Clin Orthop Relat Res (2010) 468:3028–3034
DOI 10.1007/s11999-010-1392-7

SYMPOSIUM: HIGHLIGHTS OF THE ISOLS/MSTS 2009 MEETING

Clinical and Treatment Outcomes of Planned and Unplanned Excisions of Soft Tissue Sarcomas

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Published online: 22 May 2010

Abstract

Background Soft tissue sarcomas are often inappropriately excised without adequate preoperative planning. Inappropriate (unplanned) excisions may adversely affect local recurrence, distant metastasis, patient survival, and / or postoperative function once properly evaluated.

Questions/purposes We asked whether the clinical and treatment characteristics, survival (overall, local recurrence-free, distant metastasis-free), and functional scores of patients with unplanned excisions differ from those with a planned excision.

Methods We retrospectively reviewed 128 patients with planned excisions and 63 patients with unplanned excisions at prereferral hospitals followed by additional reexcisions. We determined whether age, gender, tumor size, depth, histologic grade, operative duration, blood loss, survival, or functional scores differed between the two groups. The minimum followup was 6 months (mean, 55 months; range, 6–275 months).

Results The tumor was larger and its location deeper in the planned excision group. Overall, metastasis-free, and local recurrence-free survival were similar in the two groups: 86%, 71%, and 85% in the planned excision group and 96%, 86%, and 92% in the unplanned excision group, respectively. However, additional soft tissue reconstruction was more often necessary for patients with unplanned excisions. No difference in postoperative function was observed.

Conclusions The data suggest an adequate additional wide excision may improve the local control and survival in patients with an unplanned excision as well as the patients with a planned excision. While patients with unplanned excisions had superficial and smaller tumors, survival and postoperative function were similar to those with planned excisions.

Level of Evidence Level III, prognostic study. See the Guidelines for Authors for a complete description of evidence.

Introduction

It is not uncommon for a surgeon to operate on a presumed benign soft tissue mass without appropriate preoperative imaging or prior biopsy and then to excise the lesion without attention to the surgical margins. Such surgery has been termed an "unplanned excision" [6]. These lesions can appear deceptively straightforward to treat, perhaps owing to the rarity of soft tissue sarcomas, lack of knowledge of their implications, and frequently straightforward surgical approaches to soft tissue masses.

Several previous studies emphasize the problems of an unplanned excision showing the higher incidence of local recurrence even after additional surgery [12] or residual tumor in reexcision specimens [2, 3, 11, 17]. Several studies have evaluated the disease-specific survival, metastasis-free survival, and local recurrence-free survival of the patients with unplanned excisions for musculoskeletal tumors in comparison to the patients with planned

One of the authors (YN) has received funding from the Ministry of Education, Culture, Sports, Science and Technology of Japan (Grant-in-Aid 20591751 for Scientific Research [C]).
Each author certifies that his institution has approved the human protocol for this investigation, that all investigations were conducted in conformity with ethical principles of research, and that informed consent was obtained.

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excisions [8, 12, 16]. One of these studies suggested patients with unplanned excision followed by additional wide resection had as good or better disease-specific and metastasis-free survival compared with those with planned excision [8]. Another study of foot and ankle sarcomas concluded unplanned excisions did not affect survival [16] and resulted in similar function in patients with unplanned excisions comparing the patients with planned excisions [16]. Thus, there is controversy as to whether unplanned excisions cause higher recurrence and survival rates.

To address the controversy, we compared patients with planned and unplanned excisions of soft tissue tumors to determine any differences in (1) the treatment characteristics; (2) the survival (overall survival, metastasis free-survival, and local recurrence-free survival); and (3) the functional scores.

Patients and Methods

We retrospectively reviewed 191 patients with soft tissue sarcomas who underwent either planned or unplanned excisions followed by additional reexcisions between 1985 and 2008. During that time, 710 patients were recorded as having soft tissue sarcomas in our files. We excluded patients with distant metastases at the initial presentation (n = 88), unresectable tumors (n = 33), recurrent tumors (n = 65), or those with insufficient data (n = 333). Most of the 333 cases with missing data were diagnosed before 1995, and included 220 cases with paper-based medical records that had been discarded. Other cases with missing data included those without information of the status of the tumor or patient, without a report and/or specimens of pathology, and without information on the treatment at the prereferral hospital. This left 191 patients for review: 128 with planned excisions and 63 with unplanned excisions. The size of the tumor was determined with preoperative imaging study; the maximum diameter of all obtained sections was defined as its size. In patients with unplanned excision, it was determined with images in the prereferral hospital before the unplanned surgery. The histologic diagnoses in the planned excision group were liposarcoma (38 cases), malignant fibrous histiocytoma (22 cases), malignant peripheral nerve sheath tumor (13 cases), synovial sarcoma (eight cases), dermatofibrosarcoma protuberans (seven cases), rhabdomyosarcoma (seven cases), leiomyosarcoma (seven cases), and others (26 cases). The unplanned excision group consisted of patients with malignant fibrous histiocytoma (16 cases), liposarcoma (10 cases), dermatofibrosarcoma protuberans (nine cases), malignant peripheral nerve sheath tumor (7 cases), synovial sarcoma (five cases), leiomyosarcoma (four cases), and others (12 cases). The minimum followup was 6 months (mean, 55 months; range, 6–275 months). No patients were lost to followup in these cohorts.

The Mann-Whitney U and chi square tests showed no differences in age at surgery, gender, followup, or histologic grade between the two groups. The original tumor size in the unplanned excision group was smaller than that in the planned excision group and the tumors in the planned excision group were more often ($p < 0.001$) located in the deep layer than those in the unplanned excision group (Table 1).

In the planned excision group, surgery was performed in all patients with a wide surgical margin to the tumor and the biopsy route obtained whenever possible. A wide surgical margin was defined when a resection margin was designated outside of a reactive zone, commonly with a margin more than 3 cm, by imaging and also confirmed microscopically to be negative. In patients in the unplanned excision group, additional wide resection was performed with a 3-cm margin including the surgical scar. The muscle surrounding the scar was resected widely with a margin more than 3 cm. Any residual tumor, hemorrhage, or edema remaining from the primary procedure was evaluated before additional surgery with CT and MRI with enhancement in preparation for the wide resection.

All patients were followed every 3 months by physical examination to examine the local recurrence, the assessment of MRI of the primary site every 6 months, and CT of the chest after surgical treatment every 3 months until 2 years after surgery and every 6 months thereafter. We determined function using the International Society of Limb Salvage (ISOLS) scoring system [1, 14], which is a modification of the initial Musculoskeletal Tumor Society

Table 1. Patient demographics

Variables	PE	UE	p value
Number of cases	128	63	
Gender			
Male	70 (55%)	32 (51%)	0.612
Female	58 (45%)	31 (49%)	
Age (years, mean)	50.5	51.0	0.840
Followup (months, mean)	53.4	57.9	0.312
Depth*			
Superficial	37 (30%)	52 (87%)	< 0.001
Deep	87 (70%)	8 (13%)	
Unknown	4	3	
Size* (cm)	9.0	4.6	< 0.001
Histologic grade			
Low	49 (38%)	30 (48%)	0.218
High	79 (62%)	33 (52%)	

* Significant difference between cohorts; PE = planned excision; UE = unplanned excision.

(MSTS) score [5] and also determined a Toronto Extremity Salvage Score (TESS) [4] in a subset of the 191 patients. Among the last 100 patients surviving more than 1 year, 10 had an unknown address; for the remaining 90, we sent the MSTS and TESS questionnaires to 55 patients in the planned excision group and 35 patients in the unplanned excision group by mail. Seventy patients returned fully completed questionnaires.

We determined differences in nonnormally distributed data (operative duration, intraoperative blood loss, ISOLS score, and TESS score) between the planned excision group and the unplanned excision group using the Mann-Whitney U test. We determined differences in proportion of occurrences (rate of free skin graft or flap coverage, limb salvage, radiotherapy, chemotherapy, and complications) between the two groups using the chi square test. Survival times were determined from the date of the first visit to the date of death or last followup before study closure, and metastasis-free or local recurrence-free time was counted from the date of operation to the date of the first metastasis or the first local recurrence. We analyzed overall, metastasis-free, and local recurrence-free survival rates using the Kaplan-Meier method and determined difference in survivorship between the two groups using the log rank test. We performed multivariate analysis for factors affecting overall, metastasis-free, and local recurrence-free survival rates using stepwise Cox proportional hazards regression analysis. Statistical analysis was performed using SPSS Version 16.0 (SPSS Inc, Chicago, IL).

Results

We observed no adverse effects of unplanned excision on the treatment characteristics except for the soft tissue reconstruction. Soft tissue reconstruction with a free skin graft or flap coverage was performed more often ($p = 0.002$) in the unplanned excision group (71% versus 47%, respectively). The surgical duration was similar in the two groups (planned excisions, 343 minutes; unplanned excisions, 298 minutes) (Table 2). The intraoperative blood loss was smaller in the unplanned excision group than those in the planned (planned excisions, 328 mL; unplanned excisions, 161 mL). The incidence of postoperative complications was similar in the two groups (planned excisions, 22% versus unplanned excisions, 14%, $p = 0.189$) and the proportion of limb salvage (planned excisions 94% versus 98%, $p = 0.349$) (Table 2).

There were no differences between the two groups in overall, metastasis-free, or local recurrence-free survival. Both groups demonstrated survival ranging from 86% to 96% for overall survival, from 71% to 86% for metastasis-free survival, and from 85% to 92% for local recurrence-free survival. High-grade tumor reduced ($p = 0.026$) overall survival. Larger tumor size ($p = 0.032$) and high-grade tumor ($p < 0.001$) reduced metastasis-free survival (Table 3).

We observed no differences in function at last followup (Table 4). Given that there were differences in clinical factors, particularly tumor size and depth, between patients with planned and unplanned excisions, patients were subdivided into those with superficial and deep tumors and analyzed individually. Although tumor size was larger in planned surgery, survivals (overall, metastasis-free, local recurrence-free survivals) were similar in the two groups. The same results were obtained by the analysis for deep tumors (Table 5). We observed no differences in function with superficial tumors or deep tumors individually, and no difference in function between patients with planned surgery and those with unplanned surgery (superficial: ISOLS

Table 2. Treatment features

Variables	PE	UE	p value
Operative duration (minutes, mean)	343	298	0.107
Intraoperative blood loss† (mL, mean)	328	161	0.009
FSG or flap coverage†	47%	71%	0.002
Number of cases/total cases (unknown cases)	60/127 (1)	45/63 (0)	
Limb salvage*	94%	98%	0.349
Number of cases/total cases (unknown cases)	100/106 (0)	42/43 (0)	
Combined with radiotherapy	19%	13%	0.313
Number of cases/total cases (unknown cases)	24/126 (1)	8/61 (2)	
Combined with chemotherapy†	38%	18%	0.007
Number of cases/total cases (unknown cases)	48/128 (0)	11/61 (2)	
Postoperative complications	22%	14%	0.189
Number of cases/total cases (unknown cases)	28/125 (3)	8/57 (6)	

* Intended for patients with soft tissue sarcomas in the extremities; †significant difference between cohorts; PE = planned excision; UE = unplanned excision; FSG = free skin graft.

Table 3. Univariate and multivariate analysis of overall, metastasis-free, and local recurrence-free survival rates

Variables		Univariate						Multivariate			
		OS		MFS		LRFS		Variables	OS	MFS	LRFS
		Number		Number		Number			p value		
Group	Planned excision	127	86%	123	71%	126	85%	History of UE	0.384	0.870	0.459
	Unplanned excision	62	96%	61	86%	62	92%				
Size	= or < 5 cm	83	98%	83	85%	83	94%	Size	0.088	0.032*	0.127
	> 5 cm	94	82%	90	66%	93	82%				
Depth	Superficial	89	94%	88	85%	89	88%	Depth	0.591	0.112	0.862
	Deep	94	85%	90	66%	93	86%				
Grade	Low	79	96%	79	95%	79	95%	Grade	0.026*	< 0.001*	0.082
	High	111	81%	106	69%	110	84%				

* Statistically significant; OS = 5-year overall survival; MFS = 5-year metastasis-free survival; LRFS = 5-year local recurrence-free survival.

Table 4. Functional outcome

Scoring system	PE	UE	p value
ISOLS	80%	85%	0.252
TESS	85%	89%	0.392

PE = planned excision; UE = unplanned excision; ISOLS = International Society of Limb Salvage; TESS = Toronto Extremity Salvage Score.

p = 0.202, TESS p = 0.516; deep: ISOLS p = 0.758, TESS p = 0.693).

Discussion

Unplanned excisions of soft tissue sarcomas are frequently performed, but their influence on local recurrence, distant metastasis, and patient survival remains controversial [8, 12, 13]. Moreover, their impact on function has seldom been investigated [16]. The aims of this study were to investigate the treatment characteristics, the survivals (overall, metastasis-free, and local recurrence-free survivals), and the function of patients with unplanned excisions followed by additional reexcisions in comparison with those with planned excisions.

We recognized limitations to our study. First was the lack of standardization in regard to the adjuvant treatment. A small proportion of patients were treated with radiotherapy or chemotherapy, because these adjuvant therapies were administered selectively to the patients with tumors that were adjacent to critical organs or with inadequate surgical margins; thus, their effects on the local recurrence, distant metastasis, or patient survival could not be assessed. Second, although similar surgical procedures were performed on the patients studied, the number of patients was relatively small. To address the small number of patients in this study, we have compared the results in this study with previous studies describing unplanned excisions (Table 6). Third, a large number of cases were excluded as a result of the lack of a detailed medical record, information on

Table 5. Subgroup analysis divided into patients with superficial and deep tumors

Depth	Superficial			Deep		
Number of cases	89			95		
Group (number of cases)	PE (37)	UE (52)	p value	PE (87)	UE (8)	p value
Tumor size (cm, mean)	7.5	4.7	0.004	9.6	4.2	0.001
Operative duration (minutes, mean)	334	274	0.124	345	432	0.545
Intraoperative blood loss (mL, mean)	238	148	0.629	366	233	0.480
FSG or flap coverage (cases/total)	86% (32/37)	75% (39/52)	0.184	32% (27/85)	50% (4/8)	0.296
OS	92%	95%	0.627	83%	100%	0.287
MFS	86%	83%	0.789	64%	67%	0.324
LRFS	82%	91%	0.750	84%	100%	0.334

PE = planned excision; UE = unplanned excision group; FSG = free skin graft; OS = overall survival at 5 years; MFS = metastasis-free survival at 5 years; LRFS = local recurrence-free survival at 5 years.

Table 6. Previous studies describing patients with UE compared with those with PE

Author	Numbers		OS/DSS		MFS		LRFS		Variables significant different between two groups
	PE	UE	PE	UE	PE	UE	PE	UE	
Chui et al. [3]	19	60	74%*	98%*	57%* (event-free)	98%* (event-free)	NA	NA	Site, size
Potter et al. [12]	139	64	60%	74%	NA	NA	90%*	64%*	Size, depth, microscopic margins, flap or FSG coverage, chemotherapy, followup periods
Temple et al. [15]	17	18	NA	NA	NA	NA	NA	NA	Delay in receiving treatment, free flaps, perioperative complications
Lewis et al. [8]	685	407	70%*	88%*	63%*	83%*	NA	NA	Size, depth microscopic margins
Thacker et al. [16]	23	29	80%	73%	NA	NA	91%	79%	Free flap, radiotherapy
Arai et al. [current study]	128	63	86%	96%	71%	86%	85%	92%	Size, depth, flap or FSG coverage, chemotherapy, intraoperative blood loss

* Significant difference between cohorts; OS = 5-year overall survival; DSS = 5-year disease-specific survival; MFS = 5-year metastasis-free survival; LRFS = 5-year local recurrence-free survival; PE = planned excision; UE = unplanned excision; NA = not available, no accurate data described in the articles; FSG = free skin graft.

pathology, tumor status, and treatment at the prereferral hospital, which might influence the results of this study. However, given that cases with missing data were mostly those before 1995, we presume the inclusion of more recent patients would reduce variability in treatment. Fourth, there were difference between the groups in mean tumor size and tumor depth differed. We addressed these potential biases by subdividing patients into those with superficial tumors and deep tumors and analyzing individually. Finally, the patients were heterogeneous regarding histologic subtype. Only a study of a larger number of patients would be able to clarify the effects of histologic subtypes.

Soft tissue reconstruction was more often required in the unplanned excision group, suggesting an unplanned excision in a prereferral hospital may cause wider contamination of malignant cells, which requires wider reexcision to obtain a negative surgical margin. Considering superficial tumors may require more skin reconstruction than deep tumors, tumors were subdivided into superficial and deep tumors and analyzed individually. In superficial tumors, although tumor size was substantially smaller in the unplanned excision group, the necessity of soft tissue reconstruction was similar to the planned excision group (Table 5). A previous study reported more frequent need for soft tissue reconstruction in patients with an unplanned excision [12]. Although the study focused on only tumors of high-grade malignancy, more patients with prior unplanned excision required flap coverage and/or skin grafting in association with the additional surgery (unplanned excision group, 30%; planned excision group, 5%). In comparison to the results, the incidence of soft tissue reconstruction in the present study was much higher in the unplanned excisions group (present study: 71%; Potter et al.: 30%), whereas the incidence of local recurrence was much lower (present study: 7.8%; Potter et al.: 34%). There is a possibility that the large skin and/or soft tissue resection required to obtain a negative margin may reduce the incidence of local recurrence. The limb salvage rate is acceptable in both the planned excision (94%) and unplanned excision (98%) groups in this study. Another study reported patients with foot and ankle soft tissue sarcomas who undergo an unplanned excision receive flap or skin graft procedures more frequently and required limb amputation more frequently (nine of 18 cases) [15]. These observations suggest an unplanned excision, in particular in an anatomic location such as the foot or ankle, may thus require extensive procedures.

Our data show no adverse impact of an unplanned excision on local recurrence, distant metastasis, or patient survival. A possible explanation may be that the mean size of the primary tumors in the unplanned excision group was smaller, and the depth of the tumors was more likely to be superficial. A pediatric study reported patients with planned excisions had larger tumors than those who underwent unplanned excisions, and that resulted in poor survival in comparison to patients with an unplanned excision [3], which is inconsistent with the current observations. The largest study [8] demonstrated improved survival of patients with "two operations (unplanned excision followed by reexcision)" in comparison with that with "one operation (planned excision)" in extremity soft tissue sarcoma. In that study there were, however, differences in tumor size and depth between the groups and also potential referral and selection bias; these factors might have affected the disease-specific and metastasis-free survival. On the other hand, another study demonstrated an

adverse effect of prereferral excision on the survival of patients with superficial tumors of more than 4 cm [13]. The approach of our institution is to excise the soft tissue sarcoma very widely (commonly greater than 3-cm margin), which may obscure the difference in local recurrence-free survival between two groups. If we had performed more conventional narrow margins for patients with unplanned excision, there might be a difference in local recurrence-free survival between patients with planned excision and those with unplanned excision. There has been only one study addressing the local recurrence-free and distant metastasis-free survival of patients receiving postoperative radiotherapy after an unplanned excision without any additional surgery [7]. The rate of local control, occurrence of distant metastasis, and incidence of complications were comparable to those in the current study. However, as a result of the severity of posttherapeutic complications of irradiation, they described postoperative radiotherapy without surgical treatment should be applied to the patients with a low performance status, difficulties obtaining wide surgical margins in additional reexcision, or a severe functional impairment predicted after reexcision. On another front, local recurrence-free survival might be affected by the adjuvant radiotherapy with planned or unplanned excision. In our institution, only 19% and 13% of patients with planned and unplanned excisions received radiotherapy, respectively. We applied radiotherapy for patients with positive or marginal surgical margin of a resected specimen. This low rate of patients with radiotherapy in our institution was different from the conventional studies in Western countries. A previous study from the United States described that 58% of patients with planned and 64% with unplanned excisions had radiotherapy [12]. Considering the acceptable local control in this study, excisions with wider surgical margins in our institution may compensate for the low rate of radiotherapy. Taking all of these findings into account, the effects of an unplanned excision on local recurrence, distant metastasis, or patient survival could hardly be determined as a result of the limited data.

Related studies have not reported function of patients who underwent an unplanned excision except for one study [16] that reported only patients with foot and ankle tumors. The authors found no differences in function between patients with planned and unplanned surgery. We also observed no difference in the postoperative function between the two groups in this study. The postoperative function seems to be affected by the loss of working soft tissue (namely, the muscles) or bones at surgery. We found tumors were smaller and located more frequently in the superficial layer in the unplanned excision group. Consequently, this may lead to a lower resection volume of the muscles and it may also contribute to better function. A better postoperative function could be obtained in patients with an unplanned excision if they were primarily treated with a planned excision, because they tend to have smaller and more superficial tumors.

We observed no adverse effect of an unplanned excision on local control, distant metastasis, patient's survival, and function. However, additional reexcision for patients with an unplanned excision seems to be justified by demonstrating the similar rates of local control, distant metastasis control, patient survival, and postoperative function of patients with a planned excision. The past reports also advocate the effectiveness of an additional reexcision [2, 8–10, 17] (Table 6). However, an unplanned excision should be avoided as a result of the additional requirement for soft tissue reconstruction. An adequate additional wide excision in patients with an unplanned excision may improve local control and survival as well as in the patients with a planned excision.

Acknowledgments We thank Ms Eri Ishihara for her valuable secretarial assistance.

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