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Oncological outcome, functional results and costs after unplanned excision of musculoskeletal soft tissue sarcoma

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THESE

préparée sous la direction du Docteur Stéphane Cherix
(avec la co-direction du Professeur Alain Farron)

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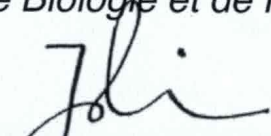
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Oncological outcome, functional results and costs after unplanned excision of musculoskeletal soft tissue sarcoma

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ABSTRACT

Background: Treatment of soft tissue sarcomas (STS) should only be initiated once the diagnosis is fully established. Resection of tumors of unknown nature should be avoided. Nevertheless, specialized centers continue to face numbers of unplanned excisions (UPE) in STS.

Aim: To compare oncologic and functional outcomes, number of surgeries, length of hospital stay and treatment costs of UPE versus planned excision (PE) in STS.

Method: A retrospective single tertiary center study was performed on 201 patients. Survival, local and distant recurrence rates were compared between PE (n = 137) and UPE (n = 64). In a subgroup analysis of 60 patients, functional outcome (MSTS and TESS scores), and socio-economic impact (number of surgeries, length of hospital stay and treatment costs) in "functional planned excision" (fPE) group (n = 30) and "functional unplanned excision" (fUPE) group (n = 29) were compared.

Results: There was no significant difference in oncological outcome between PE and UPE. In the subgroup analysis, we found a non-significant difference in functional outcome. Patients in the fUPE had significantly more surgeries (3.5 vs. 1.4; p < 0.00001) and costs of their management was 64% higher than fPE (p = 0.048). Hospital stay was longer after fUPE but not statistically significant (18.3 days vs. 11.8 days; p = 0.13).

Conclusion: Even though oncological and functional outcomes are comparable after PE and UPE of STS, the number of surgeries, length of hospital stay and treatment costs were higher in patients with UPE. Our data underscore the importance of specialized STS treatment centers including multidisciplinary management.

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Introduction

Musculoskeletal soft tissue tumors are frequent, often asymptomatic and therefore underdiagnosed. Benign lesions are much more common than malignant entities. Damron et al. estimated the incidence of benign lesions at 3/1000 persons per year, while the incidence of musculoskeletal soft tissue sarcomas (STS) is estimated at 2/100′000 persons per year [1]. History, symptoms or lesion location do not enable distinction between histotypes and in most cases not even between benign or malignant tumors. Extensive diagnostic work-up (e.g. MRI, CT, functional imaging and biopsy) is indicated in most cases to define an appropriate treatment strategy [2].

However, unplanned excisions (UPE) of STS remain frequent, occurring in up to 53% of cases [3–5]. In this setting, surgery was generally performed based on the assumption of benignity. These patients are often treated in non-specialized centers, without advanced imaging and histotype prior to surgery, as no biopsies were performed. Diagnosis is made only after surgery upon histological work-up of the specimen. As surgical margins are often insufficient (i.e. intralesional or marginal), subsequent tumor bed excision is usually necessary, with neo-adjuvant or adjuvant chemo- or radiotherapy [6–8]. Several studies have demonstrated that the oncological outcome is not different in such cases [3,9–11], whereas other authors showed that oncological results were worse after tumor bed excision [12,13] and that survival rate improved when STS were treated in a specialized center [12,13]. However, data on functional outcome in patients after UPE are currently scarce. We are aware of only one study comparing functional outcome in patients after UPE and PE of STS [9].

The purpose of this study was to assess functional and oncological outcomes as well as economic impact of STS management in patients referred to our tertiary center after UPE compared with patients who had PE in our institution.

Patients and methods

A retrospective single center study was performed in our sarcoma center. Ethical committee approval was obtained (CER-VD: 266/14).

Oncological outcome

We reviewed all patients who underwent a resection of a musculoskeletal STS or a tumor bed excision at our sarcoma center between 2000 and 2015. Oncological data were retrospectively collected from the medical files. We determined overall survival, disease-specific survival and disease-free survival (local recurrence and distant metastases).

All patients who were operated for musculoskeletal STS between 2000 and 2015 at our center were included. All patients were discussed at a multidisciplinary sarcoma board, deciding on the best (neo-) adjuvant treatment (radiotherapy, chemotherapy and ILP (Isolated Limb Perfusion)) according to the literature recommendation of the moment. Radiotherapy was given in a neo-adjuvant setting for high grade STS whenever possible (25×2 Gy $= 50$ Gy in most of cases). Since 2013, radiotherapy is no longer performed systematically in low grade STS.

Patients were divided into two groups. The first group was composed of patients who had a PE at our center i.e. established sarcoma histotype and a multidisciplinary sarcoma board discussion prior to initial resection. The second group was composed of patients who needed a re-excision after UPE i.e. the diagnosis of sarcoma was not known at the initial resection.

Patients were followed up at the Orthopedic and Oncology Departments on a 3-month schedule with clinical and radiological workups.

Functional outcome

To evaluate functional outcome, we selected a subgroup of patients in the PE group ("functional" PE = fPE) using the following inclusion and exclusion criteria and we compared it with a selected subgroup of patients in the UPE group ("functional" UPE = fUPE). This allowed us to have two groups with comparable epidemiological characteristics.

Patients' inclusion criteria for both "functional" subgroups were:

- to have had a surgical resection for a musculoskeletal STS in the orthopedic unit of our sarcoma center between 2000 and 2015
- functional outcome was considered definitive (minimum of 12 months since last surgery)
- consent to take part in the study

We excluded deceased patients, those unable to give a consent, missing data and patients lost to follow up. Patients with STS located in the wrist, hand, foot and ankle were excluded, due to the well-known negative impact on postoperative function of STS in those particular locations. In addition, lesions greater than 100 mm were excluded as they were significantly less frequently subjected to unplanned excisions than smaller lesions and would consequently induce a selection bias.

Tumor size was determined on the preoperative MRI, or, if not available (in unplanned surgeries), as reported from the pathologist's report.

Functional assessment was performed at least 12 months after the last surgery, using the patient-reported score of the Musculoskeletal Tumor Society (MSTS) [14] and the Toronto Extremity Salvage Score (TESS) [15,16].

Economic impact

Economic impact was calculated for the two functional subgroups because these two subgroup were much more statistically comparable than the overall PE and UPE groups.

We compared length of hospital stay, number of surgeries related to STS and costs. We also did multivariate analyses regarding tumor size (<5 cm vs. 5–10 cm) and depth (subcutaneous vs. underneath the fascia).

Data on cost of inpatient treatment were available in our institution only after 2002, so we were only able to establish cost for 29/31 patients in the fPE group and 25/29 in the fUPE, as they were charged to the patients' insurance according to the SwissDRG system. For the patients who had initial UPE in another center, we added the cost of outpatient excision of a benign <5 cm or >5 cm tumor, based on our national outpatient billing scheme.

Statistical analysis

Statistical analyses were performed using NCSS and Prism 8 software. Nonparametric pairwise comparisons of continuous variables were performed using Mann-Whitney U test. Fisher's exact test or chi-squared test were used for comparisons of categorical data, where appropriate. Comparison of multiple groups was performed using one-way ANOVA test. Survival was analyzed using the Kaplan-Meier method. P-values ≤ 0.05 were considered statistically significant.

Results

Oncological outcome

Two hundred and one patients were included for this part of the study. One hundred and thirty seven out of 201 patients (68.2%) underwent PE while in 64/201 patients (31.8%) the diagnosis of STS was not known at the time of initial surgery (UPE).

Demographic data and tumor characteristics are detailed in Table 1.

These two groups did not differ in terms of gender, age or tumor grade, but there was a significant difference regarding localization of the tumor, with proportionally significantly more lesions of the upper extremity in the UPE group than in the PE group (p = 0.0007). There was also a significant difference in size, with bigger tumors in the PE group (p < 0.00001).

Table 1
Patient epidemiologic data.

Variable	PE	UPE	p-value	Total	fPE	fUPE	p-value	Total
	n = 137	n = 64		n = 201	n = 31	n = 29		n = 60
Gender			0.44				0.12	
Male	79	35		114	16	21		37
Female	58	29		87	15	8		23
Age	55.9 (12–93)	52.2 (12–94)	0.11	54.7 (12–94)	50	54	0.18	(med 52)
Tumor site			0.0007				0.102	
Upper extremity	15	15		30	6	12		18
Shoulder/arm	11	4		15	5	4		9
Elbow/forearm/hand	4	11		15	1	8		9
Lower Extremity	120	45		165	25	17		42
Pelvic ring/buttock	14	4		18	4	4		8
Thigh	79	22		101	15	8		23
Knee/lower leg	22	14		36	6	5		11
Ankle/foot	5	5		10	0	0		0
Back	2	4		6	0	0		0
Depth			< 0.00001				0.02	
Superficial	26	36		62	9	18		27
Deep	111	28		139	22	11		33
Histology			0.06				0.002	
Unclassified sarcoma	41	16		57	7	6		13
Lipomatous tumors	40	11		51	11	3		14
*WDLPS/ALT**	*23*	*6*		*29*	*9*	*2*		*11*
Grade 2 or 3	*17*	*5*		*22*	*2*	*1*		*3*
Myxofibrosarcoma	11	12		23	2	10		12
Leiomyosarcoma	8	7		15	0	5		5
Synovialosarcoma	12	3		15	4	0		4
Fibromyxoid sarcoma	8	1		9	3	0		3
ES chondrosarcoma**	3	1		4	2	0		2
MPNST***	2	2		4	0	2		2
Epithelioid sarcoma	1	3		4	1	1		2
Other	11	8		19	1	2		3
Grade (FNCLCC**)**			0.98				0.42	
Low	34 (24.8%)	15 (23.4%)		49 (24.4%)	12 (38.7%)	9 (31%)		21 (35%)
Intermediate	53 (38.7%)	25 (39.1%)		78 (38.8%)	13 (41.9%)	10 (34.5%)		23 (38.3%)
High	50 (36.5%)	24 (37.5%)		74 (36.8%)	6 (19.4%)	10 (34.5%)		16 (26.7%)
Size			< 0.00001				0.12	
<50 mm	33 (24,1%)	39 (60.9%)		72 (35.8%)	15 (48.3%)	20 (69%)		35 (58.3%)
50–100 mm	47 (34,3%	14 (21.9%)		61 (30.3%)	16 (51.6%)	9 (31%)		25 (41.7%)
>100 mm	57 (41.6%)	11 (17.2%)		68 (33.8%)	0	0		0
Mean size (mm)	92	56		(med 81)	46	42		(med 44)
Mean follow up (month)	89	99		92	77	79		78

*WDLPS/ALT = Well-Differenciated Liposarcoma / Atypical Lipomatous Tumor **ES chondrosarcoma = extra skeletal chondrosarcoma ***MPNST = malignant peripheral nerve sheath tumor ****FNCLCC = Fédération Nationale des Centres de lutte Contre le Cancer.

With a median follow-up of 92 months, overall 48 patients (24%) died, 37 due to the STS (disease-specific death rate = 18.4%), 153 were alive (76%), and 120 (59.7%) were alive and disease-free. Five- and ten-year survival rates were 86.1% and 84.1%, respectively. Fifteen patients (7.5%) had local recurrence, of whom five were alive at time of last follow-up. Median time to local recurrence was 34 months. Fifty-nine patients (29.3%) had distant recurrence, of whom 28 were alive at time of follow-up. Median time to distant recurrence was 24 months. Oncological outcome for the whole cohort and the different subgroups are presented in Table 2 and in Figs. 1–3.

Functional results

Eighty-nine out of 201 patients (44.3%) met the inclusion criteria for functional analysis. Four had moved abroad, we were unable to contact 22, and 3 refused to take part in the study. Sixty patients were included and completed the patient reported outcome measures. Median follow-up was 78 months (range: 12–187 months). The cohort was divided into two subgroups consisting of 31/60 patients (51.7%) who had planned excision (fPE)) and 29/60 patients (48.3%) who had an unplanned excision (fUPE). The demographic data of these subgroups are detailed in Table 1 and were statistically comparable in term of gender (p = 0.12), age (p = 0.18), tumor site (p = 0.102), grade (p = 0.42) and size (p = 0.12). There was more superficial (localization above the fascia) in the fUPE group than in the fPE group (p = 0.02).

There was no statistical difference between fPE and fUPE regarding oncological (Table 2) and functional outcomes (Table 3). In multivariate analysis, we did not find any significant correlation between grade and functional results, but we found a trend with superficial STS having worse functional outcome in the fUPE sub-group (Table 4). On multivariate analysis, the addition of radio-therapy did not significantly influence functional results (p = 0.82 for MSTS and p = 0.62 for TESS).

Economic impact

Patients in the fUPE group had on average two more surgeries than those in the fPE group (p < 0.00001) and five more days of

Table 2
Oncological outcome.

| Variable	PE	UPE	p-value	Total	fPE	fUPE	p-value	Total
	n = 137	n = 64			n = 31	n = 29		n = 60
Survival status								
Alive	103	50		153 (76.1%)	31	29	1	60
Deceased of sarcoma	25 (24%)	12 (19%)	1	37 (18.4%)				
Total Deceased	34	14	0.72	48 (23.9%)				
Grade 1 deceased of sarcoma				0				
Grade 2 deceased of sarcoma				9				
Grade 3 deceased of sarcoma				25				
Local recurrence			0.25				1	
No	129	57		186	30	28		58
Yes	8 (6%)	7 (11%)		15 (7.5%)	1	1		2
Residue after tumour bed excision		20 (31%)				16		
Distant recurrence (metastasis)			0.25				1	
No	93	49		142	26	25		51
Yes	44 (31.7%)	15 (23.4%)		59 (29.3%)	5	4		9
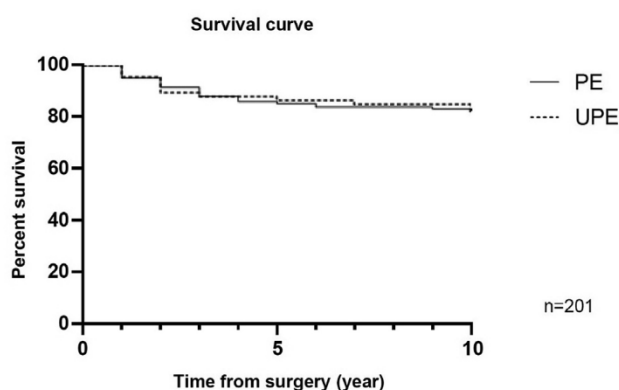
Fig. 1. 10 year survival.
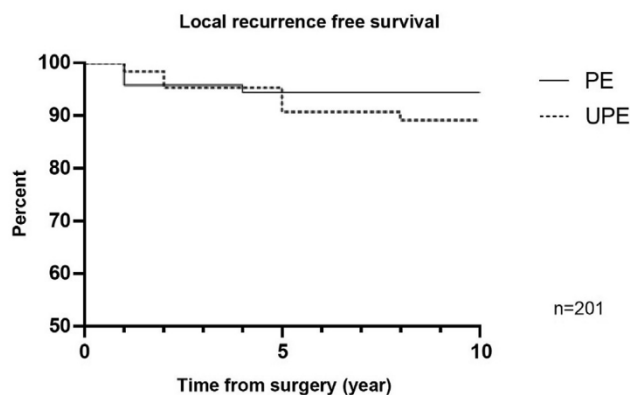
Fig. 3. 10 year local recurrence free survival.
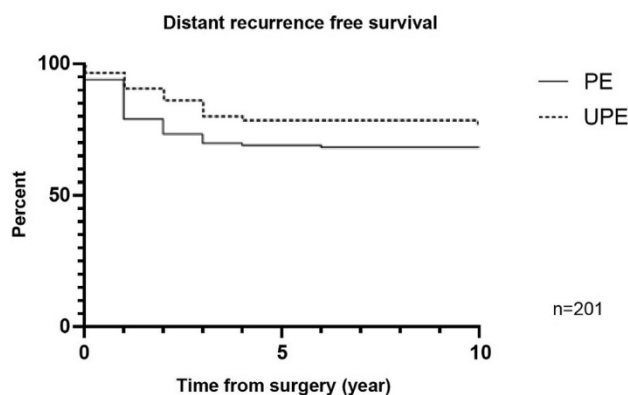
Fig. 2. 10 year distant recurrence free survival.

Table 3
Functional results.

Variable	fPE	fUPE	p-value
	n = 31	n = 29	
MSTS score	25,4	24,2	0,99
TESS	92.8	87.7	0.90
Number of surgical procedures	1,4	3,5	< 0.00001
Time of hospital stay (days)	12,8	18.3	0,13
Cost (€)	18'101	28'185	0.0477
Radiation therapy			
Neo-Adjuvant	20	21	
Adjuvant	3	1	0.61
Chemotherapy			
Neo-Adjuvant	3	1	
Adjuvant	1	1	0.74
ILP (Isolated Limb Perfusion)	1	0	1

hospitalization (p = 0.18).

Patients with high grade STS had significantly more surgeries than those with low grade (mean of 2.2 surgeries in high grade versus 1 in low grade, p = 0.03) in the fPE, but there was no correlation between grade and the number of surgeries in the fUPE (3.2 surgeries in high grade versus 3.8 surgeries in low grade, p = 0.8). We did not find any significant correlation between grade and functional results or length of hospital stay.

In the multivariate analysis, we found a significantly higher number of surgical procedures in every fUPE subgroup (<5 cm, 5–10 cm, superficial and deep), but no statistically significant difference in functional results or length of hospital stay (Table 4). We observed a trend in superficial STS in the fUPE doing worse regarding length of hospital stay and number of surgeries compared to deep lesions. All these data are described in Table 4.

When we compared deep and superficial tumors in the fUPE subgroup, we observed a significantly higher risk of secondary surgical wound closures by skin graft or flap in the superficial fUPE subgroup (p = 0.03). Twelve out of 18 patients who underwent tumor bed excision for a superficial STS needed skin graft or flap coverage whereas only 2 out of 11 patients (18%) secondarily

Table 4
Functional multivariate analysis.

	Superficial			Deep		
	fPE	fUPE	p-value	fPE	fUPE	p-value
Number of patients	9	18		21	11	
Mean age	50	42	0.13	51	51	1
Average size of tumor (mm)	39	37	0.10	38	49	0.63
MSTS score	27.6	23.8	0.33	24.6	24.8	0.51
TESS	94.2	88.1	0.37	92.5	87.2	0.57
Time of hospital stay	9	17.5	0.16	14.4	19.7	0.56
Surgical procedures	1,2	3.2	0.0002	1,5	3.9	0.0005
Tumor residue after Tumor bed excision		9 (50%)			6 (54%)	

	Tumor <5 cm			Tumor 5–10 cm		
	fPE	fUPE	p-value	fPE	fUPE	p-value
Number of patients	14	20		16	9	
Mean age	45	54	0.10	54	55	0.71
Average size of tumor (mm)	30	28	0.08	56	63	0.56
MSTS score	24	22.8	0.98	26.9	27.3	0.63
TESS	90.3	82.6	1	95.4	99.1	0.41
Time of hospital stay	15.8	19.3	0.81	10.3	16.3	0.08
Surgical procedures	1.8	3.6	0.001	1.1	3.1	0.0001
Tumor residue after Tumor bed excision		9 (45%)			6 (66%)	

needed a flap for wound coverage in the deep fUPE subgroup.

Average cost of management of a patient in the fPE group was € 18′101 whereas the management cost of a patient in the fUPE group was € 28′185 (p = 0.048), representing a 64% higher cost for fUPE.

Discussion

In our series, the proportion of UPE in STS patients was 31.8%. This is in line with the literature, with some studies reporting up to 53% of UE [3–5]. In their recent review, Grimer et al. [17] found rates between 18% and 53%, with an average of 33%. Interestingly, like in other studies, it remained stable throughout the analyzed period. Surgeons' raise of awareness to this problematic is the keypoint to decreasing this rate. Nandra et al. created an aide-mémoire, "larger than a golfball and growing", to trigger referral to tertiary tumour units [18]. To our knowledge, they have not yet published data on the efficiency of this prevention strategy.

The first part of our work consisted in comparing the oncological outcome between patients who underwent PE in our center and patients who had prior UPE in a non-specialized center, and were then referred to us for salvage treatment. All our patients were treated surgically: our study did not take into consideration patients with advanced disease and palliative treatments. Epidemiologic data for age, gender, localization, depth and histologic subtypes are comparable with the literature [19–21].

The local recurrence rate for our whole cohort was 7% at time of follow up (mean 92 months), the distant recurrence rate was 26.9%, and the disease-specific survival rate was 17%. In 1996, Pisters et al. in a cohort of 1041 surgically treated musculoskeletal STS patients, had similar results, with 17%, 22% and 24% respectively at 4 years [20]. More recent studies showed a local recurrence rate around 4.1%–10% [22–25]. A major factor affecting outcomes is the inclusion of atypical lipomatous tumors/well differentiated liposarcoma (ALT/WDLPS) in our series, as they were considered as "true" sarcomas until 2012, when the WHO declassified them into tumors of intermediate aggressiveness. On the contrary, NCCN guidelines of 2005 did not separate ALT/WDLPS from other low grade STS [26]. It is difficult to know if ALT/WDLPS were excluded or even considered

in most of the literature on STS, even in more recent publications [10], for it is generally not specified. In total, 29 ALT/WDLPS were included, 6 in the UPE and 23 in the PE groups. In our center, the last neoadjuvant radiotherapy for a ALT/WDLPS was performed in 2013, and the vast majority received complementary therapy (18 neoadjuvant and one adjuvant radiotherapy, one isolated limb perfusion). In the end, one patient presented distant metastases, and from the two ALT/WDLPS of the UPE group who had residue at tumor bed excision, one had a local recurrence. Since 2013, we do not automatically re-excise ALT/WDLPS after R1 primary excision. We generally follow them with local imaging for 2–5 years on case-by-case discussion.

In our study, the majority of patients with UPE had subcutaneous (p < 0.00001) and elbow/forearm STS (p = 0.0007) compared with patients with PE. Alamanda et al. also found an increased rate of unplanned excisions in superficial tumors and in upper extremity [27]. Forearm lumps are more frequently removed by plastic or hand surgeons than in other parts of the body: in our series, there were 9 cases of unplanned excision in the forearm, 7 of them (78%) by plastic surgeons in private practice, one by a general surgeon and one by an orthopaedic surgeon. Sensitization of plastic surgeons during continuing education and training is certainly a key, as they are on the front line for treating lumps in the upper extremities in their daily practice. Generally speaking, orthopaedic and general surgeons seem to be more at risk of performing an unplanned excision of STS, all locations included [28].

We did not find any significant difference in size or histotype, but observed a trend towards more frequent UPE of myxofibrosarcoma in our series, although the most frequent histotype was unclassified pleomorphic sarcoma. There is no evidence in the literature of an association of unplanned excision with a specific histotype: some authors found more frequent UPE of synovial sarcoma [29,30], liposarcomas [10,27,31], unclassified pleomorphic sarcoma [32] or myxofibrosarcoma [10].

Some studies showed that local recurrence rate after UPE was doubled [21]. At time of follow up (mean 92 months), we also found a two times higher local recurrence rate in the UPE group compared with the PE group (12.5% versus 6.2% p = 0.25), although it was not statistically significant, due to the small number of patients. Chandrasekar et al. Potter et al. and Noria et al. also found local recurrence rates after unplanned excision to be significantly higher [33–35].

Our distant recurrence rates were respectively 31.7% (PE) and 23.4% (UPE) (p = 0.25) and the specific mortality rates were 16% (PE) and 19% (UPE) (p = 0.69). In their study, Fiore et al. and Alamanda et al. had comparable long-term oncological outcomes when comparing PE and UPE [3,11]. On the other hand, Derbel et al. showed in a prospective study of 472 localized STS of the musculoskeletal system that treatment in a specialized center reduced disease specific mortality by 66% [13].

In our cohort of 201 patients, as in Fiore et al. and Alamanda et al., we observed a significant difference in tumor size between the two groups: 56 mm ± in the UPE group versus 92 mm in the PE group (p < 0.00001). For this reason, in the second part of the study, we aimed to compare two epidemiologically similar groups. Our cohort, even if small in size, also suggests that oncological outcomes are comparable when considering local or distant recurrence rates, whatever the initial surgery (planned or unplanned).

STS are rare and can emerge in different ways, there are more than fifty different types, they are ubiquitous and their aggressiveness is highly variable. Diagnosis itself can be challenging [36]. This heterogeneity makes it difficult to analyze the functional results after their management [37]. However, the principles of sarcoma management are quite constant, whatever the type and location, i.e. wide excision, with clear margins and limb

preservation whenever possible. Morii et al. showed that unplanned excision had no significant impact on functional results [9]. It is difficult to measure the emotional impact of secondary medical care in a specialized center by a multidisciplinary team after initial so-called whoops surgery by a "non-specialist" surgeon. To our knowledge, there is no specific score to estimate it. In their recent review article on psychological wellbeing of sarcoma patients, Storey et al. found 82 publications [38]. The main studied parameter was quality of life, but it was not possible for the authors to conclude on the psychological impact of sarcoma. The importance of being treated in a specialized center, especially after accidental "inadequate" excision of a STS may have a favorable influence on the patient when fulfilling functional score forms. We agree with Storey et al. that there is certainly a need for the inclusion of relevant psychological measurements in functional analysis of oncological treatment. They might support Morii et al. who concluded that these patients had a better emotional acceptance. Finally, esthetic results and acceptance remain largely unexplored and should be included in future patient reported outcomes.

The most important finding of our study was that patients who underwent UPE need significantly more procedures (with an average of two more surgical interventions) than PE patients, regardless of depth and size of the tumor. This is due to the fact that a tumor bed excision in this situation may involve a large cutaneous excision requiring secondary graft or flap coverage. Our study also showed that length of hospital stay was longer in case of UPE. However, our cohort was too small to reach statistical significance and further studies are needed to confirm this trend. This difference appeared to be more present for superficial tumors, where the skin defect is often more important.

The average cost of hospital care for a patient who had UPE was significantly higher than planned excision (64% more). To our knowledge, this has never been precisely measured before for STS of the extremities. Barrientos-Ruiz et al. showed that referring patients to a sarcoma center after biopsy had higher costs than before the biopsy [39], but their study was not clear about the what kind of biopsy was done in the non-reference center, i.e. if it was excisional biopsy, unplanned resection, surgical biopsy or percutaneous core-needle biopsy.

Recently, a large prospective study by Decanter et al. [40] demonstrated no metastatic free survival and overall survival benefit for systematic re-excision as compared to a "wait and see" approach after R0 and R1UPE. As systematic re-excision leads to more interventions, complex reconstructions and higher cost, as demonstrated by our study, a "wait and see" attitude might be considered in some cases, in particular in superficial low to intermediate tumors or some unfavorable deep-seated tumors. It is worse mentioning that even though the amputation rate did not raise in their series (with 23.3% of truncal sarcomas!), the functional impact of re-excision at the time of local recurrence as compared to immediately after UPE was not analyzed in their study. Neither was the cost of a "wait and see" approach determined. In our series, this strategy would have lead to a significantly higher rate of local recurrence, considering that 31% had tumor residue at re-excision. Hence, it may be premature to change our guidelines, but there is obviously space for considering no re-excision in some cases of UPE: this needs to be determined in a "case-by-case" discussion in a multidisciplinary sarcoma board.

Conclusion

Our study did not demonstrate any significant oncological or functional difference, regardless of the initial surgical management of STS of the musculoskeletal system in a reference center or by a non-specialist surgeon. However, we found a significantly higher number of surgical procedures and longer hospital stay after unplanned excision of STS, resulting in a 64% higher cost as compared to planned excision in a reference center.

The most common location for unplanned excision appears to be in the forearm. Nearly one-third (31.8%) of patients with musculoskeletal STS are referred to a specialized center after unplanned excision and we believe that providing ongoing education of non-specialists is crucial to prevent accidental excision of STS. Every patient with a suspicion of STS should be referred as soon as possible for an adequate management of the disease, as the ESMO guidelines suggests [41], in order to reduce the costs of management and to prevent additional surgeries.

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