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Follow-up for patients with extremity soft tissue sarcoma: validation of a rational schedule.

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Abstract:

Background: Patients with soft tissue sarcomas of the extremity (STS) require ongoing follow-up to detect treatment failures (local recurrence (LR) and distant metastasis (DM)). There is a significant variation in clinical practice among sarcoma specialists due to the paucity of evidence based guidelines to direct timing and duration of surveillance. A rational follow-up schedule based on annual rates of DM in one sarcoma center was proposed in 2020 but is not yet validated through data coming from a different referral center.

Questions:

- (1) What are the annual rates of LR and DM in a cohort of patients with STS from our center?
- (2) What is the proposed follow-up schedule based on the results from our cohort?
- (3) Is our proposed scheme comparable to the one proposed in 2020?

Methods: This is a retrospective review on a prospective registry in a tertiary multidisciplinary referral sarcoma center. All patients operated for a primary STS between 2004 and 2021 and with a minimum 1 year follow-up where included in this study. Patients were divided into 6 cohorts according to tumor's grade and size, and Lifetables were used to calculate the annual incidence of LR and DM in each cohort. Sub-groups that had similar annual local recurrence and metastatic risks were grouped together. Pre-determined thresholds for LR and DM annual risks were fixed a priori, based on literature review, to determine the corresponding follow-up interval. When the annual risk is >10%, follow-up every 3 months is recommended. If the annual risk is anywhere between 2.5% and 10%, a 6 months follow-up is advised. If the annual risk falls between 1 and 2.5%, annual follow-up is recommended.

<u>Results:</u> There were 407 patients that met the inclusion criteria, with a mean age of 55.8±17.2 years and a mean follow-up of 67.7±39.3 months. Fifty-eight percent of patients had large tumors (> 5cms) and 37% had grade 3 tumors. **(1)** Forty-seven patients (11.5%) in this cohort developed a LR during their follow-up while 82 patients (20%) experienced DM. **(2)** Taking into account the annual incidence of LR and DM per STS size and grade in this cohort, and abiding by the thresholds fixed a priori, patients with small, low grade STS should be followed yearly for ten years. Patients with small, intermediate/high grade STS and those with large, low grade STS should be followed every 6 months for the first two years and then yearly thereafter until 10 years post-operatively. Finally, patients with large, intermediate/high grade STS should be followed every 3 months for the first two years and then every 6 months thereafter till 10 years post-operatively (figure1). **(3)** Most of our proposed follow-up scheme is concordant with the one proposed previously, and seemingly validates it. Two differences were noted however, probably due to an under- or an over-estimation of the events annual rates between 5 to 10 years of follow-up because of the smaller number of patients at these post-operative ranges.

Conclusions: Compared to ESMO and NCCN guidelines, our proposed scheme significantly reduces hospital visits, mainly for patients with small intermediate and high-grade tumors. This protocol validates the previously published scheme despite being more conservative for small low grade tumors and large intermediate and high grade tumors. It provide a good rationale for implementing a risk based follow-up schedule instead of a generic one as currently proposed. A multicenter study including a larger number of patients and clinical settings is needed to draw stronger conclusions regarding the 5 to 10 years follow-up period; till then, the conservative approach is recommended.



Figure 1:

Figure legend:

Figure showing the proposed follow-up protocol for patients with extremity STS, based on the annual incidence of

LR and DM.