

**Title:** Soft Tissue Sarcomas of the Foot and Ankle: An Analysis of Risk Factors for Local Recurrence and Survival

**Authors:** Matthew T. Houdek, Benjamin K. Wilke, Peter Rose, Norman Turner

**Institution:** Department of Orthopedic Surgery, Mayo Clinic, Rochester, MN

**Background:** Soft tissue sarcomas of the foot and ankle are exceedingly rare. Currently there is a paucity of data examining the outcomes of treatment and prognostic variables for disease specific and overall survival.

**Purpose:** The aim of this study was to review our institution's experience with soft tissue sarcomas of the foot and ankle to identify factors affecting 1) overall survivorship, 2) disease specific survival, both local recurrence and distant disease, and 3) postoperative complications.

**Methods:** We retrospectively reviewed the records of 62 foot and ankle soft tissue sarcomas (STS) treated with definitive surgery at our institution between 1992 and 2013. Pertinent demographics as well as information regarding the surgical procedure and disease status at latest follow-up were reviewed. Cox hazard ratios were used to assess prognostic variables. Disease free survival and overall survival were estimated using Kaplan Meier method. The cohort consisted of 35 males and 27 females; with a mean age at diagnosis of 45 years (2 months-80 yrs) and a mean follow-up of 7 yrs (range 1-20 yrs).

**Results:** The most common tumor subtypes were synovial sarcoma (n=16) and leiomyosarcoma (n=9). A majority of the tumors were deep (n=40, 64%) to the fascia. At the time of presentation, two patients were noted to have distant metastases. The mean tumor volume was 241.5 cm<sup>3</sup> (range 0.01 – 6930 cm<sup>3</sup>) at the time of tumor extirpation. The mean maximum tumor dimension was 5.4 cm (range 0.3-33 cm). Ultimately; negative margins were obtained in 97% of cases. Thirty-five (56%) patients underwent a limb salvage procedure and twenty-seven patients had an amputation, either Syme, below knee or above knee. Limb salvage failed in 2 patients, necessitating amputation for local recurrence. The overall limb salvage rate was 53%.

Local recurrence was observed in 9 patients and distant metastases in 15 patients. No analyzed factor significantly affected disease specific survival (Table 1). In terms of overall survival, tumors deep to the fascia and tumor recurrence significantly increased the risk of mortality. Likewise tumor size  $\geq 3$  cm in maximal dimension increased the risk of mortality (Table 1). Reexcision of an inadvertently excised tumor and a limb salvage procedure did not adversely affect outcome. Likewise a positive margin at reexcision did not lead to an increased risk of recurrence. The 10-year overall- and disease free survival was 56% and 57% (Figure 1).

Posttreatment complications occurred in 15 (24%) patients. These included wound drainage/dehiscence (n=8), wound infection (n=3), skin graft failure (n=3), fibular overgrowth (n=1) and pseudoaneurysm of the tibial vessels (n=1). In analyzing risk factors for postoperative complications it was found that patients having neoadjuvant radiation (HR 3.33, P=0.02) were at increased risk.

**Conclusion:** Local recurrence and development of distant disease was relatively common following wide excision of a soft tissue sarcoma of the foot and ankle. A high percentage of patients underwent an amputation; however limb salvage was not associated with an increased risk of mortality. Tumors that were  $\geq 3$  cm in maximal dimension were associated with a worse overall survival. This has the potential to modify treatment, as smaller tumors (<5 cm) is a risk factor for mortality. Further studies are needed to determine if a separate grading system is needed for soft-tissue sarcomas of the foot and ankle, which accounts for these aggressive, small tumors.

Table 1: Factors Associated with Disease Recurrence and Overall Survival

Patient Factors	Disease Free Survival Hazard Ratio (95% CI)	P Value	Overall Survival Hazard Ratio (95% CI)	P Value
<b>Age</b>				
≤ 40 Years	0.85 (0.32-2.05)	0.73	0.88 (0.34-2.41)	0.80
> 40 Years	1.17 (0.48-3.08)	0.73	1.12 (0.41-2.86)	0.80
<b>Male Gender</b>	1.17 (0.49-2.98)	0.71	0.91 (0.37-2.27)	0.84
<b>Tumor Characteristics</b>				
<b>Location</b>				
Foot	0.51 (0.21-1.24)	0.13	0.82 (0.33-2.14)	0.68
Ankle	2.33 (0.96-5.57)	0.06	1.22 (0.45-3.03)	0.67
Superficial to Fascia	0.60 (0.21-1.48)	0.28	<b>0.32 (0.09-0.88)</b>	<b>0.02</b>
Deep to Fascia	1.66 (0.67-4.67)	0.28	<b>3.10 (1.12-10.91)</b>	<b>0.02</b>
Positive Surgical Margin at Reexcision	2.24 (0.12-11.46)	0.48	-	-
Metastatic Disease at Presentation	2.89 (0.67-8.57)	0.13	1.43 (0.32-4.52)	0.59
Low Grade (FNCCLC)	1.42 (0.53-3.46)	0.45	0.72 (0.23-1.88)	0.52
High Grade (FNCCLC)	0.70 (0.28-1.86)	0.45	1.38 (0.52-4.29)	0.52
AJCC Grade I/II	0.51 (0.21-1.24)	0.13	0.51 (0.20-1.31)	0.16
AJCC Grade III/IV	1.97 (0.80-4.68)	0.13	1.92 (0.75-4.81)	0.16
Disease Recurrence	-	-	<b>8.06 (3.09-24.97)</b>	<b>&lt;0.0001</b>
<b>Tumor Size (Maximal Dimension)</b>				
< 2cm	0.48 (0.11-1.46)	0.21	<b>0.26 (0.04-0.92)</b>	<b>0.03</b>
≥ 2 cm	1.87 (0.53-11.84)	0.36	1.52 (0.42-9.75)	0.55
≥ 3 cm	2.39 (0.87-8.39)	0.09	<b>3.15 (1.03-13.64)</b>	<b>0.04</b>
≥ 4 cm	2.25 (0.92-5.82)	0.07	<b>2.67 (1.06-7.23)</b>	<b>0.03</b>
≥ 5 cm	2.00 (0.80-4.82)	0.12	<b>3.51 (1.35-9.13)</b>	<b>0.01</b>
<b>Surgical Considerations</b>				
Ray Resection	0.61 (0.09-2.13)	0.49	0.58 (0.09-2.04)	0.58
Limb Salvage	0.55 (0.23-1.32)	0.18	<b>0.22 (0.07-0.57)</b>	<b>0.001</b>
Amputation	1.79 (0.75-4.32)	0.18	<b>4.46 (1.74-12.79)</b>	<b>0.001</b>
Wide Resection	0.69 (0.13-12.62)	0.73	0.60 (0.11-10.94)	0.64
Reexcision of Unplanned Excision	0.85 (0.35-2.00)	0.68	1.57 (0.64-4.21)	0.32
<b>Adjuvant Treatment Considerations</b>				
Neoadjuvant Radiation	1.53 (0.59-3.77)	0.34	1.06 (0.34-2.83)	0.90
Adjuvant Radiation	1.01 (0.16-3.51)	0.98	0.21 (0.01-1.21)	0.09
Neoadjuvant Chemotherapy	2.58 (0.84-6.62)	0.09	2.85 (0.91-7.63)	0.06
Adjuvant Chemotherapy	2.10 (0.79-5.07)	0.12	<b>3.03 (1.10-7.86)</b>	<b>0.03</b>

Figure 1: Kaplan Meir Survival Curves for Disease Free- and Overall Survival

