Research Square

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Surgical Margin Distance and Oncological Outcomes in Extremity Soft Tissue Sarcomas: A Retrospective Study

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Abstract

Background:

The prognostic significance of surgical margin distance in extremity soft tissue sarcomas remains controversial. This study aimed to investigate the effect of surgical margin distance on recurrence, metastasis, and mortality in patients with soft tissue sarcoma.

Methods:

Patients diagnosed with soft tissue sarcoma who underwent surgical treatment between 2016 and 2020 at two tertiary referral centers were retrospectively evaluated. Tumor staging was performed according to the American Joint Committee on Cancer (AJCC) staging system. Surgical margins were classified as ≤ 1 mm and > 1 mm. Demographic characteristics, tumor features, treatment modalities, recurrence, metastasis, and mortality were analyzed.

Results:

A total of 60 patients were included in the study. The mean age was 49.07 ± 21.61 years. Synovial sarcoma was the most common histopathological subtype (30.0%). According to AJCC staging, stage 3B was the most frequent stage (28.3%), followed by stage 4 disease (21.7%). Negative surgical margins > 1 mm were achieved in 81.7% of patients, whereas 18.3% had margins ≤ 1 mm. No significant differences were observed between the ≤ 1 mm and > 1 mm margin groups in terms of recurrence, metastasis, or mortality ($p > 0.05$). Advanced AJCC stage was significantly associated with worse clinical outcomes.

Conclusion:

Surgical margin distance did not significantly affect recurrence, metastasis, or mortality in patients with soft tissue sarcoma when negative surgical margins were achieved. Tumor biology and disease stage appear to play a more important role in determining prognosis than absolute margin distance.

Introduction

Soft tissue refers to the connective tissues that provide structural support to anatomical structures in the body. Soft tissue sarcoma is the term used for malignant tumors arising from these connective tissues. Soft tissue sarcomas are mesenchymal-origin malignant tumors with numerous histological subtypes, often derived from more than one tissue type, and more than 50% of them are located in the extremities (1, 2). The majority of soft tissue tumors are benign. The cure rate after surgical excision of soft tissue tumors is high (3).

Soft tissue sarcomas can occur in any part of the body and are characterized by aggressive, destructive, and invasive behavior (3). The World Health Organization (WHO) has defined more than 60 histological types of soft tissue sarcomas located in the extremities and trunk, classified into 12 distinct groups. Among these 60 histological types, 37 have been shown to possess metastatic potential and are therefore classified as malignant by the WHO (4, 5). Rhabdomyosarcoma (RMS) is the most common soft tissue sarcoma in childhood. In adults, the most common types are liposarcoma, pleomorphic sarcoma, leiomyosarcoma, and fibrosarcoma, respectively (6).

In extremity soft tissue sarcomas, metastasis most commonly occurs in the lungs (7). The most frequent route of metastasis is hematogenous, while lymphatic spread is rare (7). Imaging modalities serve as an essential guide in treatment planning (4). Accurate diagnosis is achieved through properly interpreted imaging, clinical evaluation, and histopathological assessment following biopsy (8).

In the past, amputation was the primary treatment for extremity soft tissue sarcomas. With advances in technology, treatment has evolved toward limb-sparing surgery (3). Currently, the standard treatment for extremity soft tissue sarcomas is wide surgical resection, usually combined with local radiotherapy (RT). The effectiveness of contemporary chemotherapy (CT) protocols in preventing local and systemic tumor spread remains limited and controversial. The most important cause of mortality in these patients is metastasis to vital organs, which remains a major unresolved problem in the management of soft tissue sarcomas.

The aim of this study was to investigate the effect of surgical margin distance on recurrence, metastasis, and mortality in patients with soft tissue sarcoma

Materials and Methods

Study Design and Patient Population

This study was conducted after obtaining approval from the Clinical Research Ethics Committee of Adana City Training and Research Hospital (approval date: January 13, 2021; decision no: 1215).

Patients who were admitted to the Orthopedics and Traumatology Clinics of Adana Numune Training and Research Hospital and Adana City Training and Research Hospital between 2016 and 2020, diagnosed with soft tissue sarcoma based on physical examination and imaging findings, and subsequently underwent surgical treatment were included in the study. During this period, 75 patients were identified. After applying the inclusion and exclusion criteria, 60 patients were enrolled in the study. The age and gender of all patients were recorded. Preoperative “American Society of Anesthesiologists (ASA)” scores were also documented.

Clinical and Pathological Evaluation

Tumor volume was measured and recorded for each patient. Tumor staging was performed according to the “American Joint Committee on Cancer (AJCC)” staging system. Histopathological tumor types reported in pathology reports were documented. Metastatic status at the time of diagnosis was recorded for all patients. Metastasis during follow-up was also recorded as an outcome measure. All cases consisted of histopathologically confirmed primary tumors. Bone sarcomas were excluded from the study. In addition, the type of surgery performed, duration of follow-up, preoperative and postoperative chemotherapy and radiotherapy treatments, as well as postoperative recurrence, metastasis, and mortality were evaluated as prognostic factors.

Surgical margins were assessed based on pathology reports. During gross examination, the outer surface of the specimen was inked, and the specimen was sectioned perpendicular to the painted surface. The distance between the tumor and the inked margin was measured microscopically. Based on these findings, surgical margins were classified as ≤ 1 mm and > 1 mm.

Inclusion Criteria

Patients with histopathologically confirmed primary soft tissue sarcoma who underwent surgical treatment at our institution between 2016 and 2020 were included.

Exclusion Criteria

Patients who underwent surgery at another center

Patients who were operated on due to recurrence

Statistical Analysis

Statistical analyses were performed using SPSS version 20.0 (IBM®, Chicago, USA). Descriptive statistics were expressed as frequency, percentage, mean, standard deviation, and median values.

The normality of data distribution was assessed using both visual methods (histograms) and analytical methods (Shapiro–Wilk test). For normally distributed variables, comparisons between two groups were performed using the independent samples t-test. For variables that did not show normal distribution, the Mann–Whitney U test was used.

Categorical variables were compared using the Chi-square test or Fisher’s exact test, as appropriate.

Results

A total of 60 patients were included in the study. The mean age was 49.07 ± 21.61 years. The cohort consisted of 28 females (46.7%) and 32 males (53.3%). The mean symptom duration was 6.5 ± 5.55 months, and the median tumor volume was 938.6 (IQR: 340) cm^3. (Table 1)

Table 1
Sociodemographic and Clinical Characteristics of the Study Population

Parameter	Value
Age, years	49.07 ± 21.61
Gender	
Female	28 (46.7)
Male	32 (53.3)
Symptom duration, months	6.5 ± 5.55
Tumor volume, cm^3 (median, IQR)	938.6 (340)
ASA score	
1	5 (8.3)
2	28 (46.7)
3	22 (36.7)
4	5 (8.3)
Tumor location	
Knee	11 (18.3)
Elbow	4 (6.7)
Gluteal	5 (8.3)
Upper arm	3 (5.0)
Pelvis	3 (5.0)
Lower leg	5 (8.3)
Thigh	23 (38.4)
Axilla	1 (1.7)
Foot	1 (1.7)
Ankle	1 (1.7)
Hand	1 (1.7)
Shoulder	2 (3.3)
Tumor grade	

Continuous variables are expressed as mean ± standard deviation (SD), whereas categorical variables are presented as n (%).

Parameter	Value
1	7 (11.7)
2	25 (41.7)
3	28 (46.7)
Continuous variables are expressed as mean ± standard deviation (SD), whereas categorical variables are presented as n (%).	

Regarding ASA scores, most patients were classified as ASA 2 (46.7%) and ASA 3 (36.7%), while ASA 1 and ASA 4 each accounted for 8.3% of patients. In terms of tumor location, the thigh was the most common site (38.4%), followed by the knee (18.3%). Other locations included the elbow (6.7%), gluteal region (8.3%), humerus (5.0%), pelvis (5.0%), and lower leg (8.3%), while axilla, foot, ankle, and hand were rare (each 1.7%), and the shoulder accounted for 3.3% of cases. (Table 1)

With respect to tumor grade, grade 3 tumors were the most frequent (46.7%), followed by grade 2 (41.7%) and grade 1 (11.7%). (Table 1)

Regarding histopathological diagnosis, synovial sarcoma was the most common subtype (30.0%), followed by pleomorphic sarcoma (15.0%), myxofibrosarcoma (11.7%), leiomyosarcoma (10.0%), and liposarcoma (10.0%). Fibrosarcoma accounted for 8.3% of cases, while malignant peripheral nerve sheath tumor and rhabdomyosarcoma each represented 5.0%. Angiosarcoma and infantile fibrosarcoma were less frequent, accounting for 3.3% and 1.7% of cases, respectively. (Table 2)

Table 2
Clinicopathological Characteristics, AJCC Staging, Surgical Margin Status, and Outcome Measures of the Patients

Histopathological Diagnosis				**n (%)**		
Synovial Sarcoma				18 (30.0)		
Pleomorphic Sarcoma				9 (15.0)		
Myxofibrosarcoma				7 (11.7)		
Fibrosarcoma				5 (8.3)		
Liposarcoma				6 (10.0)		
Leiomyosarcoma (LMS)				6 (10.0)		
Malignant Peripheral Nerve Sheath Tumor				3 (5.0)		
Rhabdomyosarcoma (RMS)				3 (5.0)		
Angiosarcoma				2 (3.3)		
Infantile Fibrosarcoma				1 (1.7)		
Total				**60 (100)**		
AJCC Stage				**n (%)**		
1A				4 (6.7)		
1B				3 (5.0)		
2				11 (18.3)		
3A				12 (20.0)		
3B				17 (28.3)		
4				13 (21.7)		
Total				**60 (100)**		
Surgical Margin Status				**n (%)**		
≤ 1 mm				11 (18.3)		
> 1 mm				49 (81.7)		
Total				**60 (100)**		
Outcome	**1A**	**1B**	**2**	**3A**	**3B**	**4**
Recurrence	0	0	2 (18.2)	1 (8.3)	2 (11.8)	6 (46.2)

Data are presented as number and percentage. AJCC: American Joint Committee on Cancer.

Histopathological Diagnosis				n (%)		
Metastasis	0	0	0	1 (8.3)	0	13 (100)
Mortality	0	0	0	2 (16.6)	2 (11.8)	12 (92.3)
Data are presented as number and percentage. AJCC: American Joint Committee on Cancer.						

According to AJCC staging, the majority of patients were classified as stage 3B (28.3%), followed by stage 4 (21.7%), stage 3A (20.0%), and stage 2 (18.3%). Early-stage disease was less common, with 6.7% of patients in stage 1A and 5.0% in stage 1B. (Table 2)

In terms of surgical margin status, negative margins greater than 1 mm were achieved in 81.7% of patients, whereas 18.3% had margins ≤ 1 mm. (Table 2)

When clinical outcomes were evaluated according to AJCC stages, recurrence was most frequently observed in stage 4 patients (46.2%), followed by stage 2 (18.2%) and stage 3B (11.8%). Metastasis was observed exclusively in advanced stages, occurring in 8.3% of stage 3A patients and in all stage 4 patients (100%). Mortality was also highest in stage 4 (92.3%), with lower rates observed in stage 3A (8.3%) and stage 3B (5.9%), while no mortality was recorded in stages 1A, 1B, or 2. (Table 2)

No statistically significant differences were observed between patients with surgical margins ≤ 1 mm and > 1 mm in terms of age, gender, ASA score, tumor grade, AJCC stage, symptom duration, or tumor volume (all $p > 0.05$). Although female sex and higher tumor grade appeared more frequent in the ≤ 1 mm group, these differences did not reach statistical significance. Fibrosarcoma was significantly more frequent in the ≤ 1 mm group ($p = 0.003$). (Table 3)

Table 3
Comparison of Demographic and Clinical Parameters According to Surgical Margin Status

Parameter	≤ 1 mm (n = 11)	> 1 mm (n = 49)	p-value
Age, years	53.73 ± 18.62	48.02 ± 22.27	0.407
Gender			0.055
Female	8 (72.7)	20 (40.8)	
Male	3 (27.3)	29 (59.2)	
ASA score			0.603
1	0	5 (10.2)	
2	4 (36.4)	24 (49.0)	
3	6 (54.5)	16 (32.7)	
4	1 (9.1)	4 (8.2)	
Tumor grade			0.150
1	0	7 (14.3)	
2	3 (27.3)	22 (44.9)	
3	8 (72.7)	20 (40.8)	
AJCC stage			
1A	0	4 (8.2)	0.984
1B	0	3 (6.1)	0.991
2	1 (9.1)	10 (20.4)	0.700
3A	1 (9.1)	11 (22.4)	0.435
3B	5 (45.5)	12 (24.4)	0.265
4	4 (36.4)	9 (18.4)	0.231
Symptom duration, months	5 (2–8)	5 (2–36)	0.590
Tumor volume, cm^3	1307.93 ± 1526.69	588.09 ± 1231.97	0.296
Tumor type			
Synovial sarcoma	2 (18.2)	16 (32.7)	0.478
Pleomorphic sarcoma	1 (9.1)	8 (16.3)	0.998

Data are presented as mean ± standard deviation (SD) or median (min–max) for continuous variables, and number (percentage) for categorical variables. p-values were calculated using appropriate statistical tests

Parameter	≤ 1 mm (n = 11)	> 1 mm (n = 49)	p-value
Myxofibrosarcoma	0	7 (14.3)	0.330
Fibrosarcoma	4 (36.4)	1 (2.0)	0.003
Leiomyosarcoma (LMS)	2 (18.2)	4 (8.2)	0.302

Data are presented as mean ± standard deviation (SD) or median (min–max) for continuous variables, and number (percentage) for categorical variables. p-values were calculated using appropriate statistical tests

When treatment and prognostic parameters were evaluated according to surgical margin status, postoperative radiotherapy was significantly more frequent in patients with margins ≤ 1 mm ($p < 0.001$). However, no significant differences were found between the groups in terms of the remaining treatment and prognostic variables. (Table 4)

Table 4
Comparison of Treatment and Prognostic Parameters According to Surgical Margin Status

Parameter	Category	≤ 1 mm (n = 11)	> 1 mm (n = 49)	p-value
Preoperative radiotherapy				0.421
	Yes	8 (72.7)	39 (83.0)	
	No	3 (27.3)	8 (17.0)	
Postoperative radiotherapy				< 0.001
	Yes	11 (100)	2 (4.1)	
	No	0	47 (95.9)	
Preoperative chemotherapy				0.122
	Yes	8 (72.7)	23 (46.9)	
	No	3 (27.3)	26 (53.1)	
Postoperative chemotherapy				0.481
	Yes	5 (45.5)	15 (30.6)	
	No	6 (54.5)	34 (69.4)	
Recurrence				0.989
	Yes	2 (18.2)	9 (18.4)	
	No	9 (81.8)	40 (81.6)	
Metastasis				0.264
	Yes	4 (36.4)	10 (20.4)	
	No	7 (63.6)	39 (79.6)	
Mortality				0.462
	Alive	7 (63.6)	37 (75.5)	
	Dead	4 (36.4)	12 (24.5)	

Data are presented as number (percentage). p-values were calculated using the Chi-square test or Fisher's exact test, as appropriate.

When patients were evaluated according to recurrence status, no statistically significant differences were observed in terms of age, gender, ASA score, tumor grade, tumor type, or treatment modalities (all $p > 0.05$). However, patients with recurrence had a significantly higher frequency of AJCC stage 4 disease compared to those without recurrence (54.5% vs. 14.3%, $p = 0.009$). In addition, symptom duration was significantly longer in the recurrence group ($p = 0.007$). (Table 5)

Table 5
Comparison of Demographic, Clinical, Tumor, Treatment, and Prognostic Parameters According to Recurrence Status

Parameter	Category	Recurrence (+) (n = 11)	Recurrence (–) (n = 49)	p-value
Age, years		46.27 ± 23.03	49.69 ± 21.47	0.639
Gender				0.929
	Female	5 (45.5)	23 (46.9)	
	Male	6 (54.5)	26 (53.1)	
ASA score				0.558
	1	2 (18.2)	3 (6.1)	
	2	5 (45.5)	23 (46.9)	
	3	3 (27.3)	19 (38.8)	
	4	1 (9.1)	4 (8.2)	
Tumor grade				0.361
	1	0	7 (14.3)	
	2	4 (36.4)	21 (42.9)	
	3	7 (63.6)	21 (42.9)	
AJCC stage				
	1A	0	4 (8.2)	0.984
	1B	0	3 (6.1)	0.991
	2	2 (18.2)	9 (18.4)	0.989
	3A	1 (9.1)	11 (22.4)	0.435
	3B	2 (18.2)	15 (30.6)	0.712
	4	6 (54.5)	7 (14.3)	**0.009**
Symptom duration, months		9 (3–36)	5 (2–18)	**0.007**
Tumor volume, cm³		558.90 ± 647.22	1023.24 ± 1383.51	0.104

Data are presented as mean ± standard deviation (SD) or median (min–max) for continuous variables, and number (percentage) for categorical variables. p-values were calculated using independent samples t-test, Mann–Whitney U test, Chi-square test, or Fisher's exact test, as appropriate. AJCC: American Joint Committee on Cancer.

Parameter	Category	Recurrence (+) (n = 11)	Recurrence (–) (n = 49)	p-value
Tumor type				
	Synovial sarcoma	1 (9.1)	17 (34.7)	0.148
	Pleomorphic sarcoma	1 (9.1)	8 (16.3)	0.989
	Myxofibrosarcoma	1 (9.1)	6 (12.2)	0.997
	Fibrosarcoma	2 (18.2)	3 (6.1)	0.224
	Leiomyosarcoma (LMS)	2 (18.2)	4 (8.2)	0.302
Preoperative radiotherapy				0.671
	Yes	10 (90.9)	37 (75.5)	
	No	1 (9.1)	12 (24.5)	
Postoperative radiotherapy				0.231
	Yes	4 (36.4)	9 (18.4)	
	No	7 (63.6)	40 (81.6)	
Preoperative chemotherapy				0.379
	Yes	7 (63.6)	24 (49.0)	
	No	4 (36.4)	25 (51.0)	
Postoperative chemotherapy				0.155
	Yes	6 (54.5)	14 (28.6)	
	No	5 (45.5)	35 (71.4)	
Metastasis				**0.014**
	Yes	6 (54.5)	8 (16.3)	
	No	5 (45.5)	41 (83.7)	
Mortality				**0.005**
	Alive	4 (36.4)	40 (81.6)	

Data are presented as mean ± standard deviation (SD) or median (min–max) for continuous variables, and number (percentage) for categorical variables. p-values were calculated using independent samples t-test, Mann–Whitney U test, Chi-square test, or Fisher's exact test, as appropriate. AJCC: American Joint Committee on Cancer.

Parameter	Category	Recurrence (+) (n = 11)	Recurrence (–) (n = 49)	p-value
	Dead	7 (63.6)	9 (18.4)	

Data are presented as mean ± standard deviation (SD) or median (min–max) for continuous variables, and number (percentage) for categorical variables. p-values were calculated using independent samples t-test, Mann–Whitney U test, Chi-square test, or Fisher's exact test, as appropriate. AJCC: American Joint Committee on Cancer.

Furthermore, metastasis and mortality rates were significantly higher among patients with recurrence. Metastasis was observed in 54.5% of patients with recurrence compared to 16.3% in those without recurrence (p = 0.014). Similarly, mortality was significantly more frequent in the recurrence group (63.6% vs. 18.4%, p = 0.005). (Table 5)

When patients were evaluated according to metastasis status, no significant differences were observed in demographic characteristics, tumor grade, tumor type, or treatment parameters (all p > 0.05). However, AJCC stage 4 disease was significantly more frequent in patients with metastasis (p = 0.027). (Table 6)

Table 6
Comparison of Demographic, Clinical, Tumor, Treatment, and Prognostic Parameters According to Metastasis Status

Parameter	Category	Metastasis (+) (n = 14)	Metastasis (−) (n = 46)	p-value
Age, years		49.35 ± 20.86	48.97 ± 22.05	0.937
Gender				0.348
	Female	5 (35.7)	23 (50.0)	
	Male	9 (64.3)	23 (50.0)	
ASA score				0.165
	1	0	5 (10.9)	
	2	7 (50.0)	21 (45.7)	
	3	4 (28.6)	18 (39.1)	
	4	3 (21.4)	2 (4.3)	
Tumor grade				0.915
	1	2 (14.3)	5 (10.9)	
	2	6 (42.9)	19 (41.3)	
	3	6 (42.9)	22 (47.8)	
AJCC stage				
	1A	1 (7.1)	3 (6.5)	0.350
	1B	1 (7.1)	2 (4.3)	0.556
	2	4 (28.6)	7 (15.2)	0.264
	3A	4 (28.6)	8 (17.4)	0.448
	3B	4 (28.6)	13 (28.3)	0.982
	4	13 (92.9)	0	**0.027**
Symptom duration, months		4.5 (2–18)	5.5 (2–36)	0.493
Tumor volume, cm^3		864.14 ± 882.43	960.63 ± 1396.66	0.594

Data are presented as mean ± standard deviation (SD) or median (min–max) for continuous variables, and number (percentage) for categorical variables. p-values were calculated using the independent samples t-test, Mann–Whitney U test, Chi-square test, or Fisher's exact test, as appropriate. AJCC: American Joint Committee on Cancer.

Parameter	Category	Metastasis (+) (n = 14)	Metastasis (–) (n = 46)	p-value
Tumor type				
	Synovial sarcoma	3 (21.4)	15 (32.6)	0.520
	Pleomorphic sarcoma	1 (7.1)	8 (17.4)	0.671
	Myxofibrosarcoma	2 (14.3)	5 (10.9)	0.660
	Fibrosarcoma	2 (14.3)	3 (6.5)	0.224
	LMS	3 (21.4)	3 (6.5)	0.133

Data are presented as mean ± standard deviation (SD) or median (min–max) for continuous variables, and number (percentage) for categorical variables. p-values were calculated using the independent samples t-test, Mann–Whitney U test, Chi-square test, or Fisher's exact test, as appropriate. AJCC: American Joint Committee on Cancer.

In contrast, mortality analysis revealed strong associations with disease severity and clinical outcomes. Patients with mortality had a significantly higher frequency of AJCC stage 4 disease (75.0% vs. 2.3%, $p < 0.001$) and a lower frequency of stage 2 disease ($p = 0.027$). Additionally, postoperative chemotherapy, recurrence, and metastasis rates were significantly higher in patients with mortality ($p < 0.001$, $p = 0.005$, and $p < 0.001$, respectively). (Table 6–7)

Table 7
Comparison of Demographic, Clinical, Tumor, Treatment, and Prognostic Parameters According to Mortality Status

Parameter	Category	Mortality (+) (n = 16)	Mortality (–) (n = 44)	p-value
Age, years		57.63 ± 19.75	45.95 ± 21.62	0.064
Gender				0.391
	Female	6 (37.5)	22 (50.0)	
	Male	10 (62.5)	22 (50.0)	
ASA score				0.783
	1	1 (6.3)	4 (9.1)	
	2	6 (37.5)	22 (50.0)	
	3	7 (43.8)	15 (34.1)	
	4	2 (12.5)	3 (6.8)	
Tumor grade				0.207
	1	0	7 (15.9)	
	2	9 (56.3)	16 (36.4)	
	3	7 (43.8)	21 (47.7)	
AJCC stage				
	1A	0	4 (9.1)	0.565
	1B	0	3 (6.8)	0.558
	2	0	11 (25.0)	0.027
	3A	2 (12.5)	10 (22.7)	0.486
	3B	2 (12.5)	15 (34.1)	0.120
	4	12 (75.0)	1 (2.3)	< 0.001
Symptom duration, months		5.5 (2–24)	5.0 (2–36)	0.256
Tumor volume, cm³		837.74 ± 824.7	974.55 ± 1427.1	0.594

Data are presented as mean ± standard deviation (SD) or median (min–max) for continuous variables, and number (percentage) for categorical variables. p-values were calculated using the independent samples t-test, Mann–Whitney U test, Chi-square test, or Fisher's exact test, as appropriate. AJCC: American Joint Committee on Cancer.

Parameter	Category	Mortality (+) (n = 16)	Mortality (–) (n = 44)	p-value
Tumor type				
	Synovial sarcoma	4 (25.0)	14 (31.8)	0.755
	Pleomorphic sarcoma	1 (6.3)	8 (18.2)	0.422
	Myxofibrosarcoma	4 (25.0)	3 (6.8)	0.074
	Fibrosarcoma	2 (12.5)	3 (6.8)	0.602
	LMS	3 (18.8)	3 (6.8)	0.328
Preoperative radiotherapy				0.710
	Yes	14 (87.5)	35 (79.5)	
	No	2 (12.5)	9 (20.5)	
Postoperative radiotherapy				0.088
	Yes	6 (37.5)	7 (15.9)	
	No	10 (62.5)	37 (84.1)	
Preoperative chemotherapy				0.311
	Yes	10 (62.5)	21 (47.7)	
	No	6 (37.5)	23 (52.3)	
Postoperative chemotherapy				**< 0.001**
	Yes	13 (81.3)	7 (15.9)	
	No	3 (18.8)	37 (84.1)	
Recurrence				**0.005**
	Yes	7 (43.8)	4 (9.1)	
	No	9 (56.3)	40 (90.9)	
Metastasis				**< 0.001**
	Yes	13 (81.3)	1 (2.3)	

Data are presented as mean ± standard deviation (SD) or median (min–max) for continuous variables, and number (percentage) for categorical variables. p-values were calculated using the independent samples t-test, Mann–Whitney U test, Chi-square test, or Fisher's exact test, as appropriate. AJCC: American Joint Committee on Cancer.

Parameter	Category	Mortality (+) (n = 16)	Mortality (–) (n = 44)	p-value
	No	3 (18.8)	43 (97.7)	

Data are presented as mean ± standard deviation (SD) or median (min–max) for continuous variables, and number (percentage) for categorical variables. p-values were calculated using the independent samples t-test, Mann–Whitney U test, Chi-square test, or Fisher's exact test, as appropriate. AJCC: American Joint Committee on Cancer.

No significant differences were found between mortality groups in terms of age, gender, ASA score, tumor grade, tumor type, symptom duration, or tumor volume (all $p > 0.05$). (Table 7)

Discussion

In this study, we evaluated the impact of surgical margin distance on prognosis in patients with extremity soft tissue sarcomas. Our findings demonstrated that surgical margin distance (≤ 1 mm vs. >1 mm) was not significantly associated with recurrence, metastasis, or mortality. However, postoperative radiotherapy was significantly more frequently administered in patients with margins ≤ 1 mm. In addition, advanced disease stage, particularly AJCC stage 4, was strongly associated with worse clinical outcomes, including higher rates of recurrence, metastasis, and mortality.

Previous studies have emphasized the prognostic importance of achieving negative surgical margins in the management of soft tissue sarcomas. However, the impact of margin distance remains controversial. Several studies have reported that once negative margins are achieved, the exact margin width may not significantly influence local recurrence or overall survival (9, 10). Similarly, other authors have suggested that adjuvant treatments, particularly radiotherapy, may compensate for close surgical margins and reduce the risk of local recurrence (11, 12). Our findings are consistent with these reports, as no significant association was observed between surgical margin distance and recurrence, metastasis, or mortality. This suggests that, in the presence of negative margins, tumor biology and disease stage may play a more critical role in determining prognosis than the absolute margin distance.

In the series including 53 patients conducted by Demiral et al. (13), the mean age was reported as 38 years. In a study published in the European Journal of Surgical Oncology including 1066 patients, the mean age was reported as 56 years, with the youngest patient being 19 years old and the oldest 95 years old (14). In a study published in the AOTT Journal, the mean age was found to be 51.4 years (15). In our study, the mean age of the patients was 49.07 ± 21.61 years, which is consistent with the literature. No significant association was found between age and prognosis in our study.

In the study by Harati et al. (16), when only patients with negative surgical margins were evaluated, no significant difference in survival was observed between patients with tumor sizes below and above 5 cm. Brennan et al. reported a 10-year survival rate of 75% without distant metastasis for extremity-localized high-grade lesions ≤ 5 cm, whereas the 15-year disease-free survival rate was found to be below 40% for lesions > 10 cm (7). In our study, no significant relationship was found between tumor size and

prognosis. This may be due to the presence of negative surgical margins in all patients and the relatively small sample size.

In studies evaluating soft tissue sarcomas throughout the body, the most common localization has been reported to be the lower extremity (37–62%) (17, 18). Similarly, in our study, 68% of sarcomas were located in the lower extremity, 19% in the upper extremity, and 13% in the pelvis. These findings are consistent with the literature.

In our study, metastasis and mortality were found to be higher in patients with advanced AJCC stage and lower in early-stage disease. In the study by Gross et al. (19), low histological grade was associated with higher survival. In that study, the 5-year survival rate was reported as 100% in low-grade soft tissue sarcomas, whereas it was 69.2% in high-grade sarcomas. Another study reported that survival rates decreased as tumor stage increased (17).

Among the 60 patients included in our study, the most frequently observed soft tissue sarcomas were synovial sarcoma (n = 18), pleomorphic sarcoma (n = 9), and myxofibrosarcoma (n = 7). Due to the small number of cases, other tumor types were not included in the analyses. However, no significant differences were observed among the commonly analyzed soft tissue sarcomas in terms of recurrence, metastasis, and mortality. In a study evaluating more than 12,000 cases of extremity-localized soft tissue sarcomas in adults, liposarcoma was reported in 26.2%, fibrosarcoma in 7.5%, leiomyosarcoma in 14.3%, and synovial sarcoma in 8.5% of cases (6). In another study, synovial sarcoma and liposarcoma were each observed in 25.6%, and pleomorphic sarcoma in 13% of cases, with similar mortality rates among histological subtypes (20).

In patients with high-grade extremity soft tissue sarcomas treated with wide excision and local radiotherapy, no significant difference in overall survival was observed in 10- and 20-year follow-ups (11). In a study conducted by Brennan et al., no significant difference in disease-specific survival was observed in patients treated with adjuvant brachytherapy (3). Similarly, in our study, radiotherapy was not significantly associated with recurrence or mortality in our cohort.

The effectiveness of chemotherapy in both local control and treatment of distant metastasis in soft tissue sarcomas remains controversial (21). In a recent large-scale meta-analysis including 1568 patients, the efficacy of chemotherapy was evaluated. When doxorubicin-based chemotherapy regimens were combined with surgery, local recurrence was reported as 6% and distant metastasis as 10%. However, no benefit in overall survival was observed (22). In another retrospective study conducted at Memorial Sloan-Kettering and MD Anderson Cancer Center, the effect of chemotherapy on local control, distant metastasis, and disease-free survival in stage III extremity sarcomas was investigated. A statistically significant benefit was observed in 1-year disease-specific survival; however, this benefit did not persist over time. At the fifth year, no survival advantage of chemotherapy was observed (23). In our study, consistent with the literature, no statistically significant difference was found in prognosis between patients who received adjuvant chemotherapy and those who did not.

In our study, negative surgical margins were achieved in all patients who underwent limb-sparing surgery for soft tissue sarcoma. During follow-up, no difference in prognosis was observed between patients with negative margins ≤ 1 mm and those with margins > 1 mm. Our findings demonstrated that there was no difference in recurrence, metastasis, or mortality among patients with negative surgical margins. In a comprehensive study by Harati et al. (16), 643 patients were evaluated. When patients were classified according to surgical margins as microscopically negative, microscopically positive, and macroscopically positive, better survival was reported in patients with microscopically negative margins. However, when patients with negative margins were further classified into ≤ 1 mm, 1–5 mm, and > 5 mm groups, no significant difference in prognosis was observed, similar to our findings.

There are also studies in which surgical margins were classified as positive and negative, but no association was found between surgical margins and survival. In the study by Kamat et al. (24), 55 patients operated for lower extremity soft tissue sarcoma were evaluated. Surgical margins were positive in only 6 patients. No significant difference was observed between patients with positive and negative margins in terms of local recurrence and metastasis, consistent with our findings.

In our study, with a median follow-up of 24 months, recurrence was observed in 18%, metastasis in 23.3%, and mortality in 26.6% of patients. While no recurrence was observed in AJCC stage I patients, this rate increased up to 46.2% in stage IV patients. Our findings demonstrated that mortality rates were higher in patients with advanced-stage soft tissue sarcomas. In our study, AJCC stage IV was more frequent among patients with metastasis and among those who died. In the study by Maretty-Nielsen et al. (25), 5-year mortality was reported as 32.8% and 10-year mortality as 36% in 1246 patients. Consistent with our study, mortality was reported to be higher in high-grade tumors. Additionally, it was reported that mortality rates in low-grade soft tissue sarcomas were close to those of the general population. In another study by Maretty-Nielsen et al. (26), the 5-year recurrence rate was reported as 16% and the 5-year mortality rate as 24%.

There are numerous studies investigating the effect of local recurrence on overall outcome. In one of the most reliable long-term studies conducted in recent years, patients were followed for 20 years. This study included 753 patients. According to the results, patients who developed local recurrence had a threefold higher risk of death compared to those who did not. In this study, local recurrence was identified as the most important factor affecting survival duration. Furthermore, local recurrence may occur concurrently with distant metastasis (22).

In a comprehensive analysis of 2084 patients conducted at Memorial Sloan Kettering Cancer Center (9), positive resection margins were found in 22% (n = 460) of patients. Interestingly, the local recurrence rate in patients with positive margins was 28%, meaning that 72% of patients with positive margins did not develop local recurrence. This rate is comparable to results obtained from wide resections. In another series of 1091 patients conducted by MD Anderson Cancer Center, positive resection margins were found in 22.6% (n = 247) of patients (10). However, only 15.9% (n = 173) of all patients developed local

recurrence. Therefore, although positive margins are associated with a higher risk of local recurrence, they do not necessarily lead to recurrence in every case.

Conclusions

In conclusion, our findings demonstrate that in patients with extremity soft tissue sarcomas, surgical margin distance does not appear to have a significant impact on recurrence, metastasis, or mortality, provided that negative surgical margins are achieved. These results suggest that the presence of a negative margin may be more critical than the absolute width of the margin.

Advanced disease stage, particularly AJCC stage 4, was strongly associated with worse clinical outcomes and emerged as a key prognostic factor. In addition, our findings support the limited prognostic impact of tumor size, histological subtype, and adjuvant chemotherapy in this patient population.

Although postoperative radiotherapy was more frequently administered in patients with close margins, it did not translate into a measurable difference in survival outcomes. This may indicate a compensatory role of adjuvant radiotherapy in patients with narrow surgical margins.

Overall, tumor biology and disease stage appear to play a more decisive role in determining prognosis than surgical margin distance. Further prospective studies with larger patient populations are needed to better define the prognostic significance of surgical margins in soft tissue sarcomas.

Limitations

This study has several limitations. Due to the small sample size, a comprehensive analysis according to histological subtype and stage of soft tissue sarcomas could not be performed. The fact that all patients had negative surgical margins may have prevented the identification of prognostic factors previously associated with soft tissue sarcomas. In addition, the study had a retrospective design.

Declarations

Ethics approval and consent to participate

This study was approved by the Clinical Research Ethics Committee of Adana City Training and Research Hospital (approval date: January 13, 2021; decision no: 1215). Due to the retrospective design of the study, the requirement for informed consent was waived by the Clinical Research Ethics Committee of Adana City Training and Research Hospital. All methods were carried out in accordance with relevant guidelines and regulations and in accordance with the ethical standards of the Declaration of Helsinki and its later amendments.

Consent for publication

Not applicable.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

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Authors' Contributions

İA: Conceptualization, study design, literature search, clinical studies, data acquisition, data analysis, manuscript preparation, and guarantor of the study.

AK: Conceptualization, study design, literature search, clinical studies, data acquisition, data analysis, manuscript preparation, and critical revision of the manuscript for important intellectual content.

MOT: Data analysis, intellectual contribution, critical revision of the manuscript for important intellectual content, and manuscript editing.

All authors read and approved the final manuscript and agreed to be accountable for all aspects of the work, ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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