Journal on Oncology

www.journalononcology.org

Research Article

Open Access, Volume 2

Functional Outcomes and Quality of Life in Patients who Underwent Limb Sparing Surgery for Soft Tissue Sarcomas

Manrique Gamo Elena[1]*; Echevarría Marín Marta[1]; Buendía Pérez Javier[2]; Rodríguez Zamorano Patricia[3]; García Maroto Roberto[3]; Cebrián Parra Juan Luis[3]

[1]Orthopaedic Surgery and Traumatology, Musculoesqueletal Sarcomas Department, Hospital Clínico San Carlos, Madrid, Spain.

[2]Plastic Surgery, Musculoesqueletal Sarcomas Department, Hospital Clínico San Carlos, Madrid, Spain.

[3]Orthopaedic Surgery and Traumatology, Musculoesqueletal Sarcomas Department, Hospital Clínico San Carlos, Madrid, Spain.

Abstract

The impact of soft tissue sarcoma (STS) surgery on the patient's quality of life and functional capacity after limb sparing surgery needs to be studied in greater depth due to the lack of information in the current literature.

Objective: To establish relationships between the different clinical and demographic characteristics studied and the quality of life and functional capacity of patients operated on for STS in extremities.

Materials and methods: We conducted a cross-sectional observational study where we selected a population of 68 patients operated on STS in the HCSC of Madrid from 2016 to 2021. Three questionnaires were handed out; one for quality of life (QLQ-C30) and two for functionality (TESS and MSTS).

Results: In the statistical analysis we found that a larger tumor axis (≥5 cm) (p=.048) and a larger tumor size determined in Anatomical Pathology (pT3 and pT4) (p=.008) resulted in a higher risk for worse functionality measured by the TESS. In addition, high pT values (pT3 and pT4) resulted in increased risk of scoring lower on the MSTS (p=.012). Also, having a comorbidity (p=.032) and high pT values (p=.001) were associated with a worse quality of life, measured by the QLQ-C30.

Conclusions: The results of this study show that the tumor's major axis, pT values and patient's comorbidities are related to their functional status and quality of life, while other variables such as age, sex or tumor depth are not related to the survey scores.

Keywords: Soft tissue sarcoma; Quality of life; Functional capacity; TESS; MSTS; QLQ-C30.

Abbreviations: AJCC: American Joint Committee on Cancer; NHSRC: National Health System Reference Center, Service or Unit; COPD: Chronic obstructive pulmonary disease; HCSC: Hospital Clínico San Carlos; MSTS: Musculoskeletal Tumor Society Score; IQR: Interquartile range; SD: Estandar deviation; RT: Radioterapy; SEOM: Spanish Society of Medical Oncology; STS: Soft Tissue Sarcomas; QLQ-C30: Quality of Life Core Questionnaire 30; QT: Quimiotheraphy; TESS: Toronto Extremity Salvage Score; WHO: World Health Organization.

Manuscript Information: *Received: Jun 20, 2022; Accepted: Aug 01, 2022; Published: Aug 08, 2022*

Correspondance: *Manrique Gamo Elena, Orthopaedic Surgery and Traumatology, Musculoesqueletal Sarcomas Department, Hospital Clínico San Carlos, Madrid, Spain. Tel: +34670040423; Email: manrique.elena@gmail.com*

Citation: *Elena MG, Marta EM, Javier BP, Patricia RZ, Roberto GM, et al. Functional Outcomes and Quality of Life in Patients who Underwent Limb Sparing Surgery for Soft Tissue Sarcomas. J Oncology. 2022; 2(2): 1039.*

Background

Soft tissue sarcomas (STS) are low-frequency tumors, constituting approximately 1% of all malignant tumors, and are responsible for 2% of cancer-related mortality. This, together with their clinical-histological variety, the difficulty of diagnosis and the technical complexity of treatments, makes sarcomas a pathology that requires the coordination of an expert multidisciplinary team to manage them adequately.

The estimated incidence in the European Union is about 5 new cases per year per 100,000 inhabitants. In Spain, with about 46 million inhabitants, it is expected that between 1840-2300 (mean: 2070) new cases/year of STS will be diagnosed, which would correspond to about 172 cases per month.

STS can be seen in all ages, including children and adolescents. However, the age of peak occurrence in adults is between 40 and 60 years [1]. They are slightly more frequent in men than in women, except in the age groups between 45-59 years, due to a peak incidence of gynecologic sarcomas.

Approximately 40% to 50% of STSs originate in the extremities and approximately 13% involve the trunk and 15% the retroperitoneum. Nodal metastases are very infrequent in this type of sarcoma, the most frequent being pulmonary.

Prognostic factors in patients with STS of the trunk and extremities include tumor grade, size and histologic subtype. Some studies have also found that deep location, positive margins, and lower extremity site are significantly associated with long-term outcome [1].

The fact that most are located in the extremities may condition a limitation of functional capacity and quality of life after surgical resection.

The Orthopedic Surgery and Traumatology Service of the HCSC is a Reference Unit of the National Spanish Health System for the care of patients suffering from STS, a pathology which is not very prevalent and which requires high technology and a high level of specialization for its diagnosis and treatment.

Surgery for STS, being a type of tumor that primarily affects the extremities, the type and size of the tumor and certain characteristics and comorbidities of the patient could have an impact on functional capacity and quality of life.

Few studies have been conducted that have published qualitative or quantitative data on the STS patient experience. Even knowing that STSs have a measurable impact on quality of life, there is a lack of information in the published literature [2].

Because of the above three circumstances, we have considered it relevant to carry out a determination of the different variables that could affect the patient's quality of life and functional capacity, or that could be related to a decrease in both.

Materials and methods

The aims of this study are:

- To interview and collect data from patients who have undergone STS surgery at HCSC regarding their functional capacity and quality of life.

- To establish which factors influence the quality of life of the patients who have undergone surgery.

- To determine the functional capacity of patients who have undergone STS surgery.

- To present the results on the quality of life after treatment of patients who underwent STS surgery at HCSC.

We conducted a cross-sectional observational study where we selected a population of 68 patients, obtained from a database of the Hospital Clínico San Carlos (HCSC) of Madrid from 2016 to 2021, diagnosed with SPB of different histological types in extremities. As inclusion criteria to be met by the patients, we established that they were older than 18 years, had been diagnosed and operated on for SPB in upper limbs or lower limbs at the HCSC and had been followed up for at least six months. Exclusion criteria included diagnoses of Kaposi's sarcoma, dermatofibrosarcoma protuberans, fibromatosis and angiosarcoma, as well as deceased patients and those who did not agree to answer the questionnaire.

Two quality of life questionnaires were administered in the case of an upper limb injury or three in the case of a lower limb injury. The questionnaires administered were: Toronto Extremity Salvage Score (TESS) measured functional disability in lower limb, while the Musculoskeletal Tumor Society Score (MSTS) measured functional impairment of both upper and lower limb. The European Organization for Research and Treatment of Cancer (EORTC) QLQ-C30 questionnaire measured quality of life.

For data collection, we followed the protocols established by the HCSC for accessing data from medical records in order to carry out this work. From this population we were able to obtain a sample of 44 patients due to losses due to death (n = 16) and non-response (n = 8).

With the resulting data, a statistical analysis was performed to relate the different variables with the score obtained from the TESS, MSTS and QLQ-C30 questionnaires on the patient's quality of life and functional capacity. The descriptive analysis of the data was carried out with the distribution of frequencies in the qualitative variables. For quantitative variables that are normally distributed, they are presented with mean (standard deviation); otherwise, with median [interquartile range]. For quantitative variables, such as the quality-of-life outcome variables, associations were analyzed using the Mann-Whitney U test, as quantitative variables did not conform to a normal distribution. For qualitative variables with more than 2 categories, the Kruskal-Wallis test was used. To study the correlation between all the quality-of-life outcome variables, Spearman's correlation was used because they were distributed nonparametrically. The association between qualitative variables was evaluated with the chi-square $\chi 2$ test or Fisher's exact test, in the event that more than 25% of the expected were less than 5. For all tests, a significance level of 5% was assumed. The analysis was carried out with the IBM SPSS Statistics v26 statistical software.

Results

Sixty-eight patients who met the inclusion criteria for the study were selected. Of the 68 eligible, 16 (23.5%) had died and 8 (11.8%) did not agree to participate in the study. The demographic and clinical characteristics of the patients are shown in Table 1.

The mean age of the patients was 61.65 (SD 17.56), with a higher number of males (60.3%). More than half of the patients had comorbidities (64.7%), of which the most frequent were arterial hypertension (33.8%) and dyslipidemia (22.1%). Approximately one third of the patients (32.4%) were active smokers.

The median diameter of the sarcomas was 9.7 cm (IQR (interquartile range) (4.8 - 16.0 cm), most of which were primary tumors (91.2%) and were located mainly in the lower limbs (67.6%), more specifically in the thighs (14.7%) and groins (10.3%).

In reference to the depth of the tumors, intracompartmental tumors were more frequent (79.5%), compared to extracompartmental tumors (20.6%).

Most tumors had a major tumor axis equivalent to pT2 (38.2%), followed by pT4 (26.5%) and pT1 (25%), while the minority had pT3 (10.3%). In reference to the tumor grade determined by AP, it could not be assessed in a quarter of the patients due to neoadjuvant QT and of those that could be assessed, more than half were grade 3 (54.9%), followed by grades 1 and 2 (21.6% both) and only a very low percentage presented grade 4 (2%).

Only 5.9% had lymph node metastases and 11.8% had distant metastases at diagnosis, while 25% had metastases during evolution.

Prior to surgery, 32.4% of patients received neoadjuvant treatment and after surgery, 54.4% received adjuvant treatment, either radiotherapy or chemotherapy or a combination of both.

Most patients underwent wide resection (82.4%) and the surgical edges were affected in 11.8% of patients. Collaboration with plastic surgery was required in more than half of the cases (63.2%) and only a quarter of the patients (25%) required some type of postoperative physiotherapy.

The results obtained in the three quality of life surveys are listed in Table 2. Most patients describe a good level of functioning on the surveys with the mean scores out of 100 being relatively high; 71.9 (SD 25.6) on the TESS, 83.2 (SD 12.4) on the QLQ-c30, 80.8 (SD 21.4) on the lower limbs part of the MSTS and 88.9 (SD 15.2) on the upper limb part of the MSTS.

Since the measurements are not normally distributed, the medians and interquartile ranges are also plotted in Table 2.

In the statistical analysis of demographic variables (age and sex), we found no significant correlations with the scores obtained in any of the questionnaires. Nor were significant differences found in the results according to tumor depth (intra/extracompartmental), degree of malignancy in AP (1, 2, 3 and 4) or type of adjuvant or neoadjuvant treatment received (RT, QT or both). We did detect a certain statistical trend between having received adjuvant treatment and a better score on the QLQ-C30 (p = ,075). We found significant differences between tumor major axis (<5cm, >=5cm) and functional outcome measured by TESS (p = ,048). There is a trend between resections with affected margins and having worse functional outcomes measured by MSTS for MMSS (p = ,085). We could not detect a significant difference between tumor location and the results of the different questionnaires, but we did find that having a smaller (pT1 and pT2) or larger (pT3 and pT4) AP-determined tumor size significantly influences the scores obtained in the QLQ-C30 (p = ,001), TESS (p = ,008) and MSTS for MMII (p = ,012). There is a statistically significant difference between having a comorbidity and quality of life as measured by the QLQ-C30 (p = .032), while smoking does not influence the questionnaires. These results can be summarized as follows in table 3.

Table 1: (a) Demographic data **(b)** Clinical characteristics.

VARIABLE	FREQUENCY
A) Demographic data	
Age	
Mean	61,7
Standard Deviation	17,6
Range	24,95
Sex	
Male	41
Female	27
B) Clinical characteristics	
Comorbidity	44
Dyslipidemia	15
Arterial hypertension	23
Hypo/Hyperthyroidism	6
Diabetes Mellitus 2	6
Benign prostatic hyperplasia	3
Chronic renal insufficiency	2
Atrial fibrillation	4
Obstructive sleep apnea	4
Prostate cancer	4
Pacemaker	3
COPD	3
Smoking	22
Tumor major axis (pT)	
pT1	17
pT2	26
pT3	7
pT4	18
Nodal metastases	
N0	57
N1	4
Nx	7
Anatomic pathology grade	
1	11
2	11
3	28
4	1
Not assessable	17
Primary or recurrence	
Primary	62
Recurrence	6
Metastasis	
At diagnosis	8
At evolution	17
Specific localization	
Thigh	10
Axilla	6
Groin	7
Arm	4
Elbow	4
Buttock	4
Other	33
Approximate location	
Upper	22
Lower	46
Right	36
Left	30

Major axis of tumor (cm)	
25th percentile	4,8
50th percentile	9,7
75th percentile	16
Tumor volume (cm^3)	
25th percentile	55,5
50th percentile	265,1
75th percentile	1023,8
Tumor depth	
Extracompartmental	14
Intracompartmental	54
Type of surgery	
Wide resection	56
Marginal resection	12
Surgical edges	
Free	56
Affected	12
Resection	
Bone	8
Motor nerve	14
Plastic surgery intervention	
Yes	43
No	24
Adjuvant/neoadjuvant treatment	
Neoadjuvant	22

Table 2: Functional scales scores.

Scales	N	Mean (Range; Standar Deviation)	Median (Interquarter Range)
MSTS(LOWER LIMB)	44	80,8 (26,7-100; 21,4)	87 (67-100)
MSTS(UPPER LIMB)	4 4	88,9 (40-100; 15,2)	93 (87-100)
QLQ-C30	4 4	83,2 (56,7-100; 12,4)	85 (75-94)
TESS	2 7	71,4 (10-99,2; 25,6)	81 (56-93)

Table 3: Variable statistical analysis. AP: Anatomopathological. IQR: Interquarter range. *statistical significancy (p<,050).

	N	QLQ-C30: Median (IQR)	p	MSTS: Median (IQR) Lower limb	p	MSTS Median (IQR) Upper Limb	p	TESS: Median (IQR)	p
Sex:								78 (55-93)	
Men	28	85 (73-95)	,845	93 (67-100)	,333	93 (87-100)	,664	84 (58-94)	
Women	16	85 (79-92)		85 (66-93)		97 (87-100)			
Localization:							,000	81 (75-93)	
Upper	17	87 (74-96)	,571	100 (88-100)	,000	87 (63-93)			
Lower	27	84 (75-93)		80 (63-93)		100 (93-100)		71 (47-)	
Depth:							,843	82 (56-93)	
Extracompartmental	9	84 (77-94)	,816	100 (82-100)	,124	93 (73-100)			
Intracompartmental	35	85 (77-94		87 (63-100)		93 (87-100)	,785	93 (67-98)	
Mayor axis (cm):								70 (49-919	
<5	15	89 (78-96)	,340	87 (33-100)		100 (87-100)			
>=5	29	84 (73-93)		87 (65-100)	,950	93 (87-100)			
Tumoral size AP:							,550	92 (63-96)	
Minor (pT1, pT2)	29	90 (82-96)	**,001***	93 (83-100)		93 (87-100)		64 (25-81)	
Mayor (pT3, pT4)	15	75 (66-84)		67 (53-87)	**,012***	100 (87-100)			
AP Grade:								94 (77-97)	
1	6	86 (70-99)		90 (82-95)		100 (70-100)	,778	60 (53-84)	
2	8	86 (80-90)	,915	85 (75-98)		100 (84-100)		61 (20-90)	
3	16	85 (68-93)		77 (54-100)	,710	93 (87-100)		93 (93-93)	
4	1	96 (96-96)		93 (93-93)		100 (100-100)		82 (59-93)	
Non valuable	13	82 (70-96)		93 (67-100)		87 (77-100)			
Neoadyuvancy:							,969	88 (59-95)	
No	28	86 (76-96)	,218	93 (64-100)	,691	93 (87-100)		64 (53-86)	
Yes	16	85 (67-91)		85 (67-98)		93 (87-100)			
Adyuvancy:							,617	75 (53-92)	
No	26	80 (68-91)	,075	85 (62-100)	,459	93 (86-100)		89 (64-94)	
Yes	18	91 (81-94)		93 (78-100)		93 (87-100)			
Comorbility:							,230	86 (57-95)	
No	17	91 (80-99)	**,0032***	93 (82-100)	,321	87 (85-100)		78 ((49-93)	
Yes	27	82 (69-91)		87 (63-100)		100 (87-100)			
Smoking:							,553	75 (58-94)	
No	31	84 (76-94)	,643	87 (67-100)	,695	93 (87-100)		87 (26-93)	
Yes	13	85 (70-94)		93 (57-100)		93 (87-100)			
Physical therapy:							,761	75 (56-93)	
No	32	84 (73-93)	,304	83 (58-98)	,054	93 (87-100)		86 (46-95)	
yes	12	90 (76-98)		97 (87-100)		97 (72-100)			

Discussion

The results of our study show, in terms of demographic variables, that we did not find significant differences in relation to the occurrence of sarcomas by age and sex. Although it can be seen that SPB is more frequent in men than in women (n = 41/n = 27). Our mean age of the study, was approximately 60 years (61.65 (SD 17.56)), which is in agreement with other studies [1]. For age and sex, no differences were found in the results of the quality of life and functionality questionnaires. In our study, the TESS questionnaire was found to have better functionality in women than in men, contrary to other studies [3,4].

In reference to patient-related variables, comorbidities do significantly affect quality of life (p = .032), but functionality is not altered, whether there are comorbidities or not.

Smoking is not a determinant for any of the different questionnaires. Contrary to a study claiming that smoking has an adverse effect on physical function [4].

In relation to the tumor-dependent variables, the major axis, is the parameter that most affects the TESS (p = ,048) when it is greater than 5 cm, without significantly influencing the MSTS and the QLQ-C30. This result coincides with some previous study, where it is stated that the increase in tumor size, results from a decrease in functionality [14]. Although these results are contradictory compared with the findings of other studies [3].

Regarding the location, it is concluded that the functionality, with MSTS, of the affected extremity will be lower if the sarcoma is located in the lower extremity (p50 = 80) than if it develops in the upper extremity (p50 = 86.67). This same finding has been proven in other studies where it is stated that patients with sarcomas in MMII have lower functionality and quality of life than those with sarcomas in the upper limbs [5].

However rim involvement yields worse functional outcomes for MMSS.

The pT value (tumor size determined by Anatomic Pathology), differentiating smaller (pT1 and pT2) and larger (pT3 and pT4), is the most influential data, being able to observe that tumors with higher pT value significantly affect both quality of life and functionality of the patient (QLQ p = ,010 / TESS p = ,080 / MSTS MMII p = ,120), except for MSTS in upper limbs, which is independent of the pT value.

In our study we found that tumor depth and histological grade, are not determinants in the outcome of functionality and quality of life. The findings regarding tumor depth are corroborated by some studies [5], but are contradictory to the findings of a previous study [6].

In relation to treatment, neoadjuvant, RT and QT, do not affect in TESS, MSTS, nor QLQ-C30 score. In our study we found that adjuvant does demonstrate a tendency to increase the quality of life of patients receiving treatment after surgery (p = ,074), this is supported by a meta-analysis stating that adjuvant chemotherapy was associated with a modest improvement in survival and constitutes a standard option in selected patients with high-risk STS [7].

In our results, adjuvance does not present any interest in the functionality of the different patients. This fact is contrasted, in part, with a study of 185 randomized patients, determined that postoperative RT is associated with increased functionality in relation to MSTS and TESS at six weeks after surgery [5].

Patients who have received SPB physiotherapy in MMII show a tendency (p = ,540) to improve their functionality compared to those who do not receive it; the data would be conclusive if we were to increase the study sample.

In our study we obtained that the tumor axis and the size measured in PA has an influence on the patient's quality of life and functional status. This is in agreement with the results of previous studies which conclude that tumor size, histologic type and tumor grade influence patient prognosis [1].

Conclusions

STSs affect the patient's functionality and quality of life. Therefore, management should be done in reference centers with a multidisciplinary Sarcoma Committee, with better overall survival and disease-free survival rates.

The variables that most affect functional outcome are staging, tumor axis or size.

Patient comorbidities affect quality of life but not functional outcome.

Functionality is lower if the STS is located in lower limbs

Border involvement produces worse functional outcome in upper limbs.

It is necessary to include a larger sample in the study to increase the consistency of the data.

Declarations

Ethical statement and conflict of interest: The submitting authors have not financial or personal conflict of interests. All procedures performed in studies involving human participants were in accordance with the ethical standards of the ethical committee in our hospital. The patient gave informed consent for the submission of this case study for publication. This study was performed in accordance with relevant guidelines and regulations.

References

1. Gamboa AC, Gronchi A, Cardona K. Soft-tissue sarcoma in adults: An update on the current state of histiotype-specific management in an era of personalized medicine. CA Cancer J Clin. 2020; 70: 200-229.
2. Sociedad Española de Oncología Médica. SEOM. Sarcomas de partes blandas. 2020.
3. Saebye C, Fugloe HM, Nymark T, Safwat A, Petersen MM, et al. Factors associated with reduced functional outcome and quality of life in patients having limb-sparing surgery for soft tissue sarcomas - a national multicenter study of 128 patients. Acta Oncol. 2017; 56: 239-244.
4. Heaver C, Isaacson A, Gregory JJ, Cribb G, Cool P. Patient factors affecting the Toronto extremity salvage score following limb salvage surgery for bone and soft tissue tumors. J Surg Oncol. 2016; 113: 804-10.

5. Davis AM, O'Sullivan B, Bell RS, Turcotte R, Catton CN, et al. Function and health status outcomes in a randomized trial comparing preoperative and postoperative radiotherapy in extremity soft tissue sarcoma. J Clin Oncol. 2002; 20: 4472-7.

6. Gerrand CH, Wunder JS, Kandel RA, O'Sullivan B, Catton CN, Bell RS, Griffin AM, Davis AM. The influence of anatomic location on functional outcome in lower-extremity soft-tissue sarcoma. Ann Surg Oncol. 2004; 11: 476-82.

7. Pervaiz N, Colterjohn N, Farrokhyar F, Tozer R, Figueredo A, Ghert M. A systematic meta-analysis of randomized controlled trials of adjuvant chemotherapy for localized resectable soft-tissue sarcoma. Cancer. 2008; 113: 573-81.