

The Gulf Journal of Oncology



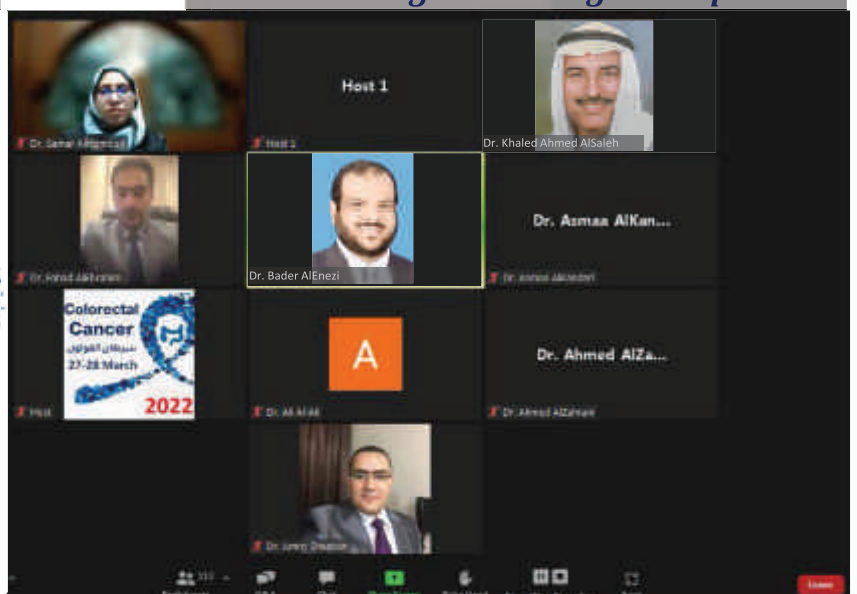
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Effects of Revision Surgery and Surgical Margins on Outcome of Peripheral Soft Tissue Sarcomas: Experience from a Tertiary Cancer Care Centre

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Abstract

Introduction: The purpose of this study is to assess the impact of revision surgery, after unplanned excision, on oncological outcome and surgical morbidity in soft tissue sarcomas and also to assess the relation between margin status and oncological outcome.

Materials and Methods: We undertook a retrospective analysis of prospectively maintained database of 153 patients with peripheral soft tissue sarcomas treated in our institute from 2006–2010.

Results: Postoperatively, 111(72.5%) patients had negative margins, 20(13.1%) had close margins and 22(14.4%) had planned positive margins. Local recurrence rate was 19.8% in patients with negative margins and

28.6% for patients with close or positive margins ($p=0.007$). There was no statistically significant difference in rates of distant metastases (18.9% vs 21.4%, p value 0.56) and five-year overall survival (82.5% Vs 79.8%, p value 0.41) between margin negative and close/positive groups. The five-year overall survival rates were 80.4 vs 77.8% ($p=0.42$) and five-year disease-free survival rates were 72.4% vs 70.2% ($p=0.3$), in the revision surgery group and primary surgery group respectively.

Conclusion: Margin status after excision of soft tissue sarcoma is not a direct predictor for overall survival or distant metastasis. Revision surgery after an unplanned excision does not carry worse survival compared to primary surgery group.

Keywords: sarcoma, reoperation, margins of excision, recurrence

Introduction

Soft tissue sarcomas, arising from mesenchymal tissues, are a diverse group of tumours that contribute to less than 1% of all new cancers^[1]. Extremities are the most common sites of origin^[2,3]. The conventional belief was that the unplanned initial excision of soft tissue sarcoma by an inexperienced surgeon may increase the local recurrence and thus adversely affect survival. So revision excision is a common practice after an unplanned excision for soft tissue sarcoma. But whether revision excisions will have the same oncological outcome as primary surgery is a matter of debate.

Aim of the study

We assessed whether revision surgery after an unplanned excision affected the oncological outcome, compared to the primary surgery. We also looked into the

effect of various factors including margin status on the outcome of surgical treatment.

Materials and Methods

This is a retrospective analysis of patients who have undergone curative surgery for soft tissue sarcoma in our institute during the period, May 2006 to April 2010. All patients with trunk, extremity and head and neck soft tissue sarcomas between 18 and 80 years were included.

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Patients who had systemic metastasis at presentation were excluded from the study.

The study was conducted after getting necessary approval from the institutional review board. Information related to each patient was retrieved from medical records using a structured proforma. Information regarding status on the last follow up was collected till August, 2019. Margin was defined as negative if it was > 1 cm, close if < 1 cm and positive if it was involved by the tumour.

Statistical analysis

Patient, disease and treatment related factors were analyzed. Comparison of categorical variables between groups (such as those with varying margin status) was done using the Chi-square test or Fisher's exact test. Z test was used to test the proportions. Kaplan-Meier method was used to calculate disease free survival (DFS) and overall survival (OS). Log-rank test was used for univariate analysis to assess the clinico-pathologic factors affecting survival. Statistical analysis was done using SPSS-20 software.

Results

One hundred and sixty-two patients were treated in our institution during the above period. Seven patients with systemic metastases and two patients with poor performance status did not undergo surgery. Among the remaining 153 patients, 103 patients underwent revision surgery after an unplanned excision and 50 patients underwent primary surgery. The demographic and treatment data are given in Table 1. Among 103 patients operated elsewhere, 96 patients (93.2%) were claimed to have definitive surgery and seven patients (6.8%) were referred after excision biopsy of the tumour. When we evaluated the operative, radiology and pathology reports, we found out that there were disparities between the procedure claimed by the referring surgeon from non-oncology departments, and the actual procedure done. Among 96 patients (93.2%) who were referred after a definitive surgery (as per the referral letter), our evaluation revealed that only five (4.8%) had undergone proper wide excision; However, all of them had at least one positive/close margin. After revision surgery, among these 96 patients (who were referred after complete excision by non-specialists) residual disease was present in 91 patients (94.8%). Also, seven patients (4.6%) underwent regional lymphadenectomy. A total of 21 patients (13.7%) required reconstructive procedures like skin graft, flap reconstruction and vascular reconstruction.

The most common histology after definitive surgery at our institute was spindle cell sarcoma (106 ,69.2%)

Characteristics		Number (%) n =153	
Mean age		48 years (19 years –78 years)	
Sex	Male	88 (57.5%)	
	Female	65 (42.5%)	
Surgery	Primary surgery	50 (32.7%)	
	Revision surgery	103(67.3%)	
Stage (AJCC 6th edition)	T stage	T1a	43(28.6%)
		T1b	15(9.8%)
		T2a	65(42.5%)
		T2b	30(19.6%)
	N stage	N0	146 (95.4%)
		N1	7(4.6%)
Grade (FNCLCC grading system)	1	18 (11.7%)	
	2	61(39.9%)	
	3	74(48.4%)	
Site	Upper limb	42 (27.5%)	
	Lower limb	71 (46.4%)	
	Trunk	36 (23.5%)	
	Head & neck	4 (2.6%)	
Depth of tumour in relation to deep fascia	Superficial	108 (70.6%)	
	Deep	45 (29.4%)	
Fixity to surrounding tissues	No	124 (81%)	
	Yes	29(19%)	
Procedure	Wide Excision	123 (80.4%)	
	Amputation	30(19.6%)	
Adjuvant Radiotherapy planned	Total 82 (53.6%)		
	Completed	71 (86.6%)	
	Refused	9(11%)	
	Incomplete	2 (2.4%)	
Adjuvant Chemotherapy planned	Total 74 (48.4%)		
	Completed	59 (79.7%)	
	Refused	9 (12.1%)	
	Incomplete	6 (8.1%)	
Margin status	Negative	111(72.5%)	
	Close	20 (13.1%)	
	Positive	22(14.4%)	
Recurrence	Local recurrence	30(19.6%)	
	Distant metastasis	26(16.9%)	
	Both	4(2.6%)	

Table 1: Baseline characteristics, treatment and results of all patients

followed by liposarcoma (15, 9.9%) and leiomyosarcoma (7, 4.3%). Patients with either margin positive excision or high grade tumour were offered adjuvant external beam radiotherapy (EBRT) with 50 Gy in 25 fractions followed by a boost of 16 Gy in 8 fractions for tumour bed. Similarly, adjuvant chemotherapy (Adriamycin 60 mg /m² & Ifosfamide 1.3g /m² for 6 cycles) was offered to all patients with grade 3 tumors . Numbers of patients who received adjuvant are given in Table 1. A total of 37 patients (24.2%) developed postoperative complications, of which seroma formation (9 patients, 5.9%) was the most common followed by wound infections and joint contracture (8 patients each, 5.2%). Base line characters and Clavien–Dindo Grade 3 complications are given in Table 2 and 3. The surgical complications were more common in the revision surgery group than in the primary surgery group.

Out of the 153 patients, 10 patients were lost to follow up. The median follow up time was 44 months. The overall survival (OS) and disease–free survival (DFS) at five years were 79.6% and 70.9% respectively. The median DFS was 22 months. Rates of local recurrence were less in the margin negative group (19.8%, 22 patients) compared to

the close margin or positive margin groups (28.6%, 12 patients) (p value 0.007) (Table 4). When we analyzed the effect of margin positivity on five–year overall survival, there was no significant difference (82.5% Vs. 79.8%, p value 0.41) between margin negative vs close/positive groups. We did univariate analysis to assess the various clinicopathological factors affecting OS and DFS, but we couldn't find a factor affecting survival except for age; a better 5–year OS for patients less than 40 years of age (Table 5). There was no statistically significant difference in 5–year OS (80.4% vs 77.8%, p=0.42) and 5–year DFS (72.4% vs 70.2%, p=0.3) between the revision surgery group and primary surgery group (Diagram 1,2). 5 year OS was statistically better in primary surgery vs revision surgery in a subgroup of patients with high grade /T2 tumours (Diagram 3).

Discussion

This is a retrospective analysis of 153 patients with soft tissue sarcoma, who underwent treatment in a tertiary cancer care center. Surgery was the mainstay of treatment. With adequate surgery and multimodality

Characteristics		Primary Surgery (n= 50)	Revision surgery (n=103)	Total	P–value
Age	<40 yrs	12 (24%)	32(31.1%)	44	0.32
	>40 yrs	38(76%)	71(68.9%)	109	
Sex	Male	27(54%)	61(59.2%)	88	0.41
	Female	23(46%)	42(40.8%)	65	
Depth of tumour in relation to deep fascia	Deep	39 (78%)	6 (5.8%)	45	< 0.05
	Superficial	11 (22%)	97 (94.2%)	108	
Fixity to surrounding tissues	No	34 (68%)	90 (87.4%)	124	< 0.05
	Yes	16 (32%)	13 (12.6%)	29	
Grade	1	2 (4%)	16 (15.6%)	18	< 0.05
	2	17 (34%)	44 (42.7%)	61	
	3	31 (62%)	43 (41.7%)	74	
T Stage	T1	9 (18%)	49 (47.6%)	58	< 0.05
	T2	41 (82%)	54 (52.4%)	95	
N Stage	N0	45 (90%)	101 (98.1%)	146	< 0.05
	N1	5 (10%)	2(1.9%)	7	
Margin status	Negative	36(72%)	75(72.8%)	111	0.91
	Close or Positive	14(28%)	28(27.2%)	42	
Adj RT completed	Yes	19(38%)	52(50.5%)	71	0.14
	No	31(62%)	51(49.5%)	82	
Adj Chemo completed	Yes	22(44%)	37(35.9%)	59	0.33
	No	28(56%)	66(64.1%)	94	

Table 2: Baseline characteristics of primary surgery and revision surgery groups

Clavien–Dindo Grade	Primary surgery (n=50)					Revision surgery (n=103)					Grand total (n =153)
	1	2	3	4	Total	1	2	3	4	Total	
All	9 (18%)	3 (6%)	3 (6%)	0	15 (30%)	6 (5.7%)	0	16 (15.%)		22 (21.4)	37 (24.2%)
Hematoma	2 (4%)	0	1 (2%)	0	3 (6%)	0	0	4 (3.8)	0	4 (3.8%)	7 (4.6%)
Seroma	4 (8%)	0	0	0	4 (8%)	1 (0.9%)	0	4 (3.8)	0	5 (4.8%)	9 (5.9%)
Wound infection	0	3 (6%)	1 (2%)	0	4 (8%)	0	0	4 (3.8)	0	4 (3.8%)	8 (5.2%)
Flap loss	0	0	1 (2%)	0	1 (2%)	0	0	3 (2.9)	0	3 (2.9%)	4 (2.6%)
Vascular injury	0	0	0	0	0	0	0	1 (0.9%)	0	1 (0.9%)	1 (0.6%)
Joint contracture	3 (6%)	0	0	0	3 (6%)	5 (4.8%)	0	0	0	5 (4.8%)	8 (5.2%)

Table 3: Comparison of postoperative complications between primary surgery and revision surgery

	Margin status		p value
	Positive or close (n=42)	Negative (n= 111)	
Local Recurrence	12 (28.6%)	22 (19.8%)	0.007
Distant Metastasis	9 (21.4%)	21 (18.9%)	0.56

Table 4: Impact of margin status on oncological outcome

treatment, we could achieve an OS of 79.6% at five years with a local recurrence rate of 19.6%. Local recurrence rate in the various retrospective series is between 16 to 20%^[4,5].

A total of 22 patients (14.4%) had margin positive resection. Our study showed a decreased rate of local recurrence in the margin negative group (19.8%, 22 patients) when compared to those with either a close margin or a planned positive margin (28.6%, 12 patients).

Factors		5 year OS	p value	5 year DFS	p value
Age	<40 vs>40	92.9% vs 74.3%	0.004	80.4% vs 67.0%	0.15
Sex	Male vs Female	79.3% vs 80.0%	0.93	68.8% vs 73.9%	0.40
T stage	T1 vs T2	78.0% vs 77.8%	0.53	70.9% vs 69.4%	0.93
Grade	Low vs High	84.0% vs 74.2%	0.27	71.3% vs 70.6%	0.62
Post op complications	Yes vs No	75.0% Vs 79.9%	0.78	70.6% vs 75.0 %	0.76
Presence of residual disease	Yes vs No	79.9% Vs 80.0%	0.73	71.0% Vs 80%	0.53
Margins status	Negative vs Close/ Positive	82.5% Vs 79.8%	0.41	79.3% vs 67.2%	0.22
Unplanned excision	Yes vs No	80.4% vs 77.8%	0.42	72.4% vs 70.2%	0.30
Adjuvant RT	Yes vs No	80.3% Vs 79.0%	0.55	74.7% vs 67.7%	0.22
Adjuvant chemo	Yes vs No	82.4% vs 78.8%	0.98	72.2% vs 66.5%	0.32

Table 5: Univariate analysis of factors affecting Five year OS & DFS

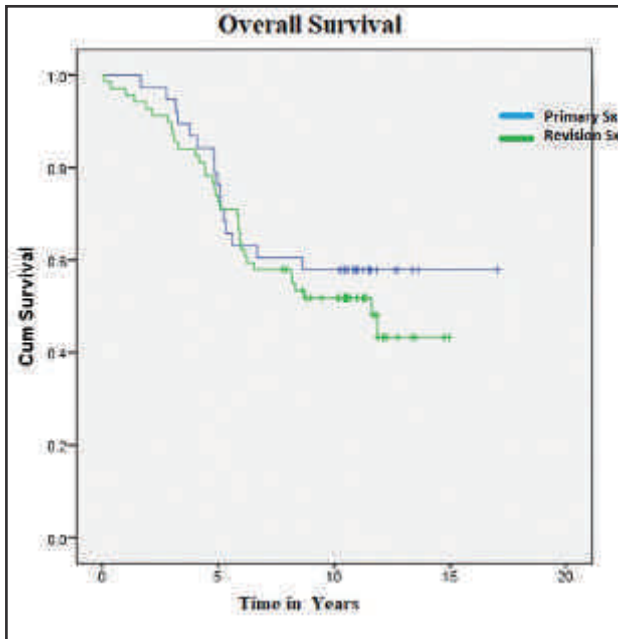


Diagram 1: 5 year overall survival in primary surgery vs Revision surgery

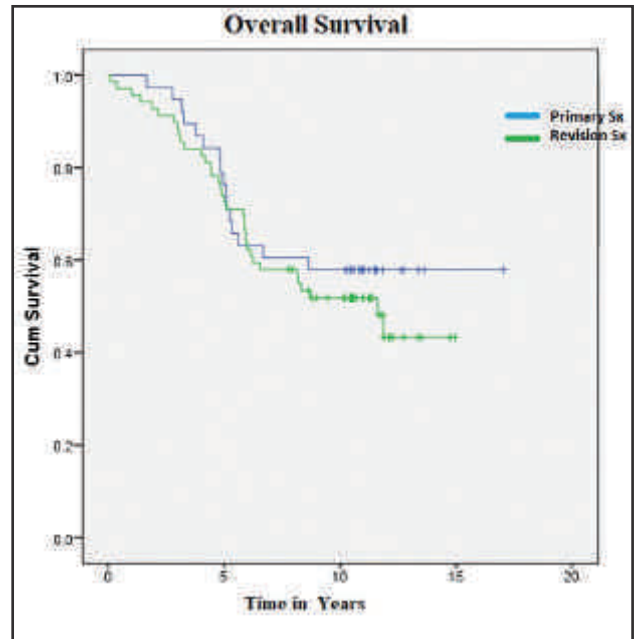


Diagram 3: Five year overall survival (primary surgery vs revision surgery) in a subgroup of patients with high grade / T2 tumours

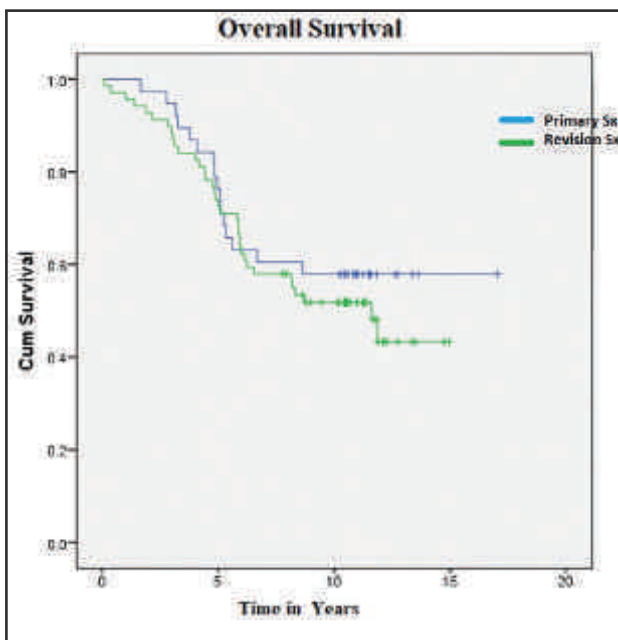


Diagram 2: Five-year disease-free survival in primary surgery vs revision surgery

Many studies also showed an increase in the rate of local recurrences after a margin positive resection in soft tissue sarcoma [6,7].

This study did not show any statistically significant difference in the rate of distant metastasis between the margin positive and the margin negative group. The result was similar to Scandinavian sarcoma group study, which could not demonstrate a significant difference in distant metastasis rate between the margin positive and the margin negative group [4].

The role of margin status on survival is controversial with various studies showing different results. In this study, there was no statistically significant difference in survival between the margin positive and the negative group (82.5% vs 79.8%, p value 0.41). Multiple studies showed that the margin positivity decreased the disease specific survival [6,7]. But another study published in 1994, showed that neither positive margin nor local recurrence affects survival [8]. The broad message from literature is that a more conservative approach, in terms of margin, holds good in case of extremity sarcoma [9]. Similarly, from our study, we can draw a conclusion that the margin positivity increased the risk of local recurrence, but it is not a risk factor for distant metastasis or overall survival.

Among 153 patients, 103 patients were referred to our hospital for adjuvant treatment after an unplanned excision elsewhere. But there was a disparity between the procedure claimed by the referring surgeon and the actual procedure done. This highlights the need for referring all patients suspected to have soft tissue sarcoma to a surgical oncologist at a dedicated cancer center before surgery and better training of general surgeons in the principles of sarcoma surgery, in case they wish to manage it.

Our analysis showed that there is no significant improvement in OS and DFS for patients who underwent revision surgery after an unplanned excision. Another important issue related to revision surgery was presence of increase in postoperative complications. Although

various studies have shown that unplanned excision is not associated with any negative outcome if re-wide excision is carried out, with revision surgery patients have to undergo two surgeries with increased risk of morbidity.

Limitations

Ours is a resource limited setting, with scarce availability of immunohistochemistry or cytogenetics, especially during the time period studied. Moreover, sample size is small in the present study. Another limitation is the retrospective nature of this study.

Conclusion

Positive Margin after excision of soft tissue sarcoma increases the local recurrence rate but margin status is not a direct predictor for overall survival or distant metastasis. Revision surgery after an unplanned excision does not carry worse survival compared to primary surgery group. However, with revision surgery after an unplanned excision, surgical morbidity and post-operative complications are more. Soft tissue sarcoma has to be managed by a surgical oncologist in a lead role at a dedicated cancer unit to avoid issues related to unplanned excision and revision surgery. There is a need for better training of general surgeons in the principles of sarcoma surgery, if they wish to manage it.

Funding and Conflict of Interest

No funding availed. All the authors declare no conflicts of interest.

References

1. National Cancer Registry Program. Consolidated Report of the Population Based Cancer Registries Incidence and Distribution of Cancer: 2012–14. New Delhi: Indian Council of Medical Research.
2. Fletcher CD, Hogendoorn P, Mertens F, Bridge J. WHO Classification of Tumours of Soft Tissue and Bone. 4th ed. Lyon, France: IARC Press; 2013.
3. Bajpai J., Khanna N., Vora T., Gulia A., Laskar S., Puri A., et al: Analysis of bone and soft tissue sarcomas registered during the year 2012 at Tata Memorial Centre, including clinical outcomes. *Indian J Cancer* 2018; 55: pp. 37–44
4. Trovik CS, Bauer HC, Alvegård TA, Anderson H, Blomqvist C, Berlin Ö, Gustafson P, Saeter G, Wallöe A. (2000) Surgical margins, local recurrence and metastasis in soft tissue sarcomas: 559 surgically-treated patients from the Scandinavian Sarcoma Group Register. *European Journal of Cancer*. Apr 30;36(6):710–6
5. Lahat, G., Tuvim, D., Wei, C. et al. (2008) New perspectives for staging and prognosis in soft tissue sarcoma. *Ann Surg Oncol* 15: 2739.
6. Novais EN, Demiralp B, Alderete J, et al.(2010) Do surgical margin and local recurrence influence survival in soft tissue sarcomas? *Clin Orthop Relat Res*;468(11): 3003–11.
7. Baldini EH et al.(1999) Long-term outcomes after function sparing surgery without radiotherapy for soft tissue sarcoma of the extremities and trunk. *J Clin Oncol*;17(10):3252
8. Tanabe KK, Pollock RE, Ellis LM, Murphy A, Sherman N, Romsdahl MM.(1994) Influence of surgical margins on outcome in patients with preoperatively irradiated extremity soft tissue sarcomas. *Cancer*.;73:1652–59.
9. Chiara Colombo 1, R Lor Randall, Robert H I Andtbacka, Alessandro Gronchi.
Surgery in soft tissue sarcoma: more conservative in extremities, more extended in the retroperitoneum. *Expert Rev Anticancer Ther* 2012 Aug;12(8):1079–87. doi: 10.1586/era.12.80.