

The width of resection margins influences local recurrence in soft tissue sarcoma patients



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Accepted 21 March 2016

Available online 12 April 2016

Abstract

Background: Patients with soft tissue sarcoma (STS) being treated following the standardized guidelines can still not be guaranteed to remain free from local recurrence (LR). A complete tumour resection has been accepted as a major prognostic factor for LR. This retrospective study was designed to analyse the influence of two different classifications of resection margins (R-classification and UICC-classification) on LR in STS patients.

Materials and methods: Of 411 patients treated at our institution for STS, 265 were eligible for statistical analysis. Kaplan–Meier curves and Cox regression models were used to assess the impact of an R0 resection according to the R-classification (resection margin clear but allowing <1 mm) and according to the UICC-classification (minimal resection margin ≥ 1 mm) on LR.

Results: Survival curves showed a lower LR rate for R0 resections in the UICC-classification, namely 1.3%, 12% and 12% as compared to 2.1%, 9.5% and 16.5% for the R-classification. In multivariate analysis calculated separately for each classification, R1 resection as defined by the R-classification (HR: 11.214; 95%CI: 2.394–52.517; $p = 0.002$) as well as by UICC-classification (HR: 15.634; 95%CI: 2.493–98.029; $p = 0.003$) remained significant.

Conclusion: In our study, margin status according to both classifications represents an independent prognostic factor for LR in patients with STS following curative surgery. Local control rates were superior after a minimal resection margin of 1 mm (R0 by UICC-classification) compared to R0 resections after the R-classification.

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Keywords: Soft tissue sarcoma; Resection margin; Local recurrence

Introduction

Soft tissue sarcomas (STS) are rare malignant tumours deriving from mesenchymal tissue and constitute a heterogeneous group of tumours. These two facts – rarity and heterogeneity – alone demand high expertise and recommend treatment by a multidisciplinary team at specialized sarcoma centres in terms of providing best medical care for patients.^{1–4} Despite improvements in imaging, surgical techniques and adjuvant treatment modalities, local

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recurrence (LR) remains a significant problem in STS patients, ranging between 5% and 18%.^{3,5}

To date, several factors associated with clinical outcome in STS patients have been identified, including age, histologic subtype, tumour size, depth, site and grade.⁶ Whilst criteria like resection margins and tumour grade are generally accepted as factors for predicting LR (and partially for survival), the value of others such as age and tumour site is more uncertain.⁷ The width of resection margins is still discussed controversially.^{8,9}

Many descriptions of what is adequate may be found,¹⁰ and from adjectives like radical, compartmental, wide or close¹¹ until metric limitations ranging from 3 cm¹² to microscopic evaluation a big variety is represented.^{5,6,13–20} A curative intent, with few exceptions, is considered as a resection with negative margins, called R0 resection.³ In the ESMO guidelines, the decision about whether a margin is adequate or not is being shifted into a multidisciplinary setting where surgeons, pathologists and radio-oncologists are to decide about the success of the resection.³ In a recent report, for example, a resection margin of 2 mm or less was considered as being “positive”.¹⁷ The comparison of positive margins with margins between 2 mm and 2 cm as well as margins wider than 2 cm revealed a significantly worse prognosis for patients with positive margins.¹⁷ On the other hand, another group used the so-called R-classification for description of tumour margins.²¹ In this classification, R0 resection characterizes surgical margins that are macroscopically and microscopically negative for tumour cells; R1 involves a surgical margin which is microscopically contaminated or marginal tumour resection along a pseudo-capsule; R2 describes an intralesional tumour resection.²¹ Conclusively, in this report the R-classification is stated as best suited for clinical needs in routine practice.²¹ In another review concerning the TNM-staging system applied by the International Union against Cancer (UICC), the category of residual tumour (R-classification) was emphasized.²² Various authors suggested and preferred a classification of residual tumour in resection specimens, which respects a 1 mm cut-off. The suggested classification – from this point called UICC-classification – states a R0 margin as margins ≥ 1 mm; R1 describes margins that are < 1 mm to the tumour and R2 involves macroscopic tumour contamination.²² Consequently, the R-classification allows margins closer than 1 mm to be regarded as R0, whereas the UICC-classification declares margins closer than 1 mm as positive resection margins (R1) (Table 1).

To the best of our knowledge, no study has been previously published that compared the prognostic value of different classifications of resection margins in STS patients. For this purpose, the aim of the present study was to investigate the prognostic impact of two different classifications of resection margins (R-classification and UICC-classification) on LR in STS patients after surgical resection.

Table 1
Definition of resection margins according to the R- and UICC-classification.

R-classification	UICC-classification
R0: Tumour does not reach intact barrier or resection margins	R0: Resection margin > 1 mm
R1: Microscopic tumour contamination of margins or resection alongside pseudo-capsule	R1: Resection margin < 1 mm
R2: Macroscopic tumour contamination	R2: Macroscopic tumour contamination

Materials and methods

Subjects

Our retrospective analysis was based on a dataset that included 411 histologically confirmed STS patients. Each patient underwent definite surgical resection between March 1998 and January 2013 at our institution. Patients who had been treated inappropriately prior to referral (e.g. inadequate resection based on the assumption that the lesion would be benign) underwent re-resection at our department. The cases were discussed during a multidisciplinary team (MDT) meeting (i.e. tumour board), with the primary intent of limb-sparing surgery under maintenance of wide surgical margins. In cases where limb salvage was not feasible amputation had to be carried out or – with regards to the patients’ individual concerns and medical condition – a possible intralesional resection was accepted. The only exceptions in the intent of surgery were atypical lipomatous tumours (also known as well differentiated liposarcomas), in accordance with modern recommendations and guidelines.³ Due to changing awareness, marginal resection was planned for atypical lipomatous tumours by the second half of the analysed period.^{3,23}

Considering these facts, patients with ablative surgery, patients that were metastasized at primary surgery, retro- or intra-abdominal sarcomas and atypical lipomatous tumours had to be excluded. Moreover, patients with a follow-up less than 12 months were excluded, with the exception of patients who had died due to their disease within the first year, resulting in 265 eligible patients.

Tumour staging was ascertained based on *magnetic resonance imaging (MRI)*, *computed tomography (CT) scans* and *chest X-rays (CXR)*. During MDTs, administration of local adjuvant radiotherapy (RTX) and systemic chemotherapy (CTX) was planned for high risk patients. The main criteria that led to adjuvant RTX were high tumour grade, large tumour size and adverse events like intraoperative tumour violation. Criteria for administration of CTX consisted of high risk for systemic disease (following nomograms and multidisciplinary evaluation), primary inoperable tumours with neurovascular involvement and

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