Why Should Unplanned Excisions Best Be Avoided In Soft-Tissue Sarcomas? Results Of A Multi-Centre Study Including 728 Patients

Orthopaedics / Musculoskeletal Tumors / Malignant Tumors

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Background
Due to their rarity and ambiguous clinical presentation, soft tissue sarcomas (STS) are often misdiagnosed. Resulting unplanned excisions (UE) mostly require additional treatment, including re-resection and radiotherapy (RTX) at tertiary tumour centres. Morbidity is definitely increased, yet results concerning the impact of UE on survival are conflicting.

Objectives
This multicentre study aims at elucidating the causality between tumour presentation, risk for UE, subsequent therapy at sarcoma centres and potential differences in prognosis among directly referred STS patients and those with prior UE.

Study Design & Methods
728 patients (352 female, 376 male; mean age: 58 years) treated for STS at three tumour centres were retrospectively included. Patient, tumour and treatment related factors were ascertained. UE was defined as an unintentionally performed resection of a subsequently histologically verified STS. Patients were followed-up to a median of 5.5 years. Chi-square and t-tests were used to evaluate differences between UE- and non-UE patients. Time-to-event analyses were calculated with Log-rank and Gray’s tests.

A propensity score of being in the UE-group was estimated, based on disparities between UE- and non-UE-patients at baseline. This score was used to generate an inverse-probability-of-UE-weight (IPUEW). Time-to-event analyses were calculated after IPUEW-weighting, thus adjusting for imbalances between UE and non-UE patients.

Results
A history of UE was present in 38.6% of patients (n=281), with similar incidences at the centres. Young age (p=0.036), male gender (p=0.05), small (p<0.005) and superficial tumours (p<0.005) with a long history of symptoms (p<0.005) predisposed to UE. Need for plastic reconstruction (p<0.005) and adjuvant RTX (p=0.041) was higher in the re-resected group as compared to patients undergoing primary surgery. Yet, postoperative complication rates were similar in both groups (p=0.73).

A significant difference in terms of overall-survival (OS) between UE and non-UE patients
was evident in univariate analysis. At 5 and 10 years, 78.6% and 63.3% of patients with prior UE were alive, as compared to 70.6% and 57.9% of directly referred ones (p=0.028). Moreover, UE-patients seemingly had a lower risk for distant metastasis (DM) than non-UE patients (p=0.01), whilst risk for local recurrence (LR) was comparable (p=0.43). Due to the strong correlation between favourable prognostic factors and a history of prior UE, time-to-event analyses were re-calculated after weighting for the IPUEW. Consequently, the prognostic benefit for UE-patients in terms of OS (p=0.241) and DM-free survival (p=0.59) disappeared following adjustment for imbalances.

**Conclusions**

Patients undergoing UE tend to have smaller, rather superficially located STS with long-standing symptoms. During definite treatment for UE, however, more aggressive approaches in relation to the actual tumour biology are chosen. Due to more favourable prognostic factors prevailing in the UE-group, a prognostic benefit is suggested by univariate analysis. After adjustment for confounding variables by IPUEW-weighting, prognosis is similar for UE and non-UE patients. Thus, one may conclude that UEs have no bearing as to prognosis. However, the crucial unanswered question remains to which extent more aggressive treatment approaches (e.g. wide resections) following UE yet compensate for inappropriate primary resections. For that reason alone, UE of STS must be avoided.