

# Superficial soft tissue sarcomas: 10-year survival outcomes

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**Abstract.** Cutaneous sarcomas comprise a broad group of rare, heterogeneous mesenchymal tumours. The present report describes a single centre experience regarding the management and the outcomes of patients with superficial soft tissue sarcomas (SSTS). Key prognostic factors in predicting overall survival (OS) and local relapse-free survival were determined. Data from 66 patients with SSTS treated surgically within Edinburgh and Lothian were collected in the context of a service evaluation. Patient demographics, tumour specifics and treatment, as well as 5-year OS and local recurrence, were analysed. Kaplan-Meier analysis was applied for survival curves, and mortality rate estimation and Cox regression were used to establish independent predictors. The mean estimated OS time was 57.2 months, with a 95% CI between 55.0 and 59.5 months. The median OS time could not be estimated because there is no time point during which the survival function has a value <50%. The death risk for a person with SSTS was increased by 7.3% (odds ratio, 1.073; 95% CI, 1.012-1.138) for every additional year of life. The estimated mean local relapse time was 58.5 months, with a 95% CI between 56 and 61 months. The median local relapse time could not be estimated since there is no time point during which the local recurrence function has

a value <50%. In conclusion, out of all independent variables considered, none could statistically significantly explicate local relapse recurrence time. It is important that these rare tumours are treated in the context of a multidisciplinary team with consensus guidelines to assist decision-making.

## Introduction

Sarcomas are solid tumours accounting for ~1% of all malignant tumours in adults within Europe and the United States (1). Superficial soft tissue sarcomas (SSTS) are a rare group of heterogeneous tumours with at least 50 histological subtypes (2,3). By definition, SSTS occur above the superficial fascia and can arise in a variety of anatomical locations (4).

The mainstay of treatment for these tumours is surgical resection, however, post-operative radiotherapy or chemotherapy may also be employed (5,6). Resection with negative margins is the primary aim of surgical management in order to minimise the incidence of local recurrence (1).

Although prognostic factors for other cancers have been well described, data regarding SSTS outcomes remain comparatively limited (7). Factors identified as predictive of local recurrence include resection margin, tumour size, depth of tumour and histological type (8-10). Size and grade of SSTS have been identified as the key factors in predicting survival whilst other studies have suggested that patient age, tumour grade, lymph node involvement, and resection margin are important prognostic factors in determining the risk of distant metastatic disease (11-14). The biology of SSTS rather than the specific medical or surgical intervention has been found to be the greatest factor in survival (2).

NICE (National Institute for Health and Care Excellence) guidelines for quality standards in the management of sarcoma, published in January 2015, advise that healthcare professionals collect and publish data about sarcoma outcomes including site-specific data (REF) (15).

We report on a 10 year experience in the management of superficial soft tissue sarcoma in Southeast of Scotland and describe the epidemiological and prognostic factors related to

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**Abbreviations:** STS, soft tissue sarcomas; SSTS, superficial soft tissue sarcomas; OS, overall survival; LR, local recurrence; M, metastasis; NICE, National Institute for Health and Care Excellence; LRFS, local recurrence-free survival; MFS, metastasis-free survival; MMS, Mohs micrographic surgery

**Key words:** superficial, soft tissue, sarcomas, survival, outcomes

disease outcome with regard to overall survival, local recurrence and metastatic disease.

## Materials and methods

**Study description.** This is a service evaluation project, rather than research, hence no ethical approval was required. The project was endorsed by the Scottish Sarcoma Network (SSN) and the key findings aimed at informing the development of the Scottish cutaneous sarcoma guidelines. Eligible patients were those referred to our cancer network with a diagnosis of SSTS. Patients surgically treated for SSTS within Edinburgh and Lothian Hospital from January 2000 to November 2010, were retrospectively identified through histopathology coding, patient notes, electronic patient notes and the institutional pathology database. For each patient, the case notes or the electronic patient record was reviewed for demographics, as well as tumour and treatment details. We recorded the following items: gender, age, histology, tumour site, diameter, treatment modality (surgery/radiation/chemotherapy), surgical margin, date of local/metastatic recurrence and death. The Enneking surgical staging system was used to classify the surgical margins used (16). If patients had more than one operation in order to achieve satisfactory resection, then the re-excision margins were used to classify the resection. Data were stored securely and accessed only by the clinical team. Descriptive statistical analysis was performed by the authors.

**Statistical analysis.** Statistical analysis was performed using SPSS version 25.0 (IBM Corp.). Continuous variables were expressed as mean  $\pm$  standard deviation and categorical variables were expressed as numbers (percentages). The 5-year survival of 66 patients was studied. The survival analysis was conducted with the Kaplan-Meier method. Multivariate Cox regression analyses were utilized to identify independent risk factors of overall survival (OS) and relapse free survival (RFS). To determine if a new model-including explanatory variables-improves upon the baseline model, the Omnibus Tests of Model Coefficients are utilized. The log-likelihoods of the baseline model and the new model are compared using chi-square tests to determine whether there is a significant difference. All analyses were conducted in the statistical package SPSS 25 (IBM Corp.). The minimum value of statistical significance (P-value) was determined at 5%.

## Results

**Overall survival.** The study sample consists of 66 patients (20 women and 46 men) with a mean age of 51.7 years (Table I). The overall survival (OS) as Kaplan-Meier evaluation is shown in Tables II and III and Fig. 1. The number of terminal events (deaths) and censored observations (alive people) is presented in Table I. For the total of cases, the percentage of living observations is 89.4%. In Table III, the descriptive measures (mean and median value with the equivalent fluctuations) of OS are reported. Mean estimated survival time is 57.2 months, with a 95% confidence interval between 55 and 59.5 months. The estimation of the average survival time is limited to the highest full time thus ignoring any longer times, but which were censored. Median survival time cannot be estimated because

Table I. Sample descriptive characteristics.

Variable	Value
Mean age $\pm$ SD, years	51.7 $\pm$ 19.1
Sex, n (%)	
Female	20 (30.3)
Male	46 (69.7)

Table II. Case processing summary.

Total, n	No. of events	Censored, n (%)
66	7	59 (89.4)

Table III. Means and medians for overall survival time.

Variable	Mean <sup>a</sup>	Median <sup>b</sup>
Estimate	57.236	.
Std. error	1.133	.
95% CI	55.015-59.457	.

<sup>a</sup>Estimation is limited to the largest survival time if it is censored.

<sup>b</sup>The median survival time cannot be calculated because there is no time point at which the survival function takes value <50%

Table IV. Case processing summary (survival time).

Variable	No. (%)
Cases available in analysis	
Event <sup>a</sup>	7 (10.6)
Censored	52 (78.8)
Total	59 (89.4)
Cases dropped	
Cases with missing values	5 (7.6)
Cases with negative time	0 (0.0)
Censored cases before the earliest event in a stratum	2 (3.0)
Total	7 (10.6)
Total	66 (100.0)

<sup>a</sup>Dependent variable: Survival time.

there is no time point during which the survival function has a value <50% (See also Table III and Fig. 1).

The OS information concerning data (Cox Proportional Risk Model) is provided in Tables IV, V and VI, and Fig. 2. There are 5 missing values (3 about age and 2 about SIMD indicator) (17), no negative time and 2 censored cases before terminal event (death) in a stratum. 7 out of totally 59 cases

Table V. Omnibus tests of model coefficients.

-2 Loglikelihood	Overall (score)			Change from previous step			Change from previous block		
	$\chi^2$	df	Sig.	$\chi^2$	df	Sig.	$\chi^2$	df	Sig.
46.758	8.005	3	0.046	9.095	3	0.028	9.095	3	0.028

df, degree of freedom; Sig. statistical significance.

Table VI. Variables in the equation.

Variable	B	SE	Wald	df	Sig.	Exp(B)	95% CI for Exp(B)
Age	0.071	0.030	5.538	1	0.019	1.073	1.012-1.138
Sex	0.164	0.842	0.038	1	0.846	1.178	0.226-6.136
SIMD	-0.513	0.451	1.294	1	0.255	0.599	0.247-1.449

B, unstandardized regression coefficient; df, degree of freedom; Exp(B), odds ratio; SE, standard error of the coefficient B; Sig., statistical significance; SIMD, Scottish Index of Multiple Deprivation.

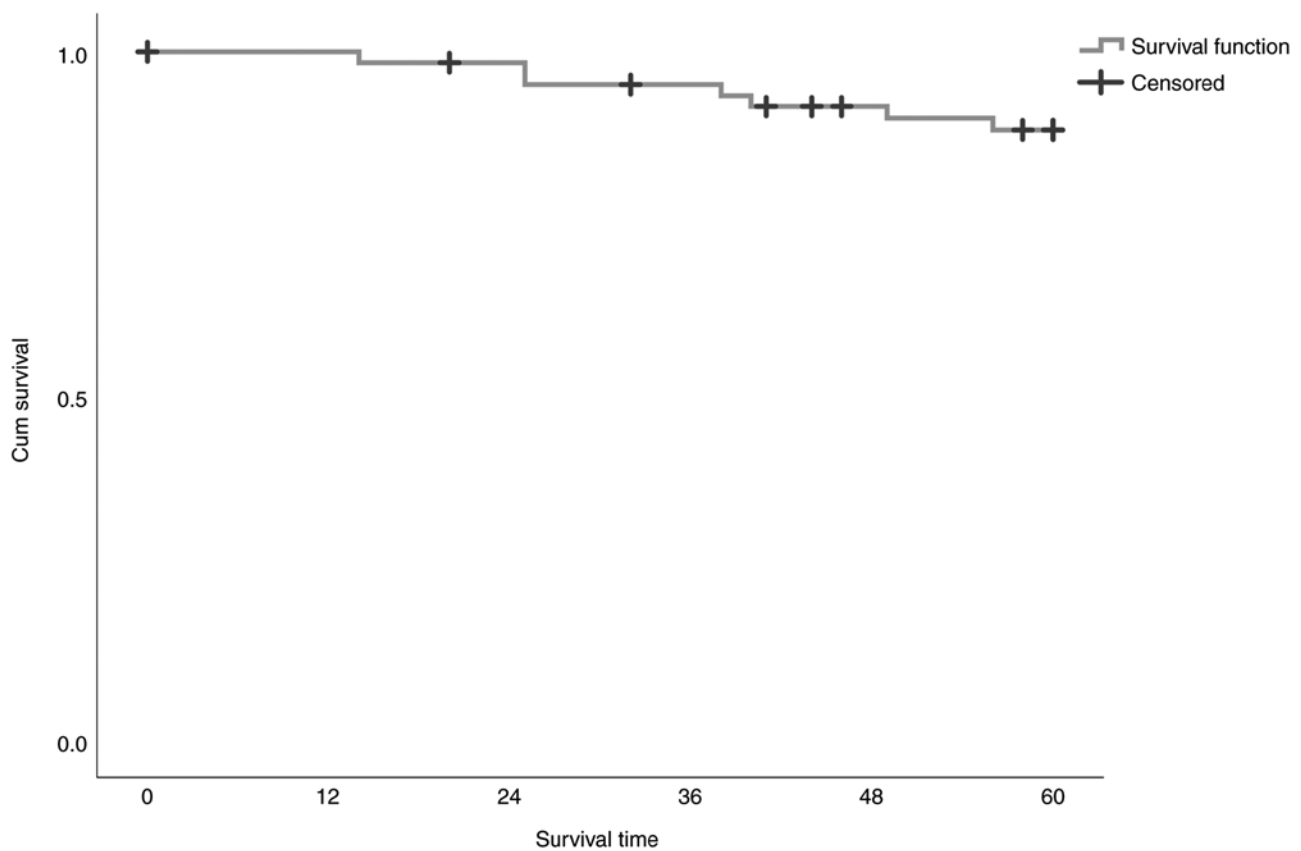


Figure 1. Overall survival function (survival curve using the Kaplan-Meier method).

(10.6%) presented this contingency while 52 (78.8%) concern censored survival time (Table IV). The independent variables chosen for Cox proportional risk model (OS) are: a) Age, b) sex, and c) SIMD indicator. In Table V there are provided the collective controls for the adjustment of the reciprocating model. Since  $\chi^2$  variation is statistically significant ( $P=0.046$ ),

the model is well adjusted. Meaning that at least one of the aforementioned independent variables significantly affects survival time (Table V). In Table VI, the assessment of the model parameters is recorded. We observe that, out of all the independent variables being in consideration, only age can statistically significantly explicate overall survival time. More

Table VII. Case processing summary (local relapse).

Total, n	No. of events	Censored, n (%)
66	3	63 (95.5)

Table VIII. Means and medians for local recurrence-free survival time.

Variable	Mean <sup>a</sup>	Median <sup>b</sup>
Estimate	58.516	.
Std. error	1.265	.
95% CI	56.036-60.996	.

<sup>a</sup>Estimation is limited to the largest survival time if it is censored.

<sup>b</sup>The median survival time cannot be calculated because there is no time point at which the survival function has a value <50%.

specifically, death risk for a person with SSTS (Superficial Soft Tissue Sarcomas) is increased by 7.3% [Exp(B)=1.073.95% CI(1.012, 1.138)] for every additional year of life. The estimated survival function, based on Cox Proportional Risk Model, is graphically presented in Fig. 2 and Table VI.

**Relapse free survival.** The local relapse free survival (Kaplan-Meier evaluation) is shown in Tables VII and VIII, and Figs. 3 and 4, as the number of terminal events (local relapse) and censored observations (people with no local relapse). The percentage of local relapse observations is 95.5%. Table VIII presents the descriptive measures (mean and median value with the equivalent fluctuations) of local relapse. The estimated mean local relapse time is 58.5 months, with a 95% confidence interval between 56 and 61 months. The estimation of mean local relapse time is limited to the maximum fulltime, thus ignoring any possibly bigger time that has been censored. Median local relapse time cannot be estimated since there is no time point during which the local recurrence function has a value <50%.

The local relapse free survival information on data (Cox Proportional Risk Model) is included in Tables IX, X and XI and Figs. 3 and 4. There are 5 missing values (3 about age and 2 about SIMD), no negative time and 2 censored cases before terminal event (local relapse) in a stratum. 3 out of 59 cases in total (4.5%) presented the contingency (local recurrence) while 56 (84.8%) are censored survival time. For Cox Proportional Risk Model (Overall Survival), we have chosen these independent variables: a) Age, b) Gender, and c) SIMD indicator. In Table X, there can be seen the collective controls for the adjustment of the reciprocating model. Since  $\chi^2$  variation is not statistically significant ( $P=0.321$ ), the model is not well adjusted. None of the aforementioned independent variables seem to significantly affect local recurrence time. In Table XI, the assessment of the model parameters is recorded. We observed that, out of all the independent variables being in consideration, none can statistically significantly explain local relapse recurrence time. The estimated survival

Table IX. Case processing summary (recurrence time).

Variable	No. (%)
Cases available in analysis	
Event <sup>a</sup>	3 (4.5)
Censored	56 (84.8)
Total	59 (89.4)
Cases dropped	
Cases with missing values	5 (7.6)
Cases with negative time	0 (0.0)
Censored cases before the earliest event in a stratum	2 (3.0)
Total	7 (10.6)
Total	66 (100.0)

<sup>a</sup>Dependent variable: Recurrence time.

function, based on Cox Proportional Risk Model, is graphically presented in Fig. 4.

## Discussion

Soft-tissue sarcomas are mesenchymal neoplasms with an incidence of <1% per year (1). SSTS are relatively rare entities and differ from deep sarcomas because they are usually smaller. Due to their small size and superficial location, these lesions are frequently treated by marginal or intralesional resection before referral to a sarcoma centre (18). SSTS present lower rates of distant metastasis and higher rates of disease-free survival (19).

Treatment of choice in patients with either SSTS or deep STS is complete surgical removal with wide negative margins (20). A sufficiently wide excision and micrographic control of margins, especially in anatomically challenging locations, should be attempted as they tend to recur locally. Mohs micrographic surgery (MMS) compared with wide local excision have shown a favourable outcome regarding local recurrence. Where available, MMS is currently the surgical treatment of choice for the majority of SSTS (especially in dermatofibrosarcoma protuberans).

In hospitals where it is not available, conventional surgery with deep margins 1 to 3 cm, is recommended (21). If resection margins are found positive in the final pathology, re-resection to obtain negative margins should strongly be advised if it will not have a significant impact upon functionality. Should excision not be feasible or adequate, radiotherapy should be employed (22). Our study established similar findings to other larger studies of prognostic factors and outcomes in SSTS (2,9,23). Age at diagnosis, tumour size and tumour grade were significantly associated with 5-year OS and LRFS.

These findings compare well with other studies in demonstrating that older age (>55 years), larger tumours and higher grade of tumour at diagnosis are all correlated to OS and LRFS (2,23,24). Other studies have demonstrated similar significance of these factors in the impact on MFS (2). As similar studies have concluded, the nature of SSTS tumours

Table X. Omnibus tests of model coefficients.

-2 Log Likelihood	Overall (score)			Change from previous step			Change from previous block		
	$\chi^2$	df	Sig.	$\chi^2$	df	Sig.	$\chi^2$	df	Sig.
19.944	3.497	3	0.321	4.032	3	0.258	4.032	3	0.258

df, degree of freedom; Sig., statistical significance.

Table XI. Variables in the equation.

Variable	B	SE	Wald	df	Sig.	Exp(B)	95% CI for Exp(B)
Age	0.078	0.049	2.495	1	0.114	1.081	0.982-1.190
Sex	0.018	1.235	0.000	1	0.988	1.019	0.091-11.450
SIMD	-0.336	0.631	0.284	1	0.594	0.714	0.207-2.460

B, unstandardized regression coefficient; df, degree of freedom; Exp(B), odds ratio; SE, standard error of the coefficient B; Sig., statistical significance; SIMD, Scottish Index of Multiple Deprivation.

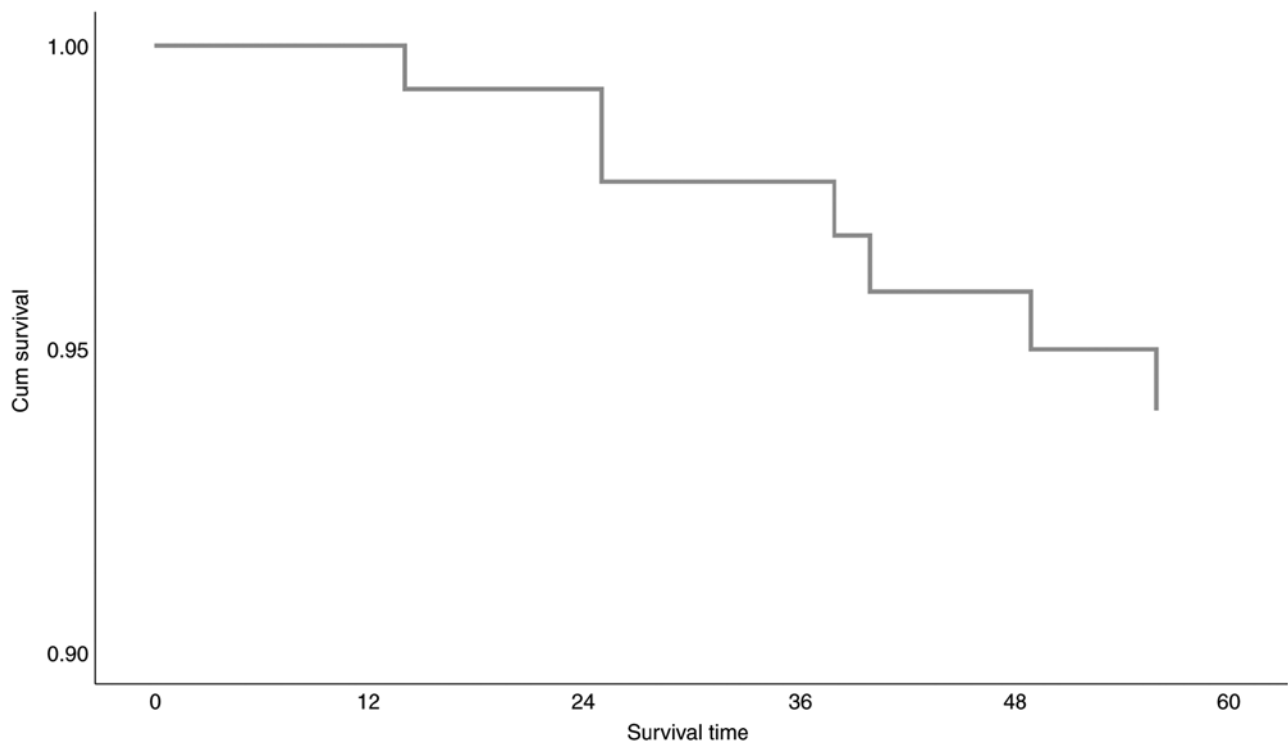


Figure 2. Survival function at mean of covariates (in months).

appears to have a significant impact on OS and LRFS (2,13). Surgical excision ensuring wide clear surgical margins remains the mainstay of local disease treatment. Wide excision and negative surgical margins are still the main goal. Radiotherapy and chemotherapy in neoadjuvant or adjuvant setting are secondary in excisable tumours and only in selected patients discussed in the MDT meeting. Our data showed a lower risk for local recurrence (6.1%) than has previously been reported (11-23%) and similar rate of overall metastasis (12.1%) (2). This

may be limited by the smaller number of cases in comparison with larger studies.

Additionally, metastatic disease at presentation was not significant in predicting OS, however, this may be skewed due to the small proportion of deaths in this study caused by SSTS and a larger case study may provide a more reliable conclusion. Like other studies, patient gender and tumour location were not significant in predicting OS or LRFS (1,2,23).

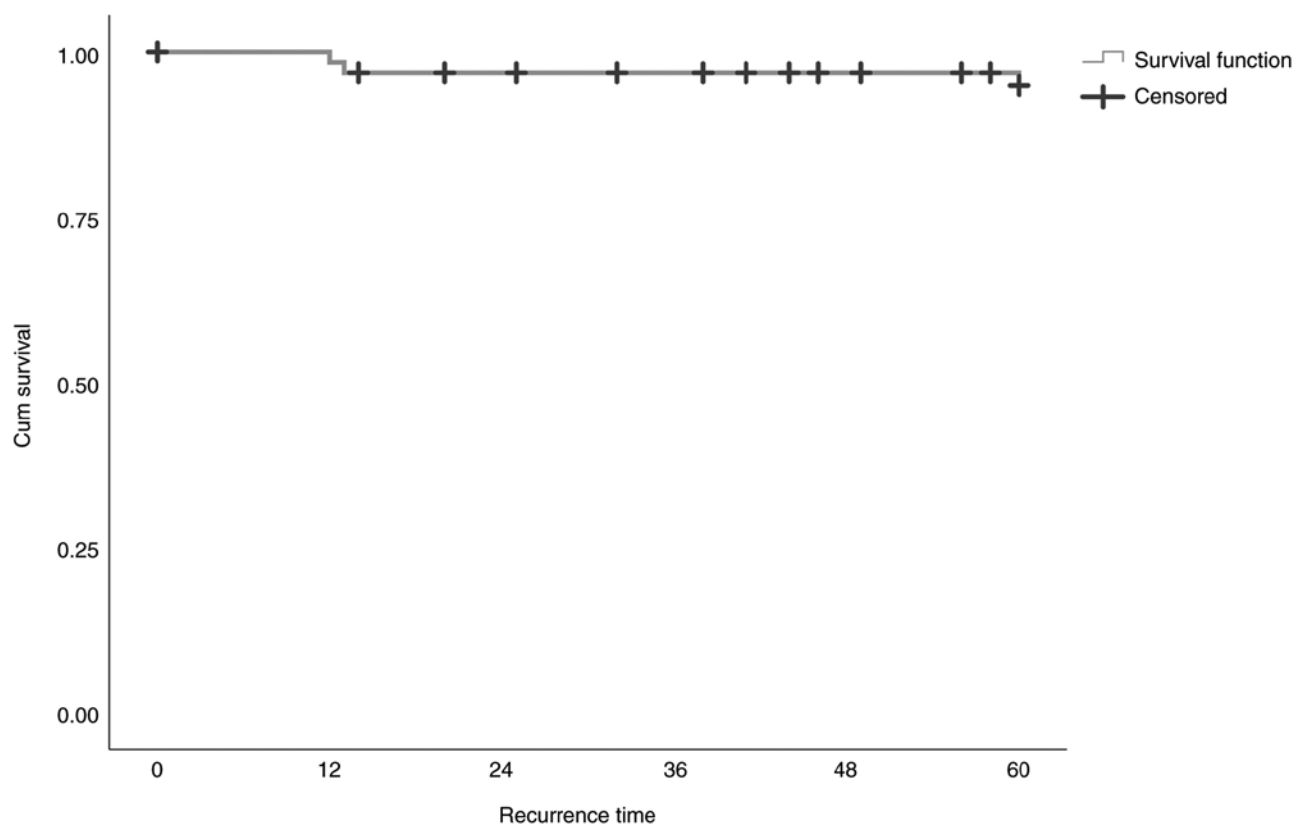


Figure 3. Local relapse-free survival function (in months).

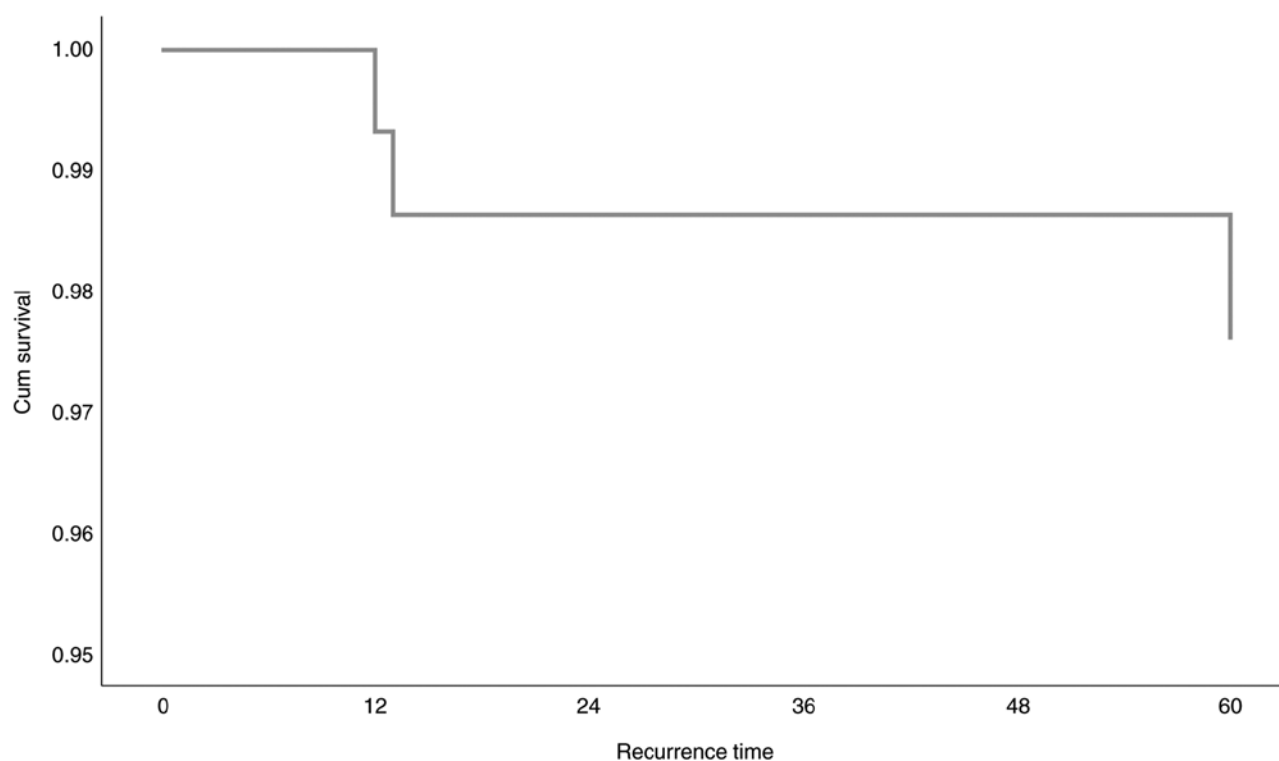


Figure 4. Local relapse-free survival function at mean of covariates (in months).

SSTS overall appear to have relatively good outcomes as demonstrated by our findings and elsewhere in the literature, with only a 6.1% mortality associated with SSTS at 5 years in

this study (11). Previous studies have alluded to the reason for this suggesting that the superficial nature of these tumours in comparison with deeper STS make them readily detectable and

comparatively easier to treat and monitor. Deeper STS tend to be larger at presentation in comparison to the average tumour size found in this study (20.7 mm) and elsewhere in the literature (2). This may be attributed to the fact that more superficial tumours can be detected by patients at an earlier stage, perhaps also explaining their superior outcomes. Other studies have found predominantly high-grade tumours in SSTS whilst we found the majority were low-grade tumours (1). However, data for tumour grade was available for only 66.6% of cases in this study.

The impact of surveillance in reducing mortality in SSTS has not been established and follow-up data in this study was insufficient for analysis. Scottish Sarcoma Network (SSN) has developed Scottish guidelines and all cases are discussed at the National Sarcoma MDT to ensure optimal care for these patients. In keeping with current UK guidelines, prospective collection of surveillance data may help to better define its significance in overall mortality in SSTS (7). As this study and others have demonstrated, significant factors relating to OS appear primarily related to the nature of the tumour (size and grade), rather than the surgical management therefore further investigation of aetiological factors may improve understanding of prognosis in these rare tumours.

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#### Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

#### Authors' contributions

MT, AG and IN conceived the study. MT, AG, LH and GG have made substantial intellectual contributions to the methodology (logic of study, research setting and participants, methods and procedures of data collection and analysis). DM and IN wrote the original draft. SP, AK, DM and IN reviewed and edited the manuscript. MT, AG and IN supervised the manuscript. IN, LH and GG confirm the authenticity of all raw data. AK and DM had a significant contribution in analysis and interpretation of data. All authors read and approved the final manuscript.

#### Ethics approval and consent to participate

Not applicable.

#### Patient consent for publication

Not applicable.

#### Competing interests

The authors declare that they have no competing interests.

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