

# Survival analysis in patients with localized extremity soft tissue sarcoma who did not receive surgical resection

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**INTRODUCTION:** Soft-tissue sarcomas (STs) are malignant tumors that comprise various histological subtypes and can be developed in any part of the body. Negative surgical margin is standard goal for localized STs, in addition, positive macroscopic margin followed by radiation therapy are reasonable in some cases. Although the advances with reconstruction surgery make it possible to cover more extensive soft tissue defects, due to critical neurovascular structure or bone, limb sparing surgery is not feasible option in some cases, accordingly, amputation surgery is still required (Ref. 1). In the meantime, there is a small number of patients for whom surgical resection is not indicated due to comorbidities or the impact of functional loss. The prognosis for such patients is one of the important factors to decide the treatment strategy, but there have been no large-scale analyses of the prognosis of non-surgical cases. The aim of this study was to investigate the survival of non-operative cases of localized extremity non-round cell sarcoma.

**METHODS:** Ethical review and approval were not required for this study on human participants in accordance with local legislation and institutional requirements. We employed Surveillance, Epidemiology, and End Results (SEER) database which was the largest public cancer database without identifiable patient data. We included all extremity STs between 2020 and 2019 according to Rare Cancer classification recode (203) developed by the Surveillance of Rare Cancer in Europe (Ref. 2). SEER employs an original histological grading system and SEER grade 1 was defined as low grade, and SEER grades 2–4 as high grade (Ref. 3). SEER\*Stat version 8.3.9.2 software (National Cancer Institute) was used to obtain the information, and a total of 24605 patients were identified for STs. After excluding cases of with metastatic lesions (1837 cases) or with unstaged lesions (4917 cases), 17671 patients were identified as localized STs. Of those, further 17225 cases with surgical intervention of unknown surgical status or unknown tumor size or unknown histological grade and AJCC<sup>8th</sup> clinical stage 1A (3 cases) were excluded. In total, 446 cases were thus enrolled in this study. Cancer specific survival (CSS) and overall survival (OS) were calculated by Kaplan-Meier survival analysis. Survival analysis was then performed by weighted Cox proportional hazards modeling to calculate hazard ratio (HR).

**RESULTS SECTION:** Of the 446 patients included, 49 (11%) patients were Stage 1B, 72 (16%) are Stage 2, 125 (28%) are Stage 3A and 200 (45%) are Stage 3B. The median age in the entire cohort was 72 years old. 129 patients (29%) received chemotherapy and 212 patients (48%) received radiation therapy and it tends to be more common in higher clinical stages. 5-year CSS was 40% in entire cohort, 80% in Stage 1B, 53% in Stage 2, 47% in Stage 3A and 22% in Stage 3B (Figure A). 5-year OS was 25% in entire cohort, 56% in Stage 1B, 31% in Stage 2, 26% in Stage 3A and 14% in Stage 3B (Figure B). In multivariate analysis, radiation therapy prolonged survivals (CSS: HR 0.7 95%CI 0.5-0.9, OS: HR 0.7 95%CI 0.6-0.98).

**DISCUSSION:** Our study clearly demonstrated that 1) 5-year OS was around one quarter, 2) radiation therapy prolonged survivals in patients who did not receive surgical resection. Regarding radiation therapy for STs, adjuvant radiation therapy has been reported to improve local control, but its impact on survivals remains unclear. In the meantime, definitive radiation therapy offers the possibility of long-term local control and overall survival for a substantial proportion of patients with unresectable primaries. In our study, we demonstrated that radiation therapy improved survivals in patients with STs in the extremities without surgical intervention. Although we did not account for the Eastern Cooperative Oncology Group Performance Status of each patient, our study, utilizing the largest population-based cancer database, provides new insights into STs patients who did not undergo surgical intervention.

**SIGNIFICANCE:** This study demonstrated that survival rates among patients with localized soft tissue sarcoma who did not undergo surgical intervention or receive radiation therapy might have significance for individuals with STs who didn't undergo surgical treatment.

**REFERENCES:** (1) Fizazi K et al. Ann Oncol 2015. (2) Gatta G et al. Lancet Oncol. 2017 (3) Matsuoka M et al. Clin Transl Oncol. 2021

