

Mapping the Course of Recovery Following Limb-Salvage Surgery for Soft-Tissue Sarcoma of the Extremities

Alexander L. Lazarides, MD, Zachary D.C. Burke, MD, Manit K. Gundavda, DNB(Orth), David C. Clever, MD, Anthony M. Griffin, MSc, Kim Tsoi, MD, PhD, Peter C. Ferguson, MD, and Jay S. Wunder, MD, MSc

Investigation performed at the University of Toronto, Toronto, Ontario, Canada

Background: Despite the goal of an acceptable functional result, the surgical treatment of soft-tissue sarcoma can portend a prolonged course of recovery. More comprehensive data on the expected course of recovery following extremity sarcoma surgery are needed to help to inform physicians and patients. The purpose of the present study was to describe the typical course of functional recovery following limb-salvage resection of a soft-tissue sarcoma and to identify factors associated with a delayed postoperative course of recovery.

Methods: A retrospective review of a prospectively maintained institutional database was performed for all patients undergoing surgical treatment with limb salvage of a soft-tissue sarcoma of the extremities or pelvis with at least 1 year of follow-up after the definitive surgical procedure. All patients were required to have preoperative functional outcomes recorded for either the Toronto Extremity Salvage Score (TESS) or the Musculoskeletal Tumor Society (MSTS) score and functional outcome measures at 1 year postoperatively. The primary outcome measures were time to recovery and maximal functional improvement.

Results: In this study, 916 patients met inclusion criteria following surgical resection of a soft-tissue sarcoma of the extremities. The median follow-up was 74 months. Patients typically achieved a return to their baseline preoperative level of function for all functional outcome measures by 1 to 2 years and achieved maximal functional recovery by 2 years postoperatively. Older age, female sex, deep tumor location, larger tumor size, pelvic location, osseous resection, motor nerve resection, free and/or rotational soft-tissue coverage, and postoperative complications were independently associated with worse TESS and/or MSTS scores ($p \leq 0.05$). Tumor recurrence was associated with worse functional outcomes scores. An analysis was performed to determine which patients had a prolonged course of recovery (i.e., were considered to still be recovering). Older age, female sex, larger tumor size, osseous resection, and motor nerve resection were associated with a delayed course of recovery ($p \leq 0.04$). Complications and tumor recurrence were associated with delayed functional recovery across all domains.

Conclusions: Most patients will achieve maximal recovery by 2 to 3 years following surgical resection for soft-tissue sarcoma of the extremities. Older age, female sex, larger tumor size, osseous resection, motor nerve resection, postoperative complications, and tumor recurrence portend poorer functional outcomes and a delayed course of recovery.

Level of Evidence: Prognostic Level IV. See Instructions for Authors for a complete description of levels of evidence.

Wide resection, with or without adjuvant therapy, is the mainstay of treatment for soft-tissue sarcoma of the extremities. Surgical options to achieve this aim include amputation or limb-salvage surgery, depending on the tumor location and the extent of the neurovascular, osseous, and soft-tissue involvement. Historically, an amputation was

considered necessary to achieve local control; however, limb salvage has emerged as the standard of care due to improved psychosocial results and superior functional outcomes^{1,2}.

Despite the goal of a cancer-free limb with good function, the surgical treatment of soft-tissue sarcoma can portend a prolonged course of recovery. Previous studies have suggested

Disclosure: No external funding was received for this work. The **Disclosure of Potential Conflicts of Interest** forms are provided with the online version of the article (<http://links.lww.com/JBJS/1152>).

TABLE I Patient, Tumor, and Treatment Characteristics for the Analyzed Cohort

No. of patients	916
Age* (yr)	54 (42 to 67)
Age†	
>40 years	706 (77%)
≤40 years	210 (23%)
Sex†	
Male	492 (54%)
Female	424 (46%)
Anatomic location†	
Upper extremity	240 (26%)
Lower extremity	643 (70%)
Pelvis	33 (4%)
Specific site††	
Wrist/hand	40 (4%)
Elbow	85 (9%)
Shoulder	114 (13%)
Pelvis	33 (4%)
Hip	259 (28%)
Knee	308 (34%)
Ankle/foot	70 (8%)
Depth††	
Superficial	286 (31%)
Deep	629 (69%)
Histological subtype†	
Liposarcoma	215 (24%)
Undifferentiated pleomorphic sarcoma	188 (21%)
Sarcoma not otherwise specified	107 (12%)
Myxofibrosarcoma	101 (11%)
Leiomyosarcoma	91 (10%)
Synovial sarcoma	63 (7%)
Malignant peripheral nerve sheath tumor	37 (4%)
Fibrosarcoma	25 (3%)
Dermatofibrosarcoma protuberans	20 (2%)
Solitary fibrous tumor	19 (2%)
Fibromyxoid sarcoma	14 (2%)
Extraskeletal myxoid chondrosarcoma	14 (2%)
Soft-tissue osteosarcoma	12 (1%)
Epithelioid sarcoma	10 (1%)
Grade†††	
1	129 (15%)
2	355 (41%)
3	398 (46%)
Tumor size* (cm)	6.4 (4.1 to 10.3)
≥10 cm†	239 (27%)
<10 cm†	658 (73%)

*continued***TABLE I (continued)**

Prior surgery††	
Yes	269 (29%)
No	643 (71%)
Surgery type†	
Primary wide resection	762 (83%)
Tumor bed re-excision	154 (17%)
Radiation therapy††	
Yes	720 (79%)
No	195 (21%)
Radiation therapy timing††	
Preoperative only	538 (59%)
Postoperative only	167 (18%)
Preoperative and postoperative	15 (2%)
None	195 (21%)
Chemotherapy†	
Yes	18 (2%)
No	898 (98%)
Osseous resection†	
Yes	53 (6%)
No	863 (94%)
Vascular resection and reconstruction†	
Yes	28 (3%)
No	888 (97%)
Motor nerve resection†	
Yes	25 (3%)
No	891 (97%)
Soft-tissue coverage†	
None	642 (70%)
Skin graft	73 (8%)
Rotational flap	137 (15%)
Free flap	64 (7%)
Resection margin status††	
Negative	776 (85%)
Positive	138 (15%)
Complications††	
Yes	271 (32%)
No	585 (68%)
Surgery for complications††	
Yes	114 (14%)
No	675 (86%)

*The values are given as the median, with the IQR in parentheses.
†The values are given as the number of patients, with the percentage in parentheses. ††The number of patients in this section does not equal 916 because of missing data.

that increasing age, larger tumor size, certain tumor locations, and motor nerve sacrifice adversely affect postoperative functional recovery³⁻⁵. Reduced functional outcomes have a negative

TABLE II Summary of Functional Outcomes Scores at Each Time Point, with Nonparametric Comparison Versus the Previous Time Point

	MSTS87 Score (Range, 0 to 5)	MSTS93 Score (Range, 0 to 100)	TESS (Range, 0 to 100)
Preoperative score			
No. of patients	897	892	810
Median*	33 (31 to 35)	100 (93 to 100)	95 (78 to 100)
3-month score			
No. of patients	648	640	577
Median*	29 (25 to 33)	83 (67 to 93)	82 (66 to 94)
P value between preoperatively and 3 months†	<0.001	<0.001	<0.001
6-month score			
No. of patients	723	715	650
Median*	31 (27 to 35)	93 (80 to 100)	90 (75 to 98)
P value between 3 and 6 months†	<0.001	<0.001	<0.001
12-month score			
No. of patients	832	827	755
Median*	31 (29 to 35)	93 (80 to 100)	92 (78 to 99)
P value between 6 and 12 months†	0.003	0.004	0.03
24-month score			
No. of patients	619	615	558
Median*	33 (29 to 35)	97 (87 to 100)	93 (82 to 99)
P value between 12 and 24 months†	0.001	0.001	0.016
36-month score			
No. of patients	454	448	416
Median*	33 (31 to 35)	97 (90 to 100)	95 (84 to 100)
P value between 24 and 36 months†	0.07	0.1	0.42

*The values are given as the median, with the IQR in parentheses. †Significant values are shown in bold.

correlation with quality of life in patients with soft-tissue sarcoma^{4,6,7}. However, more comprehensive data on the expected timelines for recovery following extremity sarcoma surgery are needed to help to inform physicians and especially patients about the potential to return to their “pre-sarcoma” baseline.

The Musculoskeletal Tumor Society (MSTS) score is a commonly used method for assessing physician-reported functional outcomes, and the Toronto Extremity Salvage Score (TESS) is a commonly used method for assessing patient-reported functional outcomes following extremity sarcoma surgery^{8,9}. Using these functional outcomes measures, the purpose of this study was to map the typical timelines for postoperative recovery following limb-salvage surgery for soft-tissue sarcomas of the extremities.

Materials and Methods

Following institutional review board approval, a retrospective review of a prospectively maintained institutional database was performed for all patients undergoing surgical treatment with limb salvage of a soft-tissue sarcoma of the extremities or pelvis between January 1, 1992, and November 15, 2020 (n = 3,021). All patients with soft-tissue sarcomas of the pelvis and extremities with at least 1 year of follow-up after the de-

finitive surgical procedure were considered eligible for inclusion; 443 patients died or were lost to follow-up within 1 year. All patients were required to have preoperative TESS or MSTS functional outcome scores^{8,9} and functional outcome measures at 1 to 2 years postoperatively, which resulted in an additional 1,220 patients being excluded. We excluded patients with a tumor location outside the extremities or pelvis, those with non-primary sarcomas, and those with well-differentiated liposarcomas, as these patients typically underwent resection in a marginal fashion and were not treated with the same surgical intent as those with a sarcoma. This resulted in excluding an additional 442 patients, leaving 916 patients eligible for analysis.

We had 3 primary questions: (1) When do patients undergoing resection of a soft-tissue sarcoma of the extremities return to baseline or reach maximal recovery? (2) What factors are associated with reduced functional outcomes measures at 1 year? (3) What factors are associated with delayed maximal recovery? We hypothesized that patients would continue to see continued functional recovery beyond 1 year and that similar patient, tumor, and treatment-related characteristics would be associated with reduced functional outcomes and prolonged functional recovery.

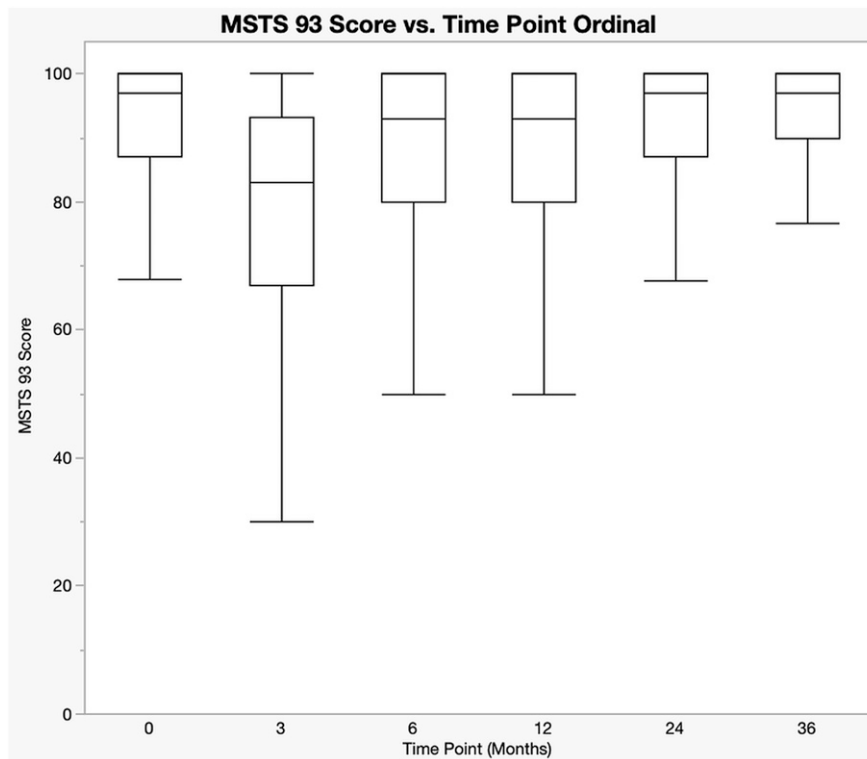


Fig. 1-A

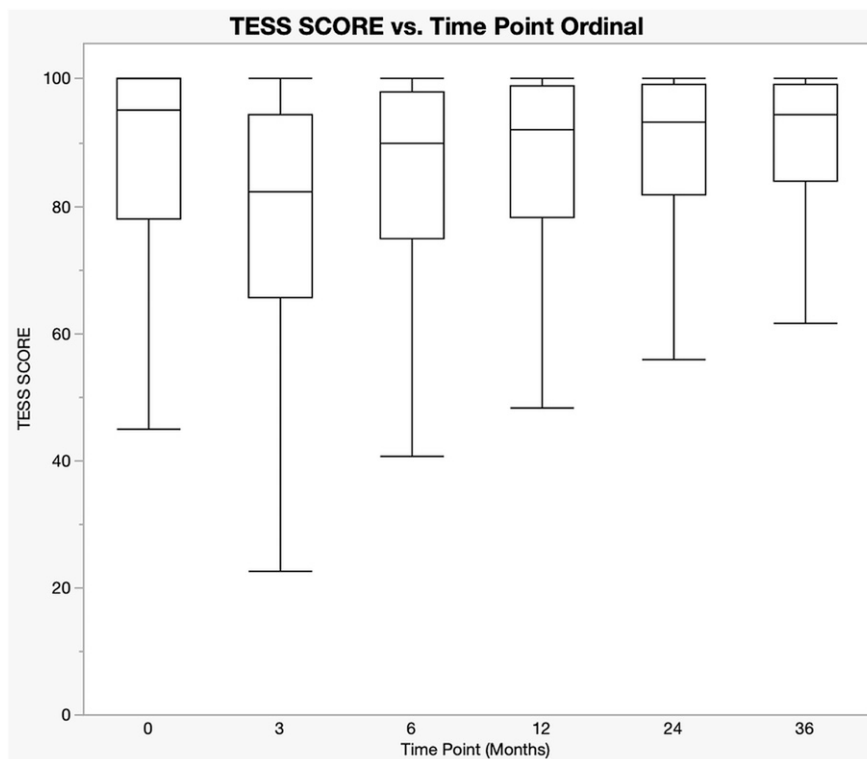


Fig. 1-B

Figs. 1-A, 1-B, and 1-C Box plots of functional outcome scores over time from the preoperative baseline function to 36 months following surgical resection. A box represents the IQR, the line within the box represents the median, and the whiskers represent the range. **Fig. 1-A** MSTS93 outcomes. **Fig. 1-B** TESS outcomes.

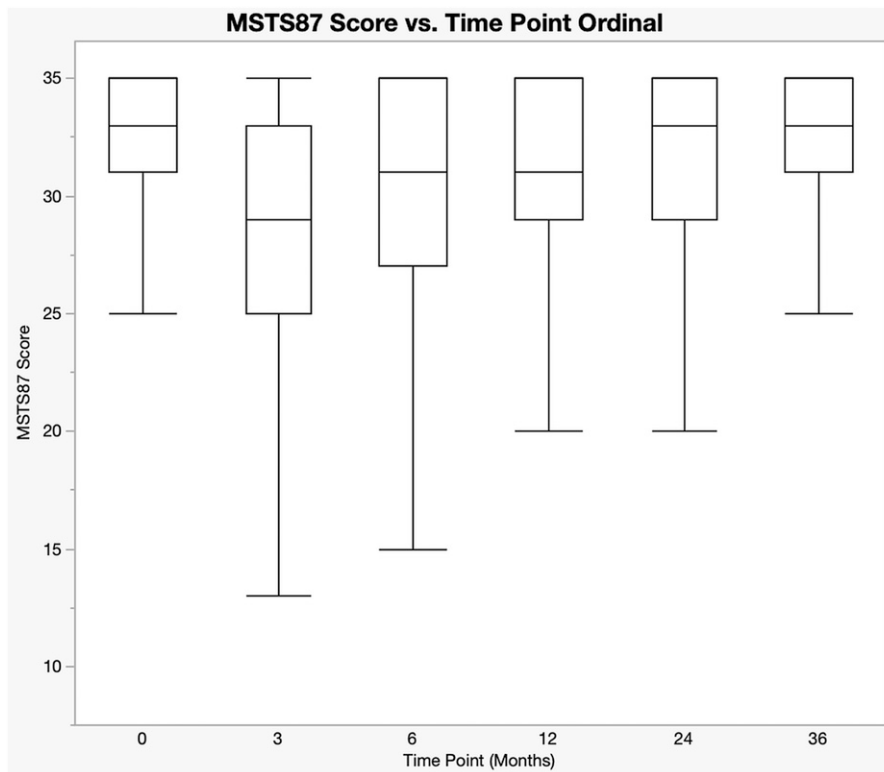


Fig. 1-C
MSTS87 outcomes.

The primary outcome measures were recovery, defined as not demonstrating improvement on 2 consecutive follow-up appointments, as defined by the TESS and MST87 score functional outcome measures, and maximal recovery, defined as achieving 90% of the patient's final maximum outcome score. This level was selected as changes above this level were believed to be unlikely to represent a minimally clinically important difference from the maximum overall score and would account for nonsignificant variation between visits once a patient had reached a plateau¹⁰.

All patients admitted to the hospital underwent postoperative inpatient physiotherapy evaluation and treatment. Postoperative disposition was determined on the basis of the inpatient postoperative assessment and, if more intensive rehabilitation was required, transfer to an inpatient rehabilitation center was provided. Outpatient physiotherapy was typically prescribed for patients at 4 to 6 weeks postoperatively during follow-up visits. Follow-up was performed on an established schedule for 5 to 10 years following surgical resection, based on tumor size and grade¹¹.

Statistical Analysis

Data were compared using unadjusted statistical methods; normally distributed continuous variables were compared using a Student t test, whereas nonparametric continuous variables were compared using a Wilcoxon-Mann-Whitney test. A chi-square test or a Fisher exact test was used to compare categorical data. A sensitivity analysis was performed for tumor size and identified that a 10-cm cutoff had the best association

with whether or not maximal recovery was achieved by 2 years, and this cutoff was used for subsequent analyses. A multivariable Poisson regression model using maximum likelihood estimation methods was used to identify factors associated with functional outcome scores at 1 year. A multivariable logistic regression model was used to compare factors associated with achieving maximal recovery by 2 years. Significance was denoted by $p \leq 0.05$. JMP Pro 15 software (SAS Institute) was used to perform all statistical analyses.

Results

We identified 916 eligible patients who underwent limb-sparing surgical resection of a soft-tissue sarcoma of the extremities (Table I) and had a median follow-up of 74 months (range, 12 to 352 months). Patients were typically older (median age, 54 years [interquartile range (IQR), 42 to 67 years]) and tended to have lower-extremity tumors (643 [70%]). Most tumors were deep to fascia (629 [69%]). Most tumors were intermediate or high grade (753 [82%]), and they had a median size of 6.4 cm (IQR, 4.1 to 10.3 cm). Most patients underwent radiation therapy (720 [79%]) and underwent margin-negative resection (776 [85%]). Postoperative complications occurred in 271 patients (30%), with 114 patients (12%) requiring a return to the operating room for management.

Course of Functional Recovery

Patients demonstrated a significant drop in all functional outcome measures from their preoperative baseline to postoperatively

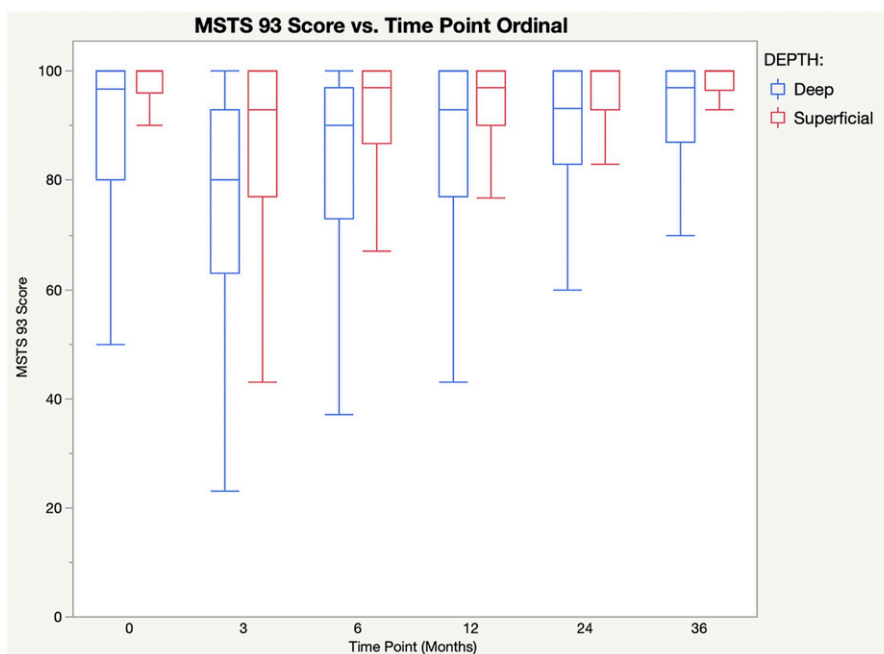


Fig. 2-A

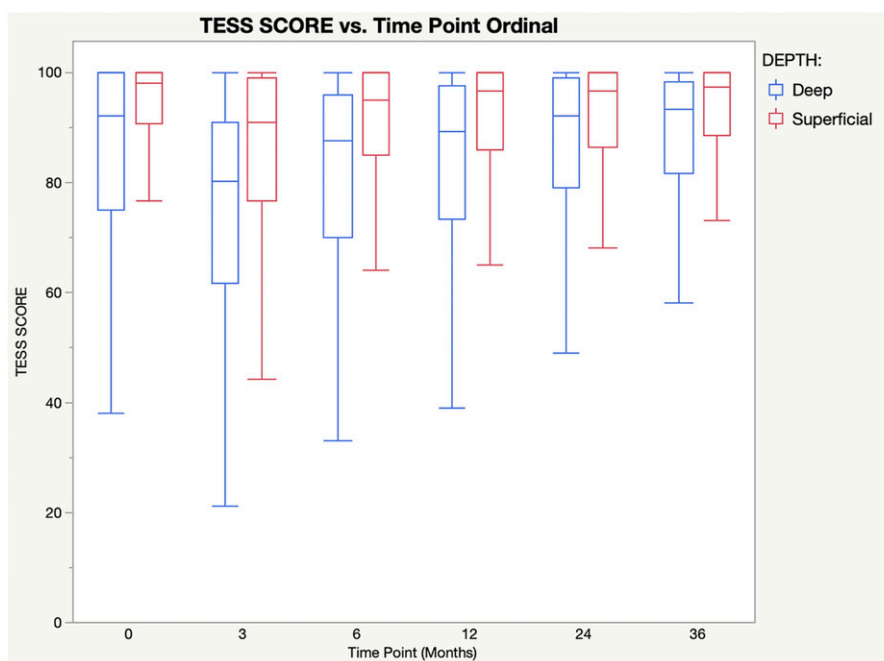


Fig. 2-B

Figs. 2-A, 2-B, and 2-C Box plots of functional outcome scores over time from the preoperative baseline function to 36 months following surgical resection, stratified by tumor depth. A box represents the IQR, the line within the box represents the median, and the whiskers represent the range. **Fig. 2-A** MSTS93 outcomes. **Fig. 2-B** TESS outcomes.

(Table II). Patients typically achieved a return to their preoperative level of function for all functional outcome measures between 1 and 2 years postoperatively (Figs. 1-A, 1-B, and 1-C). Patients typically achieved maximal functional recovery on all functional outcome measures by 2 years postoperatively. There was no significant improvement from

2 to 3 years postoperatively for any of the functional outcome measures.

When stratified by tumor depth, patients with a superficial tumor demonstrated a more rapid recovery, achieving maximal functional recovery on all functional outcome measures by 6 months postoperatively, whereas those with deep

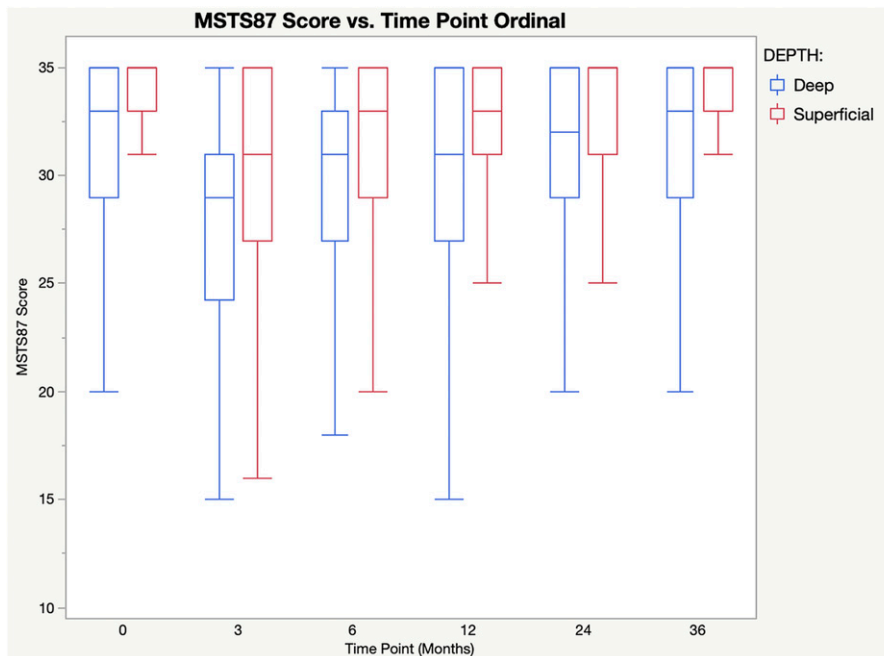


Fig. 2-C
MSTS87 outcomes.

tumors typically achieved maximal functional recovery on all functional outcome measures by 2 years postoperatively (Figs. 2-A, 2-B, and 2-C). When stratified by tumor size, those with a smaller tumor demonstrated a more rapid recovery, achieving maximal functional recovery on all functional outcome measures by 6 months postoperatively, whereas those with a tumor of >10 cm typically achieved maximal functional recovery on all functional outcome measures by 2 years postoperatively (Figs. 3-A, 3-B, and 3-C).

Factors Associated with Functional Outcomes

Scores were compared by univariate methods across a range of patient, tumor, and treatment factors (see Appendix Supplementary Table 1). A multivariable analysis was then performed to identify the factors that were independently associated with diminished functional outcomes measures at 1 year postoperatively (Table III).

Female sex, larger tumor size, and tumor recurrence within 1 year were all independently associated with worse functional outcome measures across all functional outcome domains. Older age was associated with worse MSTS93 and TESS outcomes. A pelvic location was associated with a worse TESS, whereas a deep tumor location was associated with worse MSTS93 scores. Tumors that required bone resection, motor nerve resection, or soft-tissue coverage with free or rotational flaps were associated with worse MSTS87 and MSTS93 scores. Soft-tissue coverage was also associated with worse TESS outcomes. Radiation therapy was not associated with worse functional outcomes measures. The development of complications was associated with worse MSTS93 and TESS outcomes, whereas a surgical procedure for complica-

tions was associated with worse MSTS87 and MSTS93 scores. Tumor recurrence, locally or systemically, in the first year was associated with worse functional outcome measures across all domains.

Reaching Maximal Recovery

An analysis was performed to determine which patients had a prolonged course of recovery (i.e., were considered to still be recovering). Maximal recovery was considered to be achieved when the functional outcome score reached 90% of the final recorded score of the patient. By 2 years, among patients with the respective functional outcome scores reported, 422 patients (74%) had achieved their maximal TESS, 452 patients (73%) had reached their maximal MSTS87 score, and 479 patients (78%) had achieved their maximal MSTS93 score.

We compared the patients who had not reached their maximal recovery by 2 years with patients who had achieved maximal recovery by this time point by univariate methods (see Appendix Supplementary Table 2). A multivariable analysis was then performed to identify the factors that were independently associated with a prolonged course of recovery at 2 years postoperatively (Table IV).

Older age and female sex were associated with delayed functional recovery when considering MSTS93 scores. Larger tumor size was associated with delayed functional recovery when considering both MSTS93 scores and the TESS. Osseous resection was associated with delayed functional recovery for both MSTS87 and MSTS93 scores. Postoperative complications were associated with delayed recovery for MSTS87 scores. Recurrence, locally or systemically, was associated with delayed functional recovery.

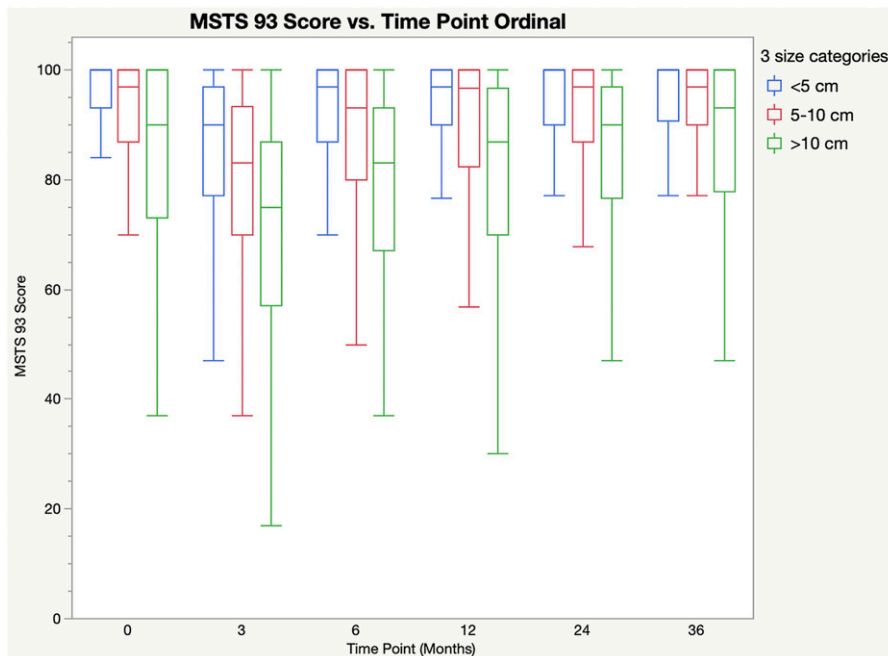


Fig. 3-A

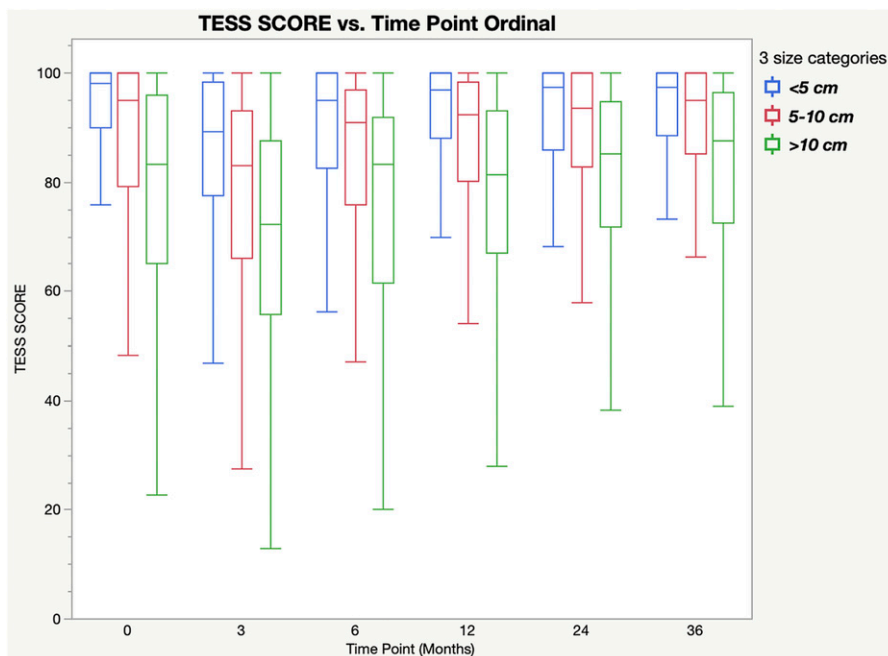


Fig. 3-B

Figs 3-A, 3-B, and 3-C Box plots of functional outcome scores over time from the preoperative baseline function to 36 months following surgical resection, stratified by tumor size. A box represents the IQR, the line within the box represents the median, and the whiskers represent the range. **Fig. 3-A** MSTS93 outcomes. **Fig. 3-B** TESS outcomes.

Discussion

Limb salvage has emerged as the standard of care for most patients with extremity and pelvic soft-tissue sarcomas. The extent of resection can be quite variable, such that the treatment of soft-tissue sarcoma can portend a prolonged course of recovery in some cases¹². The results of this study demonstrate

that most patients will return to their baseline preoperative function between 1 and 2 years postoperatively, and most patients will achieve maximal recovery by 2 years. More debilitated patients with lower preoperative functional scores predictably have lower postoperative functional outcome scores, but the majority still recover to their preoperative baselines.

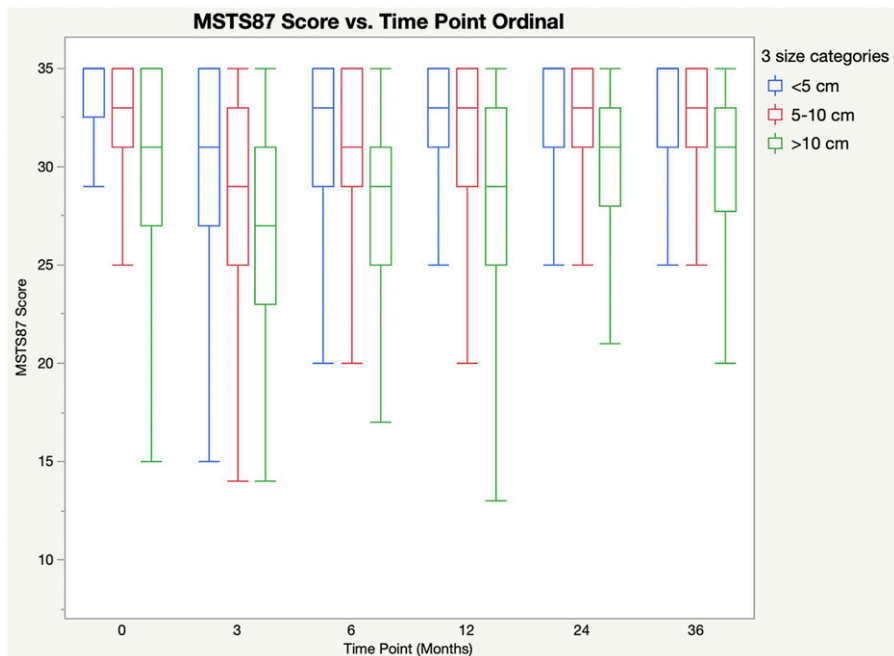


Fig. 3-C
MSTS87 outcomes.

Older age, female sex, larger tumor size, bone resection, motor nerve resection, postoperative complications, and both local and systemic tumor recurrence frequently lead to worse functional outcomes and a delayed course of recovery. Utilizing this information to set patient expectations about their anticipated level of recovery and the time it takes to achieve maximal recovery has become a valuable practice in preoperative counseling of patients with soft-tissue sarcoma.

A variety of outcome measures have been used to assess function following sarcoma surgery¹³. This study utilized 3 measures of function, the MSTS87¹⁴, the MSTS93⁸, and the TESS⁹. The TESS is designed to assess disability and has the benefit of being reported by the patients themselves. In contrast, the 2 MSTS scores are designed to assess impairment and are completed by clinicians. The MSTS87 is a joint-specific measure, whereas the MSTS93 considers the entire involved limb, thus assessing different components of physical function. Furthermore, the MSTS93 includes emotional acceptance, which is not included in the MSTS87 scores. We found that the time course of recovery did not specifically differ between these outcome measures. The implication is that the patient and clinician perspectives of recovery are similar and that recovery from impairment and from disability follow a similar time course. There are notable instances where the association of certain patient, tumor, or surgical factors with functional recovery differed between the MSTS93 and MSTS87. The contribution that emotional acceptance makes to functional recovery, which is not assessed in the MSTS87, might explain these discrepancies.

We found that patients undergoing resection of deeper and larger tumors had a more protracted course of recovery. These findings corroborate the results of prior investigations. A

study by Davis et al. found that functional scores returned to baseline levels by 1 year postoperatively³. The study additionally found that larger tumor size had a negative effect on recovery, although, interestingly, tumor depth did not. Patients undergoing resection of large, deep tumors will typically require more extensive dissections with a larger quantity of soft-tissue removal to provide a suitable resection margin. Additionally, these extensive resections were more frequently associated with the use of radiation, which itself may increase complication rates and negatively affect functional recovery.

We found that factors associated with worse functional outcomes include older age, female sex, larger tumor size, bone resection, motor nerve resection, free flap or rotational flap utilization, postoperative complications, and tumor recurrence. Many other studies have previously assessed functional outcome following sarcoma surgery. Stoeckle et al. found that predictive factors for functional impairment included postoperative complications, neoadjuvant chemotherapy, and bone or neurovascular involvement¹⁵. Importantly, they also showed that early rehabilitation after surgery led to improved outcomes. Davis et al. found that large tumor size, bone resection, motor nerve resection, and complications were associated with lower MSTS scores, whereas large tumors, high tumor grade, and motor nerve resection correlated with a lower TESS⁴. Compared with these previous studies, our current findings demonstrate that similar trends also hold true in a much larger patient cohort. Furthermore, our study characterizes the temporal impact of nonmodifiable patient, tumor, and surgical factors on recovery after the surgical procedure.

We identified some notable differences from prior investigations. Saebye et al. found that radiation therapy was

TABLE III Multivariable Analysis of the Association of Patient, Tumor, and Treatment Factors with Worse Functional Outcome Scores at 1 Year Postoperatively*

Variable	MSTS 87 Score at 1 Year		MSTS 93 Score at 1 Year		TESS at 1 Year	
	Effect Size†	P Value‡	Effect Size†	P Value‡	Effect Size†	P Value‡
Age ≥40 years	-0.01 (-0.02 to 0.01)	0.33	-0.02 (-0.03 to -0.01)	<0.001	-0.02 (-0.03 to -0.01)	0.02
Female sex	-0.03 (-0.04 to -0.02)	<0.001	-0.03 (-0.04 to -0.02)	<0.001	-0.02 (-0.03 to -0.01)	0.003
Location in an extremity, versus the pelvis	—	—	—	—	0.05 (0.01 to 0.06)	0.005
High grade	0.001 (-0.03 to 0.03)	0.38	0.001 (-0.02 to 0.02)	0.97	0.0 (-0.02 to 0.02)	0.96
Size ≥10 cm	-0.04 (-0.05 to -0.02)	<0.001	-0.05 (-0.06 to -0.04)	<0.001	-0.06 (-0.07 to -0.05)	<0.001
Had prior surgery	0.002 (-0.02 to 0.02)	0.78	0.001 (-0.01 to 0.02)	0.52	0.01 (-0.004 to 0.02)	0.72
Deep to fascia	-0.01 (-0.03 to 0.01)	0.07	-0.01 (-0.03 to -0.01)	0.004	-0.01 (-0.02 to 0.001)	0.26
Osseous resection	-0.06 (-0.1 to -0.03)	<0.001	-0.06 (-0.08 to -0.05)	<0.001	-0.03 (-0.05 to -0.01)	0.08
Vascular reconstruction	—	—	—	—	0.01 (-0.01 to 0.04)	0.45
Motor resection	-0.04 (-0.1 to -0.01)	0.002	-0.08 (-0.1 to -0.05)	<0.001	-0.02 (-0.05 to 0.01)	0.39
Received radiation therapy	-0.01 (-0.03 to -0.01)	0.07	-0.01 (-0.02 to 0.01)	0.34	-0.003 (-0.02 to 0.01)	0.65
Had soft-tissue coverage	-0.01 (-0.03 to -0.001)	0.02	-0.02 (-0.03 to -0.01)	0.002	-0.01 (-0.02 to -0.003)	0.02
Positive margin status	0.004 (-0.02 to 0.02)	0.64	0.01 (-0.003 to 0.02)	0.36	0.01 (-0.004 to 0.03)	0.21
Had complications	-0.01 (-0.04 to 0.01)	0.07	-0.03 (-0.05 to -0.02)	<0.001	-0.06 (-0.08 to -0.05)	<0.001
Surgery for complications	-0.04 (-0.07 to -0.02)	0.002	-0.02 (-0.04 to -0.003)	0.02	0.01 (-0.004 to 0.03)	0.44
Had recurrence within 1 year	-0.03 (-0.06 to -0.01)	0.02	-0.03 (-0.05 to -0.02)	<0.001	-0.04 (-0.06 to -0.03)	0.004

*The symbols — indicate that this variable was not included in the analysis for that specific patient-reported outcome measure. †The values are given as the effect size, with the 95% confidence interval in parentheses. ‡Bold values are significant.

associated with worse functional outcomes⁶, a finding that differed from the present study. Radiation therapy can lead to a variety of sequelae that can impact functional recovery and that

differ on the basis of the timing of the intervention, including an increased risk of wound complications if administered preoperatively compared with increased risks of soft-tissue

TABLE IV Multivariable Analysis of the Association of Patient, Tumor, and Treatment Factors with Not Achieving Maximal Functional Recovery by 2 Years Postoperatively*

Variable	MSTS 87 Score at 1 Year		MSTS 93 Score at 1 Year		TESS at 1 Year	
	OR†	P Value‡	Effect Size§	P Value‡	Effect Size§	P Value‡
Age ≤ 40 years	—	—	2 (1.1 to 3.5)	0.021	1.5 (0.9 to 2.5)	0.09
Female sex	—	—	1.8 (1.2 to 2.8)	0.01	—	—
Size ≥10 cm	1.5 (0.9 to 2.4)	0.1	1.7 (1.1 to 2.9)	0.035	1.6 (1.1 to 2.6)	0.036
Had prior surgery	—	—	—	—	1.4 (0.9 to 2.4)	0.15
Tumor bed re-excision	1.1 (0.6 to 2.1)	0.75	1 (0.46 to 2.1)	0.97	—	—
Deep to fascia	—	—	1.2 (0.64 to 2.2)	0.58	—	—
Osseous involvement	3.1 (1.5 to 6.5)	0.003	2.6 (1.2 to 5.7)	0.015	—	—
Motor resection	—	—	2.8 (0.9 to 7.9)	0.054	2.2 (0.7 to 6.9)	0.16
Received radiation therapy	0.8 (0.44 to 1.4)	0.43	2.1 (0.9 to 4.6)	0.065	—	—
Positive margin status	0.6 (0.35 to 1.1)	0.061	—	—	1.6 (0.9 to 2.8)	0.07
Had complications	1.9 (1.1 to 3.4)	0.036	1.5 (0.8 to 3.0)	0.22	1.5 (0.9 to 2.3)	0.051
Surgery for complications	1 (0.5 to 2.1)	0.91	1.4 (0.6 to 3.0)	0.4	—	—
Had recurrence within 2 years	1.6 (0.8 to 3.1)	0.16	2.5 (1.3 to 5)	0.007	2.5 (1.3 to 4.8)	0.005

*The symbols — indicate that this variable was not included in the analysis for that specific patient-reported outcome measure. †The values are given as the odds ratio (OR), with the 95% confidence interval in parentheses. ‡Bold values are significant. §The values are given as the effect size, with the 95% confidence interval in parentheses.

fibrosis, joint stiffness, pain, and lymphedema if given postoperatively¹⁶. However, recent work has demonstrated that radiation therapy may not, in and of itself, be a driver of worse functional outcomes. A possible explanation is that the factors that necessitate the use of radiation therapy utilization, such as larger tumor size, deep tumor location, and neurovascular and bone abutment or involvement, have a stronger correlation with functional outcomes than radiation therapy itself.


We also identified that the need for free or rotational flap coverage was associated with worse functional outcome scores at 1 year when compared with primary wound closure. These findings contrast with a prior study by Davidge et al. in which flaps were not found to be an independent predictor of worse function, but were associated with other clinical features associated with worse functional outcomes⁵, findings that were corroborated by an investigation by Slump et al.¹⁷. In contrast, Kang et al. performed a comparative analysis between patients with flaps and patients undergoing primary wound closure for soft-tissue sarcoma and showed that patients with flaps demonstrated worse functional outcome scores overall¹⁸. When considering these results, it is important to acknowledge that the use of flaps is typically dictated by tumor factors, including the extent of superficial soft-tissue involvement and anticipated skin loss, large dead spaces in irradiated wounds, and the inability to close a wound primarily.

Although this is the largest study investigating functional outcomes in soft-tissue sarcoma patients, to our knowledge, there were several limitations. First, although we observed significant differences in functional outcome measures, this study was not specifically geared to detect minimal clinically important differences between time points, as has been done for other sarcoma populations^{10,19}. Second, there was no standardized postoperative physical therapy regimen instituted for patients after they left the hospital. Although all inpatients were assessed and received physiotherapy before discharge from hospital, their ultimate disposition was heterogenous and not readily available in our database. Furthermore, with a large portion of potentially eligible patients excluded from analysis because of loss to follow-up and limited functional outcome score availability beyond 1 year, the impact on the available data, analyses, and interpretation must be considered. Finally, as this was a retrospective review, the study was subject to selection bias, which may have influenced the interpretation of the present findings. Given the

retrospective nature of the study, the results must be interpreted as hypothesis-generating rather than prescriptive and should provide a foundation of baseline data for comparison in future investigations of more specific and controlled questions.

In conclusion, most patients recovered to their baseline level of function between 1 and 2 years postoperatively, and most patients achieved maximal recovery by 2 years following surgical resection of extremity soft-tissue sarcoma. Older patient age, female sex, larger tumor size, bone resection, motor nerve resection, postoperative complications, and tumor recurrence were all associated with worse functional outcomes and a delayed course of recovery. These patient, tumor, and treatment factors should be taken into consideration when counseling patients as to their expected course of recovery following these surgical procedures.

Appendix

 Supporting material provided by the authors is posted with the online version of this article as a data supplement at <http://links.lww.com/JBJS/1153>. ■

Alexander L. Lazarides, MD^{1,2}
Zachary D.C. Burke, MD^{2,3}
Manit K. Gundavda, DNB(Orth)^{2,4}
David C. Clever, MD²
Anthony M. Griffin, MSc²
Kim Tsoi, MD, PhD²
Peter C. Ferguson, MD²
Jay S. Wunder, MD, MSc²

¹Sarcoma Department, Moffitt Cancer Center, Tampa, Florida

²University of Toronto Musculoskeletal Oncology Unit, Division of Orthopaedic Surgery, Department of Surgery, Mount Sinai Hospital, University of Toronto, Toronto, Ontario, Canada

³Department of Orthopaedic Oncology, Cleveland Clinic, Cleveland, Ohio

⁴Division of Orthopaedic Oncology, Centre for Bone and Joint Cancer, Kokilaben Dhirubhai Ambani Hospital and Medical Research Institute, Mumbai, India

Email for corresponding author: alexander.lazarides@moffitt.org

References

- Davis AM, Devlin M, Griffin AM, Wunder JS, Bell RS. Functional outcome in amputation versus limb sparing of patients with lower extremity sarcoma: a matched case-control study. *Arch Phys Med Rehabil*. 1999 Jun;80(6):615-8.
- Malek F, Somerson JS, Mitchel S, Williams RP. Does limb-salvage surgery offer patients better quality of life and functional capacity than amputation? *Clin Orthop Relat Res*. 2012 Jul;470(7):2000-6.
- Davis AM, O'Sullivan B, Bell RS, Turcotte R, Catton CN, Wunder JS, Chabot P, Hammond A, Benk V, Isler M, Freeman C, Goddard K, Bezjak A, Kandel RA, Sadura A, Day A, James K, Tu D, Pater J, Zee B. Function and health status outcomes in a randomized trial comparing preoperative and postoperative radiotherapy in extremity soft tissue sarcoma. *J Clin Oncol*. 2002 Nov 15;20(22):4472-7.
- Davis AM, Sennik S, Griffin AM, Wunder JS, O'Sullivan B, Catton CN, Bell RS. Predictors of functional outcomes following limb salvage surgery for lower-extremity soft tissue sarcoma. *J Surg Oncol*. 2000 Apr;73(4):206-11.
- Davidge KM, Wunder J, Tomlinson G, Wong R, Lipa J, Davis AM. Function and health status outcomes following soft tissue reconstruction for limb preservation in extremity soft tissue sarcoma. *Ann Surg Oncol*. 2010 Apr;17(4):1052-62.
- Saebye C, Fugloje HM, Nymark T, Safwat A, Petersen MM, Baad-Hansen T, Krarup-Hansen A, Keller J. 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 Feb;56(2):239-44.
- Schreiber D, Bell RS, Wunder JS, O'Sullivan B, Turcotte R, Masri BA, Davis AM. Evaluating function and health related quality of life in patients treated for extremity soft tissue sarcoma. *Qual Life Res*. 2006 Nov;15(9):1439-46.
- Enneking WF, Dunham W, Gebhardt MC, Malawar M, Pritchard DJ. A system for the functional evaluation of reconstructive procedures after surgical treatment of tumors of the musculoskeletal system. *Clin Orthop Relat Res*. 1993 Jan;(286):241-6.

- 9.** Davis AM, Wright JG, Williams JI, Bombardier C, Griffin A, Bell RS. Development of a measure of physical function for patients with bone and soft tissue sarcoma. *Qual Life Res.* 1996 Oct;5(5):508-16.
- 10.** Gazendam AM, Schneider P, Bhandari M, Busse JW, Ghert M; on behalf of the PARITY Investigators. Defining minimally important differences in functional outcomes in musculoskeletal oncology. *J Bone Joint Surg Am.* 2022 Sep 21;104(18):1659-66.
- 11.** Wilson DAJ, Gazendam A, Visgauss J, Perrin D, Griffin AM, Chung PW, Catton CN, Shultz D, Ferguson PC, Wunder JS. Designing a rational follow-up schedule for patients with extremity soft tissue sarcoma. *Ann Surg Oncol.* 2020 Jun;27(6):2033-41.
- 12.** Kollár A, Müller S, Limacher A, Briner I, Klenke F, Bernhard J. Return to work and quality of life in disease-free adult patients with soft-tissue and bone sarcoma of the extremity. *Praxis (Bern 1994).* 2021 Jan;110(1):22-9.
- 13.** Kask G, Barner-Rasmussen I, Repo JP, Kjälldman M, Kilk K, Blomqvist C, Tuukiainen EJ. Functional outcome measurement in patients with lower-extremity soft tissue sarcoma: a systematic literature review. *Ann Surg Oncol.* 2019 Dec;26(13):4707-22.
- 14.** Enneking W, Dunham W, Gebhardt M, Malawar M, Pritchard D. A system for the classification of skeletal resections. *Chir Organi Mov.* 1990;75(1)(Suppl):217-40.
- 15.** Stoeckle E, Michot A, Rigal L, Babre F, Sargos P, Henriques de Figueiredo B, Brouste V, Italiano A, Toulmonde M, Le Loarer F, Kind M. The risk of postoperative complications and functional impairment after multimodality treatment for limb and trunk wall soft-tissue sarcoma: long term results from a monocentric series. *Eur J Surg Oncol.* 2017 Jun;43(6):1117-25.
- 16.** O'Sullivan B, Davis AM, Turcotte R, Bell R, Catton C, Chabot P, Wunder J, Kandel R, Goddard K, Sadura A, Pater J, Zee B. Preoperative versus postoperative radiotherapy in soft-tissue sarcoma of the limbs: a randomised trial. *Lancet.* 2002 Jun 29;359(9325):2235-41.
- 17.** Slump J, Hofer SOP, Ferguson PC, Wunder JS, Griffin AM, Hoekstra HJ, Bastiaannet E, O'Neill AC. Flap choice does not affect complication rates or functional outcomes following extremity soft tissue sarcoma reconstruction. *J Plast Reconstr Aesthet Surg.* 2018 Jul;71(7):989-96.
- 18.** Kang S, Han I, Kim S, Lee YH, Kim MB, Kim HS. Outcomes after flap reconstruction for extremity soft tissue sarcoma: a case-control study using propensity score analysis. *Eur J Surg Oncol.* 2014 Sep;40(9):1101-8.
- 19.** Ogura K, Uehara K, Akiyama T, Shinoda Y, Iwata S, Tsukushi S, Kobayashi E, Hirose T, Yonemoto T, Endo M, Tanzawa Y, Nakatani F, Kawano H, Tanaka S, Kawai A. Minimal clinically important differences in Toronto Extremity Salvage Score for patients with lower extremity sarcoma. *J Orthop Sci.* 2020 Mar;25(2):315-8.