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Changes in Soft Tissue Sarcoma Volume During Neoadjuvant Therapy: Predictors and Clinical Importance.

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Background:

Complete surgical resection is the cornerstone of treatment for localized extremity soft tissue sarcomas (STS). Neoadjuvant therapy (NT) is increasingly used in patients with STS to reduce post-surgical local recurrence rates and/or treat potential micro-metastases. Nomograms can help support clinical decisions on employing different types of NT including a single or combination regimen of chemotherapy, radiation, or chemoradiation. NT often leads to changes in size of STS that remain difficult to predict. These changes may affect surgical planning and patient counseling.

Purpose:

We sought to investigate the impact of histologic subtype, grade, and treatment modality in predicting radiographic changes in tumor volume and surgical outcomes.

Patients and Methods:

In this IRB-approved retrospective case series, we identified all soft tissue sarcomas resected at a single institution between 2017 and 2021. Patients who did not receive NT, which included chemotherapy, radiotherapy, or a combination of treatment modalities, and those who did not have an MRI immediately preceding and following NT were excluded. Patient demographics, treatment modality, and tumor characteristics were recorded. Contrast enhanced sequences of tumors were volumetrically segmented using semi-automated software. Wound closure type (simple including adjacent soft tissue re-arrangement vs complex including local and free muscles flaps) and 30-day post-operative wound complication rate was recorded.

Results:

Thirty-five patients met inclusion criteria. Mean age was 59 (range 19 to 87) and presented mainly in males (60%). The majority of tumors were grade 3 (22/32, 68.8%), and myxofibrosarcoma (9/35, 25.7%) and synovial sarcoma (5/35, 14.3%) were the most common histologic subtypes.

Pre-treatment tumor volume averaged 480 cm³ (range 1 to 2,783 cm³) and mean percent change in volume was +15% (range -86% to +367%). There was no correlation between change in tumor volume and pre-treatment volume (r = -0.068, p = 0.689) or percent tumor necrosis (r = 0.083, p = 0.637). We also found no association among the various histologic subtypes (H = 2.131 (2), p = 0.345) or NT with radiation versus chemoradiation (U = 65, p = 0.112) and change in tumor volume.

Alternatively, there was a positive correlation between histologic grade and percent volume change (r = 0.363, p = 0.032). Complex closures (n = 15, 43%) were significantly associated with higher post-treatment volumes compared to simple closures (U = 68, p = 0.007). There were five (9%) postoperative complications, which were associated with larger post-treatment volumes (U = 37, p = 0.077).

Conclusion:

The use of neoadjuvant therapy in patients with STS is increasing as an effort to reduce post-surgical local recurrence and treat potential micro-metastases. STS represents a diverse family of rare tumors, which may explain the difficulty in predicting changes in tumor size during NT. The present study suggests that higher tumor histologic

grade correlates with an increased percent volume change following NT. These tumors are associated with more complex closure types, which has clinical implications related to surgical planning, post-operative complications, the necessity of complex wound closures, and patient counseling prior to starting NT. Limitations of the study include small sample size from a single institution. Future studies, with larger sample sizes across multiple institutions, are necessary for further investigation of potential predictors.



Figure 1. Average percent volume change and tumor necrosis among included histology subtypes.

MYX = Myxofibrosarcoma

SS = Synovial Sarcoma

*All Others = Dedifferentiated Liposarcoma (n = 2), Ewing Sarcoma (n = 2), Extraskeletal Myxoid Chondrosarcoma (n = 1), Fibroblastic/Myofibroblastic Sarcoma (n = 1), Fibroblastic Sarcoma (n = 3), Leiomyosarcoma (n = 1), Myxoid/Round Cell Liposarcoma (n = 3), Myofibrosarcoma (n = 1), Pleomorphic Liposarcoma (n = 3), Rhabdomyosarcoma (n = 3), Undifferentiated Round Cell Sarcoma (n = 1)