

Foot and Ankle Soft Tissue Sarcomas – Treatment and Oncologic Outcomes: A Systematic Review of the Literature

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INTRODUCTION: Foot and ankle soft tissue sarcomas (STS) are rare neoplasms associated with a high risk of local recurrence and metastasis. Treatment consists of tumor resection with negative margins through either limb-salvage surgery or amputation. Whether amputation is associated with higher local control rates than limb salvage therapy remains under debate. Our systematic review sought to identify risk factors for 1) overall death, 2) local recurrence, 3) metastasis, and 4) assess whether the type of surgery (amputation or limb-salvage) affected survival.

METHODS: This systematic review was conducted following PRISMA guidelines. Our study was registered in PROSPERO (415624). A comprehensive search of the PubMed, Embase, and Scopus databases from inception to May 1, 2023 was performed. To be included, studies had to provide individualized data on either local recurrence, metastasis, or overall survival by type of treatment (limb salvage or amputation), include at least 10 patients with foot and ankle STS, have a minimum follow up of 12 months, and be published in a peer-reviewed journal. Case reports and non-peer-reviewed publications were excluded. Quality assessment of studies was performed using the STROBE checklist. Crude (univariate) and adjusted (multivariate) logistic regression was used for risk factor analysis. For survival analysis according to treatment type, the Kaplan-Meier method was used.

RESULTS:

A total of 7 studies and 123 patients were included (Figure 1). The foot was the most common location (78.1%) and synovial sarcoma was the most common histology (48.1%). The median tumor size was 3.75 cm. History of previous unplanned excision was present in 48% of patients and positive surgical margins were found in 20% of patients (Table 1). Patients with history of previous unplanned excision had a higher rate of local recurrence (21% vs. 4%, $p=0.010$). Five- and 10-year overall survival were 73% and 57%, respectively (Figure 2). Patients with metastases were almost 160 times more likely to die (OR=159.93, $p<0.001$)(Table 2). A trend toward higher likelihood of dying was seen with deep tumors and tumors ≥ 6 cm; however, this was not found to be statistically significant ($p=.093$ and $p=.075$, respectively). Unplanned excision (OR=22.29, $p=0.009$) and positive margins (OR=64.48, $p=0.011$) were associated with higher risk of local recurrence (Table 3). Patients with high-grade tumors (OR=13.22, $p=0.023$) and tumors ≥ 6 cm (OR=7.40, $p=0.022$) were more likely to develop metastases (Table 4). Amputation was not associated with higher risk of death ($p=0.098$) after adjusting for age, sex, and presence of metastasis.

DISCUSSION AND CONCLUSION: Our findings show that metastasis was the single most important risk factor for death in foot and ankle soft tissue sarcoma. Besides positive margins, history of previous unplanned excision was also a risk factor for local recurrence. The most important risk factors for metastasis were tumor grade and size ≥ 6 cm. Surgeons should be aware of the higher accuracy of the 6-cm size threshold when assessing the risk of metastasis. Amputation *per se* was not associated with a higher risk of death. Future studies should focus on determining the role of (neo)-adjuvant radiation therapy on the local control of these tumors.

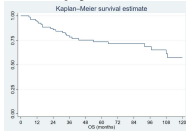
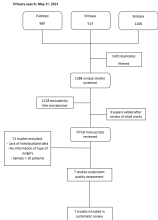


Table 1. Demographic, clinical and treatment characteristics of patients included

Characteristic	Frequency	%
Age (years)	46 (43.8%)	46 (37.4%)
Female sex	52 (42.3%)	52 (42.3%)
Location		
Foot	96 (78.1%)	96 (78.1%)
Ankle	27 (21.9%)	27 (21.9%)
History of previous unplanned excision	59 (47.9%)	59 (47.9%)
Unplanned excision	10 (8.1%)	10 (8.1%)
Planned excision	49 (39.8%)	49 (39.8%)
Positive surgical margins	24 (19.5%)	24 (19.5%)
Negative surgical margins	99 (80.5%)	99 (80.5%)
Tumor size (cm)		
0-2	15 (12.2%)	15 (12.2%)
2-4	44 (35.8%)	44 (35.8%)
4-6	33 (26.8%)	33 (26.8%)
6-8	22 (17.8%)	22 (17.8%)
8-10	7 (5.7%)	7 (5.7%)
>10	2 (1.6%)	2 (1.6%)
Depth		
Superficial	41 (33.3%)	41 (33.3%)
Intermediate	44 (35.8%)	44 (35.8%)
Deep	38 (30.9%)	38 (30.9%)
Grade		
Low grade	5 (4.1%)	5 (4.1%)
Intermediate grade	51 (41.5%)	51 (41.5%)
High grade	67 (54.4%)	67 (54.4%)
Primary site		
Foot	80 (65.1%)	80 (65.1%)
Ankle	43 (34.9%)	43 (34.9%)
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OR, Odds Ratio; CI, Confidence Interval; STS, soft tissue sarcoma; p, p-value

*Odds ratios to analyze values and interpretative ranges between brackets.