%)	12 (6.2%)	26 (9.5%)	28 (7.5%)	69 (6.3%)
RT					
Not carried out	169 (67.6%)	123 (63.4%)	134 (48.9%)	150 (40.0%)	576 (52.7%)
Preoperative/pre- and postoperative	2 (0.8%)	0 (0%)	9 (3.3%)	47 (12.5%)	58 (5.3%)
Combined with CT	1 (0.4%)	0 (0%)	6 (2.2%)	45 (12.0%)	52 (4.8%)
Postoperative	79 (31.6%)	71 (36.6%)	131 (47.8%)	179 (47.6%)	460 (42.0%)
Combined with CT	3 (1.2%)	12 (6.2%)	26 (9.5%)	28 (7.5%)	69 (6.3%)

IQ, interquartile range; MPNST, malignant peripheral nerve sheath tumor; MFH, malignant fibrous histiocytoma.

and fourth period, respectively 52, 33, 58, and 64 patients had only DMs, while 30, 25, 22, and 12 had a LR and DMs, as reported above.

The 5- and 10-year CCI estimates according to period are reported in Table 2. CCI curves (Figure 1, panel C) were not significantly different according to period ($P = 0.266$).

Table 2. Number of events according to calendar time of operation and corresponding incidence estimates

		No. of events		5-Year estimates		10-Year estimates	
	No. of patients	Overall	First event	CCI	CI	CCI	CI
1987–1992	250						
SSM		67	–	23.0%	18.1, 29.2%	29.5%	24.0, 36.2%
LR		56	41	15.1%	11.2, 20.4%	17.5%	13.2, 23.1%
DM		82	67	26.8%	21.7, 33.1%	28.2%	23.0, 34.5%
1993–1997	194						
SSM		46	–	19.8%	14.8, 26.5%	23.2%	17.8, 30.2%
LR		46	38	18.3%	13.5, 24.7%	19.4%	14.5, 26.0%
DM		58	41	18.4%	13.6, 24.8%	21.9%	16.7, 28.8%
1998–2002	274						
SSM		59	–	19.4%	15.2, 24.9%	23.0%	18.3, 29.0%
LR		39	28	9.8%	6.8, 14.1%	11.0%	7.7, 15.6%
DM		80	69	24.3%	20.0, 30.1%	26.2%	21.3, 32.1%
2003–2007[a]	376						
SSM		27	–	9.2%	6.2, 13.7%	–	–
LR		24	18	6.0%	3.6, 9.8%	–	–
DM		76	70	22.2%	17.5, 28.2%	–	–

[a]Due to the short follow-up in this subgroup, the CCI was not extrapolated to 10 years.
CCI, crude cumulative incidence; CI, CCI 95% confidence interval; LR, local recurrence; DMs, distant metastases; SSM, sarcoma-specific mortality.

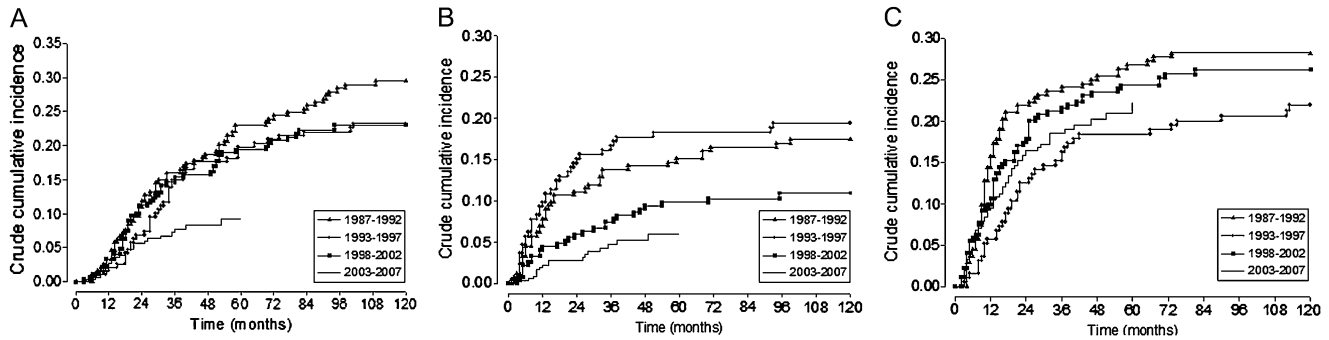

Figure 1. Crude cumulative incidence of sarcoma-specific mortality (panel A), local recurrence (panel B), and distant metastases (panel C) by calendar time of operation.

Table 3 shows the results from the Cox multiple regression model. Significant prognostic factors were size, histological grade, and histological subtype, but not period of the first treatment.

DMs-free survival, taking into account all DMs (either occurred as first event or not), showed a significant better outcome in the fourth period in comparison with all the three previous ones (Figure 2; $P = 0.020$).

The median time from metastases to death was 17 months in the first three periods of time and approached 31 months in the last one (Figure 3).

The above findings were confirmed also on both the high-grade and the deep-tumor subgroups (data not shown).

discussion

Over a period of 20 years, in a single-institution series of patients with primary localized ESTS, the 5-year LR and cause-specific death incidence dropped from 15% and 23%, respectively, to 6% and 9%. Both improvements were statistically significant and hold true even in the subgroups of grade III and deep tumors.

All retrospective analyses have obvious weaknesses. A Will Rogers phenomenon [21] could be advocated to explain the improved outcome. Nevertheless if that was real, we would expect to observe an overall improvement even in the CCI of DMs, which did not occur. On the other hand, an absolute improvement in the 10% range in both LR and survival is worthy of notice. No known breakthrough in ESTS treatment has occurred in the same time interval as to justify such a difference. Institutional learning curves do exist, of course, and may improve outcomes over time. If so, it would be noteworthy as well, implying that room for improvement does exist for sarcoma institutions at the best of current knowledge. Indeed, there was a higher resort to reconstructive surgery in the last period (from <10% of the cases in the first periods to >20% in the last one). This was accompanied by a decrease in amputations (which dropped to 0.8%), and may have thus resulted in more aggressive, albeit conservative, surgery. Another major difference in treatment among the four time

Table 3. Analysis of the effect of calendar time of operation on SSM, LR, and DM by multivariable Cox models

	SSM			LR			DMs		
Factor	HR	CI	*P*	HR	CI	*P*	HR	CI	*P*
Calendar time			0.005			0.006			0.278
1987–1992 versus 2003–2007	1.67	0.98, 2.83		2.68	1.42, 5.02		1.25	0.84, 1.86	
1993–1997 versus 2003–2007	2.00	1.17, 3.43		2.79	1.50, 5.17		1.12	0.73, 1.72	
1998–2002 versus 2003–2007	2.38	1.46, 3.89		1.71	0.93, 3.14		1.41	0.99, 2.01	
Age, years									
64 versus 36[a]	1.13	0.86, 1.48	0.678	1.80	1.26, 2.56	0.005	1.01	0.80, 1.29	0.880
Tumor size, cm									
10 versus 3[a]	2.62	1.75, 3.92	<0.001	1.35	0.85, 2.15	0.248	3.23	2.20, 4.75	<0.001
Depth									
Deep versus superficial	1.86	1.00, 3.45	0.051	1.28	0.72, 2.27	0.401	1.02	0.65, 1.61	0.928
Grading			<0.001			0.209			<0.001
II versus I	3.53	1.73, 7.18		1.61	0.89, 2.91		2.98	1.68, 5.29	
III versus I	6.29	3.11, 12.71		1.22	0.66, 2.27		5.08	2.87, 8.98	
Histotype			<0.001			0.102			<0.001
Myxoid/round cell liposarcoma versus MFH	1.50	0.76, 2.96		0.54	0.27, 1.06		1.44	0.82, 2.52	
Dedifferentiated liposarcoma versus MFH	1.90	0.94, 3.85		0.60	0.27, 1.35		1.61	0.86, 3.01	
Synovial sarcoma versus MFH	3.90	2.23, 6.82		1.01	0.54, 1.88		2.86	(1.73, 4.73)	
Leiomiosarcoma versus MFH	2.93	1.73, 4.97		0.54	0.30, 0.99		3.06	1.98, 4.72	
MPNST versus MFH	2.63	1.43, 4.84		0.77	0.39, 1.53		1.58	0.86, 2.93	
Vascular sarcoma versus MFH	6.49	2.72, 15.49		1.30	0.45, 3.74		3.98	1.65, 9.64	
Other versus MFH	2.06	1.18, 3.59		0.45	0.24, 0.87		2.18	1.38, 3.46	
Surgical margins									
R1 versus R0	1.49	1.02, 2.16	0.037	2.52	1.62, 3.90	<0.001	1.17	0.82, 1.69	0.385
Interaction preoperative CT–RT			0.015			0.334			0.055
Preoperative CT			0.048			0.511			0.150
Yes versus no, without preoperative RT	1.19	0.80, 1.78		0.86	0.43, 1.69		1.15	0.80, 1.66	
Yes versus no, with preoperative RT	0.24	0.07, 0.84		0.21	0.01, 3.50		0.36	0.11, 1.14	
Preoperative RT			0.027			0.334			0.028
Yes versus no without preoperative CT	4.00	1.40, 11.43		1.12	0.15, 8.61		4.06	1.42, 11.60	
Yes versus no, with preoperative CT	0.79	0.34, 1.83		0.27	0.03, 2.20		1.28	0.68, 2.39	
Postoperative CT									
Yes versus no	0.91	0.61, 1.36	0.642	1.60	0.87, 2.94	0.134	0.80	0.56, 1.14	0.208
Postoperative RT									
Yes versus no	0.90	0.65, 1.24	0.523	0.73	0.48, 1.09	0.123	1.26	0.93, 1.70	0.134

[a]Modeled as continuous variable (see 'Statistical methods' section); the two values are third and first quartiles, respectively.
HR, hazard ratio; CI, HR 95% confidence interval; *P*, two-sided Wald test *P* value; LR, local recurrence; DMs, distant metastases; SSM, sarcoma-specific mortality; MPNST, Malignant Peripheral Sheath Tumor; MFH, Malignant Fibrous Histiocytoma.

cohorts was the introduction at our institution of preoperative combined chemoradiation therapy in the latter period (practically never employed in the first three periods, while used in 12% of the cases in the last one). The choice to do a preoperative combined treatment was not randomized, even when it was made within a clinical study, and was mainly based

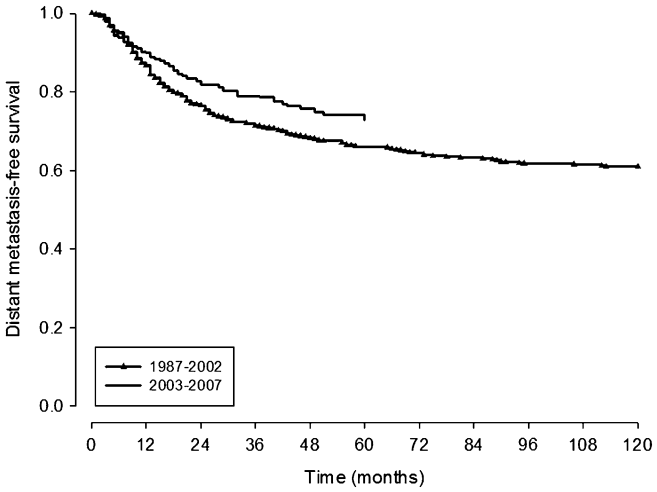

Figure 2. Distant metastases-free survival by period of primary treatment.

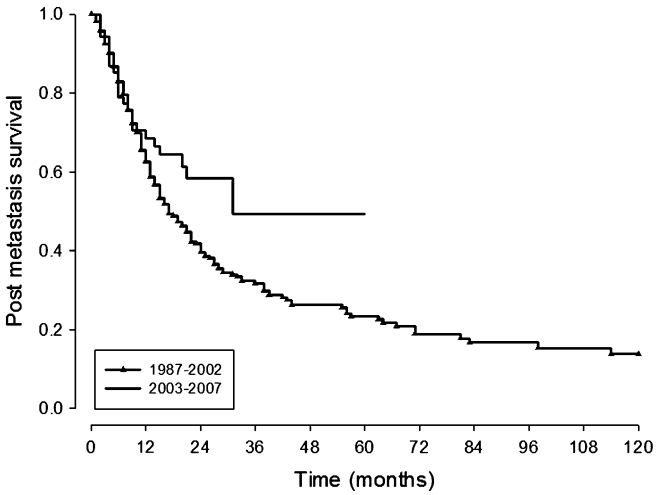

Figure 3. Postmetastases survival by period of primary treatment.

on the clinical perception of a higher risk or tumor volume. We do not have data formally proving the added value of preoperative radiation therapy [19]. Indeed, the role of radiation therapy as such in complementing surgery was proved by small, though convincing, randomized trials more than a decade ago [8, 9]. Whether doing radiation therapy pre- or postoperatively makes a difference in terms of local outcome has been addressed in part by a randomized trial [22]. The study focused on differences in complications but was not powered enough to say if the local control was affected by the pre- versus postoperative placement of radiation therapy. Yet several groups have started to employ radiation therapy in the preoperative setting, reporting lower local failures [19, 23, 24] in comparison to previous historical series [4, 18, 25, 26]. These studies are small and not conclusive. On the other hand, the role of adjuvant chemotherapy in STS has been debated for years without any definitive conclusion [27, 28]. A recent meta-analysis [29] of all published studies suggested a minor improvement in outcome, both through a local and a distant effect. All the more, whether its placement preoperatively makes a difference is unknown (even in osteosarcoma, where a much more effective CT is available, a randomized trial did not show any difference between pre- and postoperative chemotherapy [30]). In the end, it is possible that exploiting at best reconstructive surgery and preoperative combined radiochemotherapy may make a difference in some patients. At least, our institutional improvement in local control suggests to assess this hypothesis.

In addition to a better local control, we saw an improvement in cause-specific mortality, in the lack of any improvement in the incidence of DMs as the first failing event. In principle, the most logical explanation would be that a better local control gives also a survival improvement. As well-known, no definitive formal demonstration of this is available at the moment, although this has been the subject of continuous controversy in the sarcoma community. Some believe that LR is just a marker of tumor aggressiveness [18, 25, 31]. Others believe that, though minor, a causative effect on distant spread might be in place [10, 23]. Far from saying a final word on this, in the last period we observed an absolute reduction in DMs (from 34% to 27% at 5 years, Figure 2), in the face of the same rate of DMs as a first event in the four periods. In practice, we cannot rule out that the absence of LRs in a number of patients may have prevented them from developing metastases thereby.

At least, in this series we saw that a small fraction of patients experiencing a LR die because of it, without developing any distant failure, as we already reported [32]. In this series, these patients represent 20% of those having LRs. It is therefore quite reasonable to think that, by reducing the LR rate, some patients were cured, who would have developed a LR and died from it. However, this may account for only 1%–2% improvement in 5-year mortality (the 3% rate of patients who died in the first three periods for locoregional recurrences without metastatic spread dropped to 1.2% in the last period).

Finally, we observed a longer postmetastasis survival, which definitely may have contributed to an overall survival improvement at 5 years (although this improvement, obviously, will not hold at a longer interval). In fact, median survival of metastatic patients in the previous years was 17 months, while it was 31 months in the last period. This improvement might reflect a more individualized approach to the medical therapy of metastatic disease in the most recent years. Indeed, new agents, tailored to the histological subtype, have been entering our everyday practice in the last years [14]. As well-known, even the superiority of multiagent chemotherapy over single-agent doxorubicin in first line has long been debated in STS. However, the availability of histology-driven salvage therapies has recently added to the armamentarium of the medical oncologist [33–36]. In a patient setting marked by preserved performance status across the advanced stages of disease, their use may result in some survival prolongation. Likely, it will be difficult to prove this in subgroups of patients, within a rare group of diseases like sarcomas. Thus, signals like this institutional improvement in the 5-year postmetastasis survival may be of interest to the sarcoma community.

In conclusion, sarcoma institutions should know that there is room for improving their local control rate and possibly their final outcome. Reconstructive surgery and possibly preoperative therapies may have a crucial added value. Even

postmetastasis survival might be currently improving, possibly thanks to a refined, histology-driven approach to the medical therapy of advanced sarcomas. At least, these are suggestions drawn from the retrospective analysis of a single-institution series. Other institutions may be willing to look at their data in order to confirm this, while hypotheses suggested from these data may drive prospective studies, challenging though they may be in a rare family of 50-plus histological subgroups of tumors.

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disclosure

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