Case Series
Volume 11:02, 2025

Archives of Surgical Oncology

ISSN: 2471-2671 Open Access

Wound Complications after Soft Tissue Sarcoma Resection: A Single-centre Retrospective Analysis

Carolina Curioni[1], Tim Pruimboom[2], Robert JCMF de Kleijn[1], Christel Meers-Haekens[1], Frederik WK Wesseling[3], Kristien Keymeulen[1], Marc HA Bemelmans[1], Shan Shan Qiu[2] and Sanne M. E. Engelen[1*]

[1]Department of General Surgery, Maastricht University & Maastricht University Medical Center, Maastricht, The Netherlands
[2]Department of Plastic, Reconstructive and Hand Surgery, Maastricht University & Maastricht University Medical Center, Maastricht, The Netherlands
3Department of Radiation Oncology (Maastro), GROW School for Oncology and Reproduction, Maastricht University Medical Center+, Maastricht, The Netherlands

Abstract

Background: The treatment of high-grade soft tissue sarcoma of the extremities and abdominal/trunk wall requires neoadjuvant radiotherapy followed by surgical resection. Neoadjuvant Radiotherapy (RTx) may result in closer resection margins and a more function-preserving approach. However, radiotherapy has a detrimental effect on tissue vascularization, leading to a higher incidence of Postoperative Wound Complications (PWC). Wound complications can increase morbidity, decrease quality of life and may require additional interventions. In this study we examine the postoperative wound complication rate in patients who underwent sarcoma resection in Maastricht University Medical Center (MUMC+) in the past ten years. Moreover, we aim to determine the effect of neoadjuvant radiotherapy and Plastic Surgical Reconstruction (PSR) on wound complications.

Methods: 260 patients who underwent soft tissue sarcoma resection at our center between 2014 and 2023 were retrospectively analyzed. The total wound complication rate was recorded per complication, and the patient cohort was subdivided into groups of patients who received neoadjuvant radiotherapy or not and/or plastic surgical reconstruction or not. Wound complications were scored as no wound complications, Minor Wound Complication (MiWC) and major wound complication (MaWC).

Results: Postoperative wound complications were recorded in 44.6% of patients, including infection (23%), wound dehiscence (17%), seroma (13%), and skin necrosis (8%). Neoadjuvant radiotherapy and plastic surgical reconstruction were both associated with an increased overall wound complication incidence (OR: 3.75, 95% CI: 2.08–6.74, p<0.001 and OR: 1.85, 95% CI: 1.05–3.28, p=0.034, respectively). In the radiotherapy group, infection was the most prevalent complication (OR: 2.78, p=0.004). The patients in the plastic surgical reconstruction group experienced predominantly minor wound complications. Dehiscence was the most prevalent complication in this group of patients (OR: 3.48, p=0.002).

Conclusion: This study showed that neoadjuvant radiotherapy and plastic surgical reconstruction for sarcoma patients are both associated with an increase in wound complication rate. Plastic surgical reconstruction was predominantly associated to minor complications. Future studies should focus on lowering the wound complication rates and improving care for sarcoma patients.

Keywords: Sarcoma • Wound complications • Neoadjuvant radiotherapy

Abbreviations: BMI: Body Mass Index; DDLS: Differentiated Pleiomorphic Liposarcoma; ESMO: European Society for Medical Oncology; FNCLCC: Fédération Nationale des Centres de Lutte Contre le Cancer; FTG: Full Thickness Graft; GIST: Gastrointestinal Stromal Tumor; Gy: Gray; ICGA: Indocyanine Green Angiography; LMS: Leiomyosarcoma; MaWC: Major Wound Complication; MiWC: Minor Wound Complication; MUMC+: Maastricht University Medical Center+; NCCN: National Comprehensive Cancer Network; PSR: Plastic Surgical Reconstruction; PWC: Postoperative Wound Complications; RTx: Radiotherapy; SFT: Solitary Fibrous Tumor; SSG: Split Thickness Skin Graft; STS: Soft Tissue Sarcoma: UPS: Non-Differentiated Pleiomorphic Sarcoma; WDLS: Well Differentiated Pleiomorphic Liposarcoma

Introduction

Sarcomas are a heterogeneous group of rare malignant tumors originating from soft tissue. They can differentiate into different cell types, including visceral tissues, bone, and connective tissues (such as lipocytes, fibrous supporting structures, and muscle). Soft tissue sarcomas only account for 1.5% of all cancers, with an estimated incidence of 4-5 per 100,000 per year in Europe [1-3]. According to the 2020 WHO classification, there are over seventy subtypes of Soft Tissue Sarcomas (STS) [4,5]. Liposarcomas and Leiomyosarcomas (LMSs) are the most prevalent types, with an incidence of less than 1 per 100,000 per year [2,5]. Although their anatomical location may vary, sarcomas predominantly affect the extremities [1,6].

Treatment of high-grade soft tissue sarcoma of the extremities and abdominal wall or trunk consists of surgery after neoadjuvant radiotherapy [7-9]. The use of neoadjuvant radiotherapy allows for closer resection margins and a more function-preserving surgery, improving long-term functional outcomes [10,11]. According to the National Comprehensive Cancer Network (NCCN) and the European Society for Medical Oncology (ESMO) guidelines, neoadjuvant radiotherapy is recommended in the treatment of high-grade sarcomas (Stage II and III disease), particularly for tumors that are deep located or with a volume greater than 5 cm in diameter, as it helps achieve local tumor control [2,9,10,12].

For patients requiring soft tissue sarcoma resection, neoadjuvant radiotherapy has several advantages over postoperative radiotherapy, including a lower radiation dose, a smaller volume of irradiated tissue, reduced toxicity, and no therapeutic delay [9,10]. Even without regression of the tumor, neoadjuvant radiotherapy can initiate fibrosis and necrosis, reducing the number of viable cells on the surface of the tumor. This facilitates surgical resection, increasing the chance of tumor free margins (R0) and thereby reducing the risk of recurrence [7,9]. Despite these advantages, neoadjuvant radiotherapy can lead to a higher Postoperative Wound Complication (PWC) rate when compared to adjuvant radiotherapy (35% *vs*. 17% respectively) [1,7,9]. The most common complications include wound infection, skin necrosis,

***Address for Correspondence:** Sanne M. E. Engelen, Department of General Surgery, Maastricht University & Maastricht University Medical Center, Maastricht, The Netherlands, E-mail: sanne.engelen@mumc.nl*

Received: 01 April, 2025, Manuscript No. aso-25-165166; **Editor Assigned:** 03 April, 2025, PreQC No. P-165166; **Reviewed:** 15 April, 2025, QC No. Q-165166; **Revised:** 22 April, 2025, Manuscript No. R-165166; **Published:** 29 April, 2025, DOI: 10.37421/2471-2671.2025.11.157

wound dehiscence, seroma and hematoma. Overall, the postoperative wound complication rate following sarcoma resection ranges from 16% to 56% in the current literature [9,13,14].

Several studies have investigated the contributing factors to wound complications in patients who underwent STS resection [6,13-16]. Among the potential risk factors identified, neoadjuvant radiotherapy has been shown to have a particularly detrimental effect on soft tissue vascularization, leading to impaired wound healing [13,17]. The location of the tumor has also been identified as a factor that has a significant impact on the wound healing process [13]. Higher wound complications rates were found after sarcoma resection in the lower extremity, particularly in the upper thigh area when compared to the upper extremities (43% *vs.* 5%) [7]. Moreover, tumors of 8 cm and greater in size, and with closer proximity to the skin (less than 3 mm) have been associated with higher complication rate [6,15].

Perioperatively, the surgeon should be able to assess tissue perfusion and remove skin that is perfused insufficiently. The gold standard for skin perfusion assessment is clinical evaluation, including examination of the skin color, temperature, and capillary refill. However, this is an unreliable and subjective method, as it depends mostly on the surgeon's eye and experience [18,19]. For this reason, indocyanine green angiography using intravenous Indocyanine Green (ICG) as a contrast agent, is more frequently applied in order to assess skin vascularization during sarcoma resection more objectively, and directly remove non-viable tissue [14,18]. Objective tissue perfusion assessment could represent a pivotal step in reducing postoperative wound complication rates after sarcoma resection.

If the resulting defect following sarcoma resection is too large for primary closure, consultation with a plastic and reconstructive surgeon is recommended to achieve closure [14]. The advantage is that the incorporation of Plastic Surgical Reconstruction (PSR), particularly techniques such as free flap reconstruction, also has been shown to have a protective effect against postoperative wound complications [7,20,21]. The use of well-vascularized tissue in these reconstructive procedures are proposed to enhance healing by promoting adequate blood supply, thereby mitigating the risk of infection, necrosis, and delayed healing. This factor is a critical determinant in optimizing patient outcomes, as it ensures both functional and durable tissue closure.

This study aims to investigate the postoperative wound complication rate in patients who underwent sarcoma resection over the past 10 years in Maastricht University Medical Center (MUMC+). Furthermore, we investigate the effect of both neoadjuvant radiotherapy and plastic surgical reconstruction on the wound complication rate. We hypothesize to confirm existing literature that neoadjuvant radiotherapy may have a negative effect on postoperative wound healing outcomes; while we propose that plastic surgical reconstruction serves as a protective factor, owing to its beneficial vascularization properties.

Methods

The MUMC+ database was reviewed to include all patients who underwent surgical resection for soft tissue sarcoma treatment in the past 10 years (2014 to 2023). All procedures performed in this study were in accordance with the ethical standards of the institutional research committee (Medical Ethics Committee in Maastricht: METC 2023-0102). We included patients of 18 years or older, who underwent surgical resection for soft tissue sarcoma, Solitary Fibrous Tumors (SFT), haemosiderotic fibrolipomatous tumors, or Inflammatory Myofibroblastic Tumors (IMT). Exclusion criteria were patients under the age of 18 years, benign soft tissue lesions, intermediate tumors (see Appendix), all Gastrointestinal Stromal Tumors (GIST), and retroperitoneal or intrapelvic tumors. Patients who did not undergo surgical intervention (due to unresectable tumors or palliative care status), and patients who underwent local dermatological excision, were also excluded. In total, 2672 patients were screened. Based on the in- and exclusion criteria 260 patients were eligible for inclusion. See Table 1 for the Patients' Demographics and Table 2 for the Tumor Characteristics.

According to the Fédération Nationale des Centres de Lutte Contre le Cancer (FNCLCC) grading system, we divided the tumors into low (G1), intermediate (G2), high (G3), or no grade specified based on biopsy results. Tumor size encompassed two to three measurements: initial radiological size (according to MRI or CT imaging), size of the pathology sample post-resection, and radiological size after restaging for sarcomas that received neoadjuvant radiotherapy. All measurements were recorded in centimeters according to their largest diameter. Tumor depth was categorized as cutaneous, subcutaneous, or deep to the fascia. Tumor response to radiotherapy was defined as the percentage of tumor necrosis or fibrosis in the pathology sample post-resection. A positive response to radiotherapy was defined as the presence of necrotic or non-viable tissue in the pathology report. Reconstruction by plastic surgery was categorized in the following treatment options: Split Skin Graft (SSG), Full-Thickness Graft (FTG), local transposition, pedicle flap and free flap (Table 3).

The following postoperative wound complications were recorded: infection, hematoma, skin necrosis, flap necrosis, wound dehiscence, and seroma. Delayed wound healing was defined as a healing process of more than two weeks, due to wound complications. In addition, complications requiring antibiotic therapy, readmission to the hospital, or additional surgical interventions were registered. All complications were classified according to the Clavien-Dindo grading system, based on their severity and type of intervention required [22].

The total wound complication rate was recorded per complication, and the patient cohort was subdivided into groups of patients who received neoadjuvant radiotherapy or not (RTx group *vs.* no-RTx group, respectively) and patient who underwent plastic surgical reconstruction or not (PSR group *vs.* no-PSR group, respectively).

All postoperative complications were divided into two groups based on clinical relevance and impact on patient outcome: Minor Wound Complication (MiWC) and Major Wound Complication (MaWC). Minor wound complications were defined as any surgical wounds managed conservatively (i.e. Clavien-Dindo grade I, II). Major wound complications were defined as any wound requiring secondary surgical intervention under regional or general anesthesia (i.e. Clavien-Dindo grade III, IV). The mean time interval (in days) between the surgery and onset of complications was recorded for all patients. Data on wound complications were retrieved from patient records with a follow-up period of 6 months.

Statistical analysis

Descriptive statistics were used to report all patient characteristics and the total incidence of complications. Numerical continuous variables were presented as means and Standard Deviations (SD), categorical variables as frequencies and percentages. Comparative analyses between wound complications rates (in percentages) were conducted using the Chi-square test for independence. Binary logistic regression analysis was conducted to identify independent predictors. Additionally, a multinomial logistic regression analysis was performed to assess the likelihood of three possible outcomes: no wound complications, Minor Wound Complications (MiWC), and Major Wound Complications (MaWC). Results were reported as odds ratios (OR) with 95% confidence intervals (CIs) and percentages of incidence and deemed significant when the p value was<0.05. SPSS© software (version 27) was used for all statistical analyses. For this retrospective study, no sample size calculation was performed. All patients who underwent surgical sarcoma resection over the past ten years were included.

The outcome measure was the postoperative wound complication rate following sarcoma resection (including infection, skin necrosis, wound dehiscence, seroma, and hematoma) and the effect of neoadjuvant radiotherapy and plastic surgical reconstruction on the wound complication rate. To analyze this effect, the patient cohort was subdivided into groups of patients who received radiotherapy or not (RTx group and no-RTx group, respectively) and who underwent plastic surgical reconstruction or not (PSR group *vs.* no-PSR group, respectively).

Results

Patients' characteristics

Between 2014 and 2023, 260 patients with a mean age of 70 years old,

underwent surgical resection for Soft Tissue Sarcomas (STS), excluding intrathoracic, retroperitoneal or intrapelvic resections. Around 53% of the patients were males. Approximately one-third of the study population had passed away at the time of inclusion (28.8%), which predominantly were disease related deaths (Table 1).

A total of 126 patients (48.5%) received neoadjuvant radiotherapy, predominantly a dose of 50 Gy. Almost all patients within this group (91%) exhibited a positive response to neoadjuvant radiotherapy, with a mean tumor necrosis percentage of 66%.

Table 1. Patients' demographics.

Patients' Characteristic		Total N (%) (% on total N. patients)	Mean (SD)
Patients Total		**260 (100%)**	
Gender	Female	123 (47.3%)	
	Male	137 (52.7%)	
	Age (years)	-	70 (15.2)
	BMI (Kg/m^2)	-	26.2 (4.7)
	Obesity (>30 Kg/m^2)	43 (16.5%)	
Smoking	Current	37 (14.2%)	
	Past	91 (35.0%)	
	Never	123 (47.3%)	
	Missing	9 (3.5%)	
	Diabetes	28 (10.8%)	
	Cardiovascular Comorbidities	116 (44.6%)	
	Hypertension	111 (42.7%)	
	Hypercholesterolemia	62 (23.8%)	
	Myocardial infarct	12 (4.6%)	
	Peripheral arterial disease	2 (0.8%)	
	Atrial Fibrillation	19 (7.3%)	
	TIA / CVA	13 (5.0%)	
	Anticoagulation	70 (26.9%)	
	DOAC *	19 (27.1%)	
	VIT-K antagonist *	10 (14.3%)	
	Antiplatelet inhibitors *	41 (58.5%)	
	Overall mortality	75 (28.8%)	
	Cancer Specific Mortality*	52 (69.3%)	

BMI: Body Mass Index; CVA: Cerebrovascular Accident; DOAC: Direct Oral Anticoagulants; TIA: Transient Ischemic Attack; *: Percentages within group

Most included patients (76.5%) had a primary tumor resection with a mean initial diameter of 7.6 centimeters, without the presence of distant metastases. Most sarcomas were found in the lower extremity, were classified as high grade, and extended deep to the fascia. See Table 2 for the tumor characteristics. When concerning the wound closure, slightly more than half (50.4%) of the patients underwent primary closure of the wound following sarcoma resection. The other patients underwent immediate or delayed plastic surgical reconstruction (Table 3). Free flap reconstruction with or without a skin graft, was the most frequent performed type of reconstruction.

Postoperative Wound Complications (PWC)

One or more wound complications occurred in 45 percent of all patients. Wound infection was the most prevalent wound complication, followed by dehiscence and seroma (22.7%, 17.3% and 12.7%, respectively) (Table 4). More than half of these patients (54.7%) experienced a minor complication defined as Clavien Dindo grade I or II. No patient experienced a Grade IV or higher complication (Table 5). Approximately one third of patients experienced delayed wound healing and one fourth of patients required antibiotic treatment (Table 6).

Neoadjuvant Radiotherapy (RTx): Overall, neoadjuvant Radiotherapy (RTx) was significantly associated with a higher postoperative wound complication rate, when compared to no-radiotherapy (60.3% *vs.* 30.6%; p<0.001). The most prevalent complication was infection, followed by dehiscence and skin necrosis. Binary logistic regression analysis confirmed a statistically significant higher chance of developing wound complications in patients who received neoadjuvant radiotherapy (OR: 3.45, 95% CI: 2.07–5.74, p<0.001) (Table 7). After adjusting for confounding variables (i.e. PSR, current smoking, diabetes, initial tumor size, and postoperative radiotherapy), it remained significant (OR: 3.75, 95% CI: 2.08–6.74, p<.001). Multinomial logistic regression (also adjusted for confounders) confirmed a significantly higher risk of both minor (OR: 4.03, 95% CI: 1.97–8.26, p<0.001) and major (OR: 4.25, 95% CI 1.64 - 7.46, p=0.001) postoperative wound complications in patients who received neoadjuvant radiotherapy (Table 7).

Plastic Surgical Reconstruction (PSR): Overall, plastic surgical reconstruction was significantly associated with a higher postoperative wound complication rate (OR: 2.06, 95% CI: 1.25–3.38, p=0.005). The most prevalent wound complication was wound dehiscence, followed by infection (Table 8). This association remained statistically significant after adjusting for the confounders (i.e. RTx, current smoking, diabetes, initial tumor size, and postoperative radiotherapy) (OR: 1.85, 95% CI: 1.05–3.28, p=0.034) (Table 8). The patients in the plastic surgical reconstruction group experienced more minor and major complication, when compared to the non-plastic surgical reconstruction group (31% and 23% *vs*. 18% and 17.6%, respectively, p=0.01). Multinomial regression analysis indicated a strong correlation between plastic

Table 2. Tumor characteristics.

Tumor Characteristics		Total N (% on total N. patients)	Mean (Range)
Presentation	**Primary**	**199 (76.5%)**	
	Recurrence	59 (22.7%)	
	Metastasis	2 (0.8%)	
Tumor Grade	Low	31 (11.9%)	
	Intermediate	33 (12.7)	
	High	113 (43.5%)	
	No Grade Specified	83 (31.9%)	
Tumor depth	Cutaneous	11 (4.2%)	
	Subcutaneous	49 (18.8%)	
	Deep to fascia	200 (76.9%)	
Tumor size	Initial max diameter (cm)		7.623 (0,7-30.0)
	Restaging max diameter (cm)		8.948 (1.1-24.0)
	Pathology max diameter (cm)		7.745 (0.2-27.0)
Tumor Location	Upper extremity	41 (15.8%)	
	Lower extremities	123 (47.3%)	
	Head/neck	27 (10.4%)	
	Trunk	56 (21.5%)	
	Genitalia	13 (5.0%)	
Tumor type (Histology)	Leiomyosarcoma	19 (7.3%)	
	DDLS	26 (10.0%)	
	WDLS	15 (5.8%)	
	Myxoid liposarcoma	14 (5.4%)	
	Myxofibrosarcoma	43 (16.5%)	
	Synovial sarcoma	5 (1.9%)	
	Angiosarcoma	17 (6.5%)	
	UPS (NOS)	47 (18.1%)	
	SFT	7 (2.7%)	
	Rhabdomyosarcoma	7 (2.7%)	
	Dermal sarcoma	8 (3.1%)	
	Spindle cell sarcoma	19 (7.3%)	
	Others*	33 (12.7%)	
Metastasis	None	172 (66.2%)	
	One	70 (26.9%)	
	Two	14 (5.4%)	
	Three or more	4 (1.5%)	

DDLS: Dedifferentiated Liposarcoma; WDLS: Well-Differentiated Liposarcoma; UPS: Undifferentiated Pleomorphic Sarcoma; NOS: Non-Otherwise Specified; SFT: Solitary Fibrous Tumor; *Others: Fibromyxoid, undifferentiated myxoid, Myxoinflammatory Fibroblastic Sarcoma (MIFS), atypical inflammatory myofibroblastic tumor, chondrosarcoma, histiocytic, mesenchymal, haemosiderotic fibrolipomatous tumor, Ewing, Kaposi sarcoma

surgical reconstruction and minor complication (MiWC), also after correcting for confounders (OR: 2.01, 95% CI: 1.02 - 3.94, p=0.043). However, the association between plastic surgical reconstruction and major complications (MaWC) was not found to be statistically significant (OR: 1.86, 95% CI: 0.98–3.51, p=0.057) (Table 8).

The effects of various types of reconstructions on wound complications were also analyzed. Multinomial logistic regression, adjusted for confounders, revealed no statistically significant association with either minor or major wound complications for the free flap reconstruction, pedicle flap reconstruction, and the reconstruction using a transposition flap. In the group of patients who only underwent reconstruction using an SSG, a statistically significant association between SSG and minor complications was found (OR: 8.20, 95% CI: 1.96–34.48, p=0.004) (Table 9).

Neoadjuvant Radiotherapy (RTx) and Plastic Surgical Reconstruction (PSR): Within the group that received neoadjuvant radiotherapy (N=126), patients who required plastic reconstruction (N=67) develop more wound complications, when compared to patients who did not undergo reconstruction (67.2% *vs.* 52.5%, respectively), but the difference was not statistically significant (Table 10). When analyzing the postoperative wound complications separately, only wound dehiscence was found to be significantly associated to the combination of neoadjuvant radiotherapy and plastic reconstruction (Table 11).

Table 3. Treatment characteristics.

Treatment		Total N (% on total N. patients)	Mean (SD)
	Primary closure	131 (50.4%)	
	Reconstruction by plastic surgery	129 (49.6%)	
	SSG*	45 (34.9%)	
	SSG alone	18 (13.9%)	
	FTG (full thickness graft)	3 (2.3%)	
	FTG alone*	1 (0.8%)	
	Local Transposition	23 (17.8%)	
	Free flap	51 (39.5%)	
	Pedicle Flap	36 (27.9%)	
Radicality	R0	216 (83.1%)	
	R1	39 (15.0%)	
	Dubious	5 (1.9%)	
	Blood loss (ml)		443.93 (410.26)
	Neoadjuvant Radiotherapy (RTx)	126 (48.5%)	
	Total dose 50Gy* (2Gy × 25 fractions)	117 (94.4%)	
	Total dose 36Gy* (1.8Gy × 20 fractions)	7 (5.6%)	
	Missing dose	2 (1.5%)	
	Time RTx–Surgery (weeks)		8.68 (2.89)
Response to RTx	Yes	115 (91.1%)	
	No	11 (8.1%)	
	% Necrosis		60.9 (33.87)
	Adjuvant Radiotherapy	28 (10.8%)	
	Postoperative Prophylactic AB	67 (25.8%)	

AB: Antibiotics; FTG: Full Thickness Graft; RTx: Radiotherapy; R0: Resection Free Margin; R1: Microscopic residual tumor; SSG: Split Skin Graft; *: % within group

Table 4. Wound complications.

Wound Complications	Total N=260 (%)
Patients total	117 (45.0%)
Infection	59 (22.7%)
Dehiscence	45 (17.3%)
Seroma	33 (12.7%)
Skin necrosis	20 (7.7%)
Hematoma	17 (6.5%)
Flap necrosis	8 (6.2%*)

*: Percentage calculated over total amount of patients with flap reconstruction (Free flap, Pedicle flap, Transposition flap)

Table 5. Clavien Dindo classification of wound complications.

Clavien-Dindo Classification	Total N=117 (% on total number of patients with WC)
Grade I	31 (26.5%)
Grade II	33 (28.2%)
Grade IIIa	13 (11.1%)
Grade IIIb	40 (34.2%)

WC: wound complications

Table 6. Postoperative course of wound complications.

Wound Complications	Total N=260 (% on total number of patients)
Delayed wound healing*	96 (36.9%)
Antibiotic Treatment	64 (24.6%)
Oral	43 (67.1%**)
Intravenous	21 (32.8%**)
Reoperation	40 (15.4%)
Readmission to hospital (other reasons)	3 (1.2%)
Time Surgery–Complication, days (mean, SD)	28.5 (36.90)

*Due to infection, dehiscence, seroma, hematoma, and necrosis
**Percentage calculated over patients who received antibiotic treatment

Table 7. Neoadjuvant Radiotherapy effect on wound complications.

	No-RTx	RTx	OR (95% C.I.)	p	OR (95% C.I.)	p*
	N (%)	N (%)			Adjusted*	pp
WC BLR	41 (30.6%)	76 (60.3%)	3.45 (2.07–5.74)	<.001	3.75 (2.08–6.74)	<.001
MiWC MLR	21 (15.7%)	43 (34.1%)	3.80 (2.04 - 7.09)	<.001	4.03 (1.97 - 8.26)	<.001
MaWC MLR	20 (14.9%)	33 (26.2%)	3.07 (1.59 - 5.88)	<.001	4.25 (1.64 - 7.46)	0.001
Days after Surgery - WC Mean, days (SD)	29.2 (42.9)	27.7 (33.5)		0.831		

BLR: Binary Logistic Regression; MaWC: Major Wound Complications; MiWC: Minor Wound Complications; MLR: Multinomial Logistic Regression; RTx: Radiotherapy; WC: Wound Complications
*Confounders: Current Smoking, Diabetes, Initial Tumor Size, Plastic surgical reconstruction, Postoperative Radiotherapy

Table 8. Plastic surgical reconstruction effect on wound complications.

	No-PSR N (%)	PSR N (%)	OR (95% C.I.)	p	OR (95% C.I.) Adjusted*	p*
WC BLR	47 (35.9%)	70 (54.3%)	2.06 (1.25–3.38)	0.005	1.85 (1.05–3.28)	0.034
MiWC MLR	24 (18.3%)	40 (31.0%)	2.37 (1.29 - 4.34)	0.005	2.01 (1.02 - 3.94)	0.057
MaWC MLR	23 (17.6%)	30 (23.3%)	1.86 (0.98–3.51)	0.043	1.83 (0.89–3.76)	0.099
Days After Surgery - WC Mean, days (SD)	32.4 (38.4)	25.4 (35.9)		0.318		

BLR: Binary Logistic Regression; MaWC: Major Wound Complications; MiWC: Minor Wound Complications; MLR: Multinomial Logistic Regression; RTx: Radiotherapy; WC: Wound Complications
*Confounders: Current Smoking, Diabetes, Initial Tumor Size, Neoadjuvant radiotherapy, Postoperative Radiotherapy

Table 9. Plastic surgical reconstruction types effect on wound complications.

	PSR types (total N)	N (%) (Per PRS type)	OR (95% C.I.)	p	OR (95% C.I.) Adjusted*	P*
Free flap (51)	MiWC	16 (31.4%)	2.09 (0.98–4.46)	0.057	1.56 (0.66–3.68)	0.309
	MaWC	12 (23.5%)	1.83 (0.81–4.18)	0.148	1.39 (0.55–3.51)	0.481
Pedicle flap (36)	MiWC	7 (19.4%)	1.21 (0.46–3.20)	0.693	0.99 (0.35–2.79)	0.985
	MaWC	12 (33.3%)	2.49 (1.05–5.85)	0.037	2.27 (0.89–5.75)	0.085
Transposition flap (23)	MiWC	5 (21.7%)	1.21 (0.40–3.20)	0.735	1.51 (0.43–5.32)	0.516
	MaWC	6 (26.1%)	1.69 (0.58–4.93)	0.335	2.33 (0.72–7.52)	0.157
SSG (18)	MiWC	9 (50%)	3.40 (1.20–9.71)	0.021	8.20 (1.96–34.48)	0.004
	MaWC	1 (5.6%)	0.45 (0.05–3.80)	0.467	X**	X**

MaWC: Major Wound Complications; MiWC: Minor Wound Complications; PSR: Plastic Surgical Reconstruction; SSG: Split Skin Graft
*Confounders: Current Smoking, Diabetes, Initial Tumor Size, Postoperative Radiotherapy, Neoadjuvant radiotherapy
**: No statistical analysis possible due to insufficient number of events

No neoadjuvant Radiotherapy (No-RTx) and Plastic Surgical Reconstruction (PSR): Within the group that did not receive neoadjuvant radiotherapy (N=134), patients who required plastic surgical reconstruction (N=62) seemed more likely to develop any wound complication, when compared to patients who did not undergo surgical reconstruction (40.3 *vs.* 22.2%, respectively). Although the association for any wound complication was not significant, there was a strong association between plastic surgical reconstruction and minor complications after correction for confounder variables (OR: 6.62, 95% CI: 1.62 - 27.03, p=0.007) (Table 10).

Discussion

In this retrospective study, the overall postoperative wound complication rate following surgical resection for soft tissue sarcoma was 45%. Most of these patients developed a minor wound complication. Neoadjuvant radiotherapy was found to be independently associated with wound complications.

Table 10. Plastic surgery influence on wound complications in RTx group and no-RTx group.

RTx group	Non-PSR N (%)	PSR N (%)	OR (95% C.I.)	p	OR (95% C.I.) Adjusted*	P*
WC BLR	31 (52.5%)	45 (67.2%)	1.85 (0.90 - 3.80)	0.096	1.76 (0.84–3.71)	0.134
MiWC MLR	20 (33.9%)	23 (34.4%)	1.46 (0.64–3.32)	0.362	1.37 (0.59–3.17)	0.466
MaWC MLR	11 (18.6%)	22 (32.8%)	2.54 (1.02–6.37)	0.045	2.54 (0.98–6.58)	0.055
No-RTx group	**No-PSR N (%)**	**PSR N (%)**	**OR (95% C.I.)**	**p**	**OR (95% C.I.) Adjusted***	**P***
WC BLR	16 (22.2%)	25 (40.3%)	2.36 (1.14 - 5.02)	0.025	2.20 (0.89–5.43)	0.086
MiWC MLR	4 (5.5%)	17 (27.4%)	6.45 (2.00–20.83)	0.002	6.62 (1.62 - 27.03)	0.007
MaWC MLR	12 (16.7%)	8 (12.9%)	1.01 (0.38-2.70)	0.986	0.81 (0.24 - 2.75)	0.734

BLR: Binary Logistic Regression; MaWC: Major Wound Complications; MiWC: Minor Wound Complications; MLR: Multinomial Logistic Regression; RTx: Radiotherapy; WC: Wound Complications

*Confounders: Current Smoking, Diabetes; Initial Tumor Size, Plastic Surgical Reconstruction, Postoperative Radiotherapy

Table 11. Effect of Neoadjuvant radiotherapy and plastic surgery on development of infection, dehiscence and skin necrosis.

		Infection		Dehiscence		Skin Necrosis	
		Tot % (p)	OR (p)*	Tot % (p)	OR (p)*	Tot % (p)	OR (p)*
	RTx (+)	32.5% (<.001)	2.78 (0.004)	23.0% (0.018)	3.23 (0.007)	11.1% (0.045)	3.49 (0.053)
	RTx (-)	13.40%		11.90%		4.50%	
	PRS (+)	25.4% (0.270)	1.208(0.558)**	25.6% (<.001)	3.48 (0.002)**	10.1% (0.152)	2.30 (0.139)**
	PRS (-)	19.80%		9.20%		5.30%	
RTx (+)	PSR (+)	31.3% (0.760)	0.93 (0.858)	34.3% (0.001)	5.122 (0.002)	14.9% (0.147)	2.72 (0.136)
	PSR (-)	33.90%		10.20%		6.80%	
RTx (-)	PSR (+)	19.4% (0.062)	2.19 (0.188)	16.1% (0.165)	1.65 (0.486)	4.8% (1.00)	1.39 (0.759)
	PSR (-)	8.30%		8.3		4.20%	

RTx: Radiotherapy; PSR: Plastic Surgical Reconstruction

*Corrected for confounders: Current Smoking, Diabetes, Initial Tumor Size, Plastic Surgical Reconstruction, Postoperative Radiotherapy

** Corrected for all aforementioned confounders + RTx

Furthermore, we found a higher complications rate in the PSR group, although we hypothesized that plastic surgical reconstruction would decrease wound complications [20,23,24]. We believe that the higher complication rate is primarily caused by the major selection bias in this group. PSR is only applied in select cases where the surgical defect is either too large or in an anatomically challenging site to primarily close. The decision to proceed with plastic surgical reconstruction was made empirically and subjectively, based on multidisciplinary case discussions, in which the anticipated inability to achieve tension-free primary closure was considered. Consequently, these results reflect the complexity and extensiveness of the procedures that were performed. This observation is consistent with previous studies that have reported higher rates of postoperative wound complications following more extensive reconstructive surgeries, particularly those preceded by neoadjuvant radiotherapy [25-27].

Moreover, we observed that plastic surgeons tended to adopt a more meticulous and detailed approach to documenting postoperative wound complications compared to oncologic surgeons. This variability highlights a limitation inherent to the retrospective nature of the study, namely the absence of a standardized scoring system for wound assessment and complication reporting. Also, while these findings suggest an increased rate of minor complications following surgical reconstruction, this should not undermine the potential benefits of plastic surgical reconstruction. Most importantly plastic surgical reconstruction allows for more extensive surgical resection margins, defect closure, regain of function using innervated muscle flaps, and at times prevents primary limb amputation.

When concerning the subtypes of plastic surgical reconstruction, the patients who received only an SSG had the highest wound complication rate. This can be explained by the fact that a split-thickness skin graft offers the least durable coverage for the wound and does not add well-vascularized soft tissue to the defect.

Although comparable retrospective studies did not find a statistically significant association between plastic surgical reconstruction and the rate of wound complications, some evidence suggests a trend toward reduced complication rates when plastic surgery is involved [23,24,28]. Tseng, et al. also hypothesized that early involvement of reconstructive techniques could potentially reduce the risk of wound complications. However, their findings did not demonstrate a significant difference in complications between primary closure and plastic surgical reconstruction. This outcome may be attributed to the inherent differences between the groups, as high-risk sarcomas were predominantly assigned to the plastic surgical reconstruction group [28]. Notably, unlike our study, Tseng, et al. focused exclusively on major wound complications, similar to Chan, et al., who analyzed only a cohort receiving neoadjuvant radiotherapy and flap reconstruction. Chan, et al. reported a lower major complication rate (25%) and reoperation rate (14%) compared to existing literature [23]. Likewise, Rosenberg, et al. observed a lower reoperation rate with plastic surgical reconstruction, though the results were not statistically significant [24]. Unlike our study, both Chan, et al. and Rosenberg, et al. included only patients undergoing preoperative radiotherapy and focused on major wound complications.

Nonetheless, we acknowledge the potential for inherent selection bias among patients undergoing plastic surgical reconstruction, which may have influenced our results. Plastic surgery is generally indicated in cases where primary wound closure is not feasible due to tumor location or size of the resection specimen. This scenario is more commonly encountered with larger tumors, which are often associated with greater disease severity and, consequently, a more complex wound healing process [26, 29,30].

In addition, neoadjuvant radiotherapy was associated with a 4 times higher incidence of minor wound complications, and even a 4.3 times higher incidence of major complications. These findings are consistent with previous studies reporting a greater risk of wound infection and dehiscence than

patients without radiotherapy [15,16,23,24,28,31-33]. This is most likely due to the negative impact of neoadjuvant radiotherapy on tissue oxygenation and microvascular blood flow [33-35].

In general, our study observed a higher incidence of minor complications compared to major complications in both the radiotherapy and plastic reconstruction group. The predominance of minor complications is clinically relevant as they are generally easier to manage compared to major complications. Notably, this outcome is particularly important in the context of radiotherapy where the primary goal of treatment, which is disease control and achieving resection free margins, takes precedence over the management of (minor) wound complications. The Clavien-Dindo classification system applied in our study further supports this observation, as all complications recorded were of grade 3b or lower, indicating limited impact on patient outcomes.

The limitations of this retrospective study have already been pointed out above: Due to its retrospective nature, the study was subject to inherent biases, namely selection bias, as previously mentioned, and recall bias due to possible incomplete, or inaccurate reports of postoperative care and complications during follow up appointments. In addition, our analyses considered several confounding variables (e.g., smoking status, diabetes, tumor size and postoperative radiotherapy). These were chosen based on our assumptions about their potential higher clinical influence, and comparable studies. Nonetheless, our outcomes might have been affected by the presence of other not evaluated variables.

The data of this study, irrespective of the potential biases, forces us to further refine our surgical treatment options to decrease postoperative complications in this challenging group of patients. We believe that intra-operative tissue perfusion assessment is crucial for the detection and, subsequently, excision, of the areas with poor tissue perfusion. Intraoperative angiography Indocyanine Green (ICG) as a contrast agent, is an effective novel technique that allows visualization in objective assessment of tissue perfusion. This method, already implemented in several surgical specialties, has shown to be a promising approach in the prediction of wound healing problems. To date, only one prior prospective study has reported that indocyanine green fluorescence imaging exhibits a high positive predictive value (100%) and a moderate negative predictive value (70%) for predicting wound complications following resection of soft tissue sarcomas in the lower extremity [14]. However, these findings are based on a limited sample size of 23 patients. Therefore, future research ought to focus on larger, multicenter, prospective trials that corroborate these findings and explore the potential implementation of novel techniques, like ICG angiography, to minimize postoperative wound complications problems, enhancing surgical outcomes in patients with sarcoma.

Conclusion

This study affirms a strong correlation between neoadjuvant radiation therapy and a higher incidence of postoperative wound complications after surgery for soft tissue sarcoma, mostly infection. Additionally, patients undergoing plastic surgical reconstruction following sarcoma resection, experienced higher wound complication rates, especially wound dehiscence. This indicates that plastic surgical reconstruction, while beneficial in many aspects, still carries a notable risk of wound complications, potentially due to the complex nature of the procedures involved. However, the predominance of minor complications, which are generally manageable, suggests that the benefits of radiotherapy and plastic surgical reconstruction in improving disease resectability and control and preservation of function justify their clinical application.

Declarations

Ethics approval and consent to participate

All procedures performed in this study were in accordance with the ethical standards of the institutional research committee (Medical Ethics Committee in Maastricht: METC 2023-0102).

Consent for publication

Not applicable.

Availability of data and materials

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

Acknowledgement

We thank Francesco Innocenti for the statistical support.

Conflict of Interest

The authors declare that they have no competing interests.

Funding

No funding was used for this publication.

Authors' Contributions

Carolina Curioni: Collection and interpretation of data, study design, writing of the manuscript; Tim Pruimboom: Collection and interpretation of data, study design, writing of the manuscript; Robert JCMF de Kleijn: Interpretation of data, writing of the manuscript; Christel Meers-Haekens: Collection of data; Frederik WK Wesseling: Collection of data, review of the manuscript; Kristien Keymeulen: Collection of data, review of the manuscript; Marc HA Bemelmans: Collection of data, review of the manuscript; Shan Shan Qiu: Collection of data, review of the manuscript; Sanne ME Engelen: Collection and interpretation of data, study design, review of the manuscript.

References

1. Ducimetière, Françoise, Antoine Lurkin, Dominique Ranchère-Vince and Anne-Valérie Decouvelaere, et al. "Incidence of sarcoma histotypes and molecular subtypes in a prospective epidemiological study with central pathology review and molecular testing." *PloS One* 6 (2011): e20294.
2. Gronchi, Alessandro, Abhishek B. Miah, Angelo P. Dei Tos and Nicolas Abecassis, et al. "Soft tissue and visceral sarcomas: ESMO-EURACAN-GENTURIS clinical practice guidelines for diagnosis, treatment and follow-up (☆)." *Ann Oncol* 32 (2021): 1348-1365.
3. Goedhart, Liset M., Valesca K. Y. Ho, Pieter D. S. Dijkstra and H. W. B. Schreuder, et al. "Bone sarcoma incidence in the Netherlands." *Cancer Epidemiol* 60 (2019): 31-38.
4. Sbaraglia, Mauro, Elisabetta Bellan and Angelo P. Dei Tos. "the 2020 who classification of soft tissue tumours: News and perspectives." *Pathologica* 113 (2021): 70-84.
5. Bansal, Anuj, Saurabh Goyal, Amit Goyal and M. Jana, et al. "WHO classification of soft tissue tumours 2020: An update and simplified approach for radiologists." *Eur J Radiol* 143 (2021): 109997.
6. Korah, Michael P., A. T. Deyrup, D. K. Monson and S. V. Oskouei, et al. "Anatomic tumor location influences the success of contemporary limb-sparing surgery and radiation among adults with soft tissue sarcomas of the extremities." *Int J Radiat Oncol Biol Phys* 82 (2012): 933-939.
7. Demetri, George D., Laurence H. Baker, David Beech and Robert Benjamin, et al. "Soft tissue sarcoma clinical practice guidelines in oncology." *J Natl Compr Canc Netw* 3 (2005): 158-194.
8. Gómez, Julio and Panagiotis Tsagozis. "Multidisciplinary treatment of soft tissue sarcomas: An update." *World J Clin Oncol* 11 (2020): 180-189.
9. Spałek, Mateusz J., Krzysztof Kozak, Anna M. Czarnecka and Ewa Bartnik, et al. "Neoadjuvant treatment options in soft tissue sarcomas." *Cancers (Basel)* 12

(2020): 2292.

10. Ouyang, Zhichao, Sean Trent, Claire McCarthy and Tom Cosker, et al. "The incidence, risk factors and outcomes of wound complications after preoperative radiotherapy and surgery for high grade extremity soft tissue sarcomas: A 14-year retrospective study." *Eur J Surg Oncol* 49 (2023): 107086.
11. Kim, Yong Bae, Kyung Hwan Shin, Jong Seok Seong and Jae Kwan Roh, et al. "Clinical significance of margin status in postoperative radiotherapy for extremity and truncal soft-tissue sarcoma." *Int J Radiat Oncol Biol Phys* 70 (2008): 139-144.
12. Casali, Paolo G., Nicolas Abecassis, Hannu T. Aro and Stephan Bauer, et al. "Soft tissue and visceral sarcomas: ESMO-EURACAN clinical practice guidelines for diagnosis, treatment and follow-up." *Ann Oncol* 29 (2018): iv51-iv67.
13. Moore, Jeff, Mark Isler, John Barry and Stephane Mottard, et al. "Major wound complication risk factors following soft tissue sarcoma resection." *Eur J Surg Oncol* 40 (2014): 1671-1676.
14. Wilke, Benjamin K., Daniel S. Schultz, Maria T. Huayllani and Daniel Boczar, et al. "Intraoperative indocyanine green fluorescence angiography is sensitive for predicting postoperative wound complications in soft-tissue sarcoma surgery." *J Am Acad Orthop Surg* 29 (2021): 433-438.
15. Baldini, Elizabeth H., Mark R. Lapidus, Qian Wang and Jane Manola, et al. "Predictors for major wound complications following preoperative radiotherapy and surgery for soft-tissue sarcoma of the extremities and trunk: importance of tumor proximity to skin surface." *Ann Surg Oncol* 20 (2013): 1494-1499.
16. Schwartz, Alan, Ashley Rebecca, Alexander Smith and William Casey, et al. "Risk factors for significant wound complications following wide resection of extremity soft tissue sarcomas." *Clin Orthop Relat Res* 471 (2013): 3612-3617.
17. Cammelli, Stefano, Alessandro Cortesi, Marco Buwenge and Alessio Zamagni, et al. "The role of radiotherapy in adult soft tissues sarcoma of the extremities." *Eur J Orthop Surg Traumatol* 31 (2021): 1583-1596.
18. Liu, Derek Z., Douglas W. Mathes, Michael R. Zenn and Peter C. Neligan, et al. "The application of indocyanine green fluorescence angiography in plastic surgery." *J Reconstr Microsurg* 27 (2011): 355-64.
19. Jallali, Nabil, Hisham Ridha and Peter E. Butler. "Postoperative monitoring of free flaps in UK plastic surgery units." *Microsurgery* 25 (2005): 469-472.
20. Chao, Alexander H., David W. Chang, Syed W. Shuaib and Matthew M. Hanasono, et al. "The effect of neoadjuvant *vs*. adjuvant irradiation on microvascular free flap reconstruction in sarcoma patients." *Plast Reconstr Surg* 129 (2012): 675-682.
21. Peat, Brian G., Robert S. Bell, Aileen Davis and Barry O'Sullivan, et al. "Wound-healing complications after soft-tissue sarcoma surgery." *Plast Reconstr Surg* 93 (1994): 980-987.
22. Clavien, Pierre A., Jeffrey Barkun, Maria L. de Oliveira and Jean-Nicolas Vauthey, et al. "The Clavien-Dindo classification of surgical complications: Five-year experience." *Ann Surg* 250 (2009): 187-196.
23. Chan, Lok W.M., Jun Imanishi, D.G. Grinsell and Peter Choong, et al. "Preoperative radiotherapy and wide resection for soft tissue sarcomas: Achieving a low rate of major wound complications with the use of flaps. results of a single surgical team." *Front Surg* 4 (2017): 79.
24. Rosenberg, Lori A., Richard J. Esther, Kourosh Erfanian and Robert Green, et al. "Wound complications in preoperatively irradiated soft-tissue sarcomas of the extremities." *Int J Radiat Oncol Biol Phys* 85 (2013): 432-437.
25. Lese, Ioana, Cristina Baesu, Ignacio A. Hoyos and Maria A. Pais, et al. "Flap reconstruction outcome following surgical resection of soft tissue and bone sarcoma in the setting of (Neo) adjuvant therapy: A sarcoma center experience." *Cancers (Basel)* 15 (2023).
26. Hoang, Minh N., Elin Nyqvist, Anna C. Hesla and Panagiotis Tsagozis, et al. "Wound healing after surgery for soft tissue sarcomas and the effect of primary plastic reconstruction - A retrospective cohort study." *Eur J Surg Oncol* 50 (2024).
27. Perrault, Daniel P., Geoffrey K. Lee, Richard P. Yu and Amanda L. Carre, et al. "Risk factors for wound complications after soft tissue sarcoma resection." *Ann Plast Surg* 86 (2021): S336-S341.
28. Tseng, Jennifer F., Matthew T. Ballo, Howard N. Langstein and Jeffrey D. Wayne, et al. "The effect of preoperative radiotherapy and reconstructive surgery on wound complications after resection of extremity soft-tissue sarcomas." *Ann Surg Oncol* 13 (2006): 1209-15.
29. Davidge, Kristen M., Jay Wunder, Gail Tomlinson and Rebecca Wong, et al. "Function and health status outcomes following soft tissue reconstruction for limb preservation in extremity soft tissue sarcoma." *Ann Surg Oncol* 17 (2010): 1052-1062.
30. Cannon, Christopher P., Melissa T. Ballo, Gary K. Zagars and Adeel N. Mirza, et al. "Complications of combined modality treatment of primary lower extremity soft-tissue sarcomas." *Cancer* 107 (2006): 2455-2461.
31. Tsagozis, Panagiotis, Otte Brosjö and Martin Skorpil. "Preoperative radiotherapy of soft-tissue sarcomas: Surgical and radiologic parameters associated with local control and survival." *Clin Sarcoma Res* 8 (2018): 19. LeBrun, Drake G., David M. Guttmann, Jacob E. Shabason and William P. Levin, et al. "Predictors of wound complications following radiation and surgical resection of soft tissue sarcomas." *Sarcoma* 2017 (2017): 5465130.
32. O'Sullivan, Brian, Aileen M. Davis, Robert Turcotte and Robert Bell, et al. "Preoperative *vs*. postoperative radiotherapy in soft-tissue sarcoma of the limbs: A randomised trial." *Lancet* 359 (2002): 2235-2241.
33. Payne, Wyatt G., Deepak K. Naidu, Chad K. Wheeler and David Barkoe, et al. "Wound healing in patients with cancer." *Eplasty* 8 (2008): e9.
34. Deptuła, Milena, Jacek Zieliński, Anna Wardowska and Michał Pikuła, et al. "Wound healing complications in oncological patients: perspectives for cellular therapy." *Postepy Dermatol Alergol* 36 (2019): 139-146.

How to cite this article: Curioni, Carolina, Tim Pruimboom, Robert JCMF de Kleijn and Christel Meers-Haekens, et al. "Wound Complications after Soft Tissue Sarcoma Resection: A Single-centre Retrospective Analysis." *Arch Surg Oncol* 11 (2025): 157.

Appendix

Appendix 1: List of excluded intermediary tumors

Excluded intermediary tumors
ALT (Atypical Lipomatous Tumor)
AFX (Atypical Fibroxanthoma)
Neurofibromas
TGCT (Tenosynovial Giant Cell Tumors)
Borderline Phyllodes
DFSP (Dermatofibrosarcoma Protuberans)
Desmoid fibromatosis
MPNST (Malignant Peripheral Nerve Sheath Tumor)