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Patient, tumour and treatment factors affect complication rates in soft tissue sarcoma flap reconstruction in a synergistic manner



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Abstract

Introduction: Flap reconstruction plays an essential role in the management of soft tissue sarcoma, facilitating wide resection while maximizing preservation of function. The addition of reconstruction increases the complexity of the surgery and identification of patients who are at high risk for post-operative complications is an important part of the preoperative assessment. This study examines predictors of complications in these patients.

Methods: 294 patients undergoing flap reconstruction following sarcoma resection were evaluated. Data on patient, tumour and treatment variables as well as post-operative complications were collected. Bivariate and multivariate regression analysis was performed to identify independent predictors of complications. Analysis of synergistic interaction between key patient and tumour risk factors was subsequently performed.

Results: A history of cerebrovascular events or cardiac disease were found to be the strongest independent predictors of post-operative complications (OR 14.84, p = 0.003 and OR 5.71, p = 0.001, respectively). Further strong independent tumour and treatment-related predictors were high grade tumours (OR 1.91, p = 0.038) and the need for additional reconstructive procedures (OR 2.78, p = 0.001). Obesity had significant synergistic interaction with tumour resection diameter (RERI 1.1, SI 1.99, p = 0.02) and high tumour grade (RERI 0.86, SI 1.5, p = 0.01). Comorbidities showed significant synergistic interaction with large tumour resections (RERI 0.91, SI 1.83, p = 0.02).

Conclusion: Patient, tumour and treatment-related variables contribute to complications following flap reconstruction of sarcoma defects. This study highlights the importance of considering the combined effect of multiple risk factors when evaluating and counselling patients as significant synergistic interaction between variables can further increase the risk of complications.

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Keywords: Soft tissue sarcoma; Flap reconstruction; Complications

Introduction

Wide surgical resection is the cornerstone of management for most patients with soft tissue sarcoma (STS) and in many cases this would not be possible without the addition of soft tissue reconstruction.^{1,2} Plastic surgery plays a

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key role in the multidisciplinary management of sarcoma patients as advances in reconstructive techniques facilitate the ability to perform extensive resections while still providing coverage for vital structures and prostheses.^{3–5} This combined approach enables effective oncological ablation while maximizing preservation of function.^{4,6,7}

Although the benefits of soft tissue reconstruction are clear, the addition of free or pedicled flaps increases the

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complexity of the surgery, which extends both the operative and recovery times.^{4,8,9} Identifying patients who are at high risk for post-operative complications is important in the preoperative assessment. Even in cases where the surgical strategy will not change, accurate and personalized estimation of risk is a critical component of effective preoperative counselling to ensure that patients understand the risks and benefits of the proposed treatment and so that any reversible or modifiable medical conditions can be addressed.^{10–13}

The complications of complex soft tissue reconstruction in the context of sarcoma ablation are poorly characterized in the current literature. Similarly the factors that may predispose to such complications are infrequently investigated in this patient population.^{9,14,15} The primary objective of this study was to identify independent predictors of postoperative complications in patients undergoing flap reconstruction following wide resection of soft tissue sarcoma. We specifically examine the significance of patient, treatment and tumour factors and determine if there is a synergistic interaction between these variables in patients with multiple risk factors.

Methods

Institutional research ethics board approval was obtained for this study. Patients who underwent resection of a soft tissue sarcoma from the extremities or trunk and required soft tissue reconstruction with a pedicled or free flap between January 2006 and January 2015 were identified from a prospectively maintained database at Mount Sinai Hospital, Toronto, Canada.

Patient demographics (age, sex, body mass index [BMI] and smoking status), comorbidities and medications, tumour variables (histology, location, tumour depth, stage, grade and diameter of resected tissue; this includes the tumour together with the surrounding soft tissue), adjuvant therapies (radiation, chemotherapy) and operative details (primary or secondary excision, tissues resected, timing of reconstruction, flap details, additional reconstructive procedures and duration of surgery) were collected from the database and retrospective chart review. All postoperative surgical and medical complications were recorded and graded according to the Clavien–Dindo classification of surgical complications.¹⁶

Statistical analyses were performed using SAS v9.4 (SAS institute; Cary, NC). The mean, standard deviation and range of all continuous variables and frequency of all categorical variables were calculated. Bivariate analysis was performed to determine the association between variables and post-operative complications. Wilcoxon rank sum test was used for continuous variables and Chi-square test and Fisher's exact test were used for categorical variables to determine the significance of the association, with p-values <0.05 considered significant. Multivariate logistic regression models were then constructed to identify

independent predictors of post-operative complications. The accuracy of the model was confirmed using the Hosmer–Lemeshow goodness of fit test and c-statistics.¹⁷

To determine whether there were interactions between significant predictors of complications, three measures of interaction were calculated. The relative excess risk due to interaction (RERI) measures the extent to which risk increases in the presence of two risk factors compared to the sum of the individual risks. The attributable proportion (AP) standardizes the RERI as a proportion of risk due to the interaction of two risk factors and the synergy index (SI) is the ratio of the risk of the joint effect to the sum of the individual risks. A RERI or AP > 0 and SI > 1 indicates positive synergistic interaction between risk factors.¹⁸

Results

A total of 294 patients underwent STS resection followed by flap reconstruction and were evaluated in this study. The study group included 164 males and 130 females with a mean age of 58.9 years (\pm 18.9, range 18–97) and mean BMI of 26.9 (\pm 6.6, range 15–63.8). Almost half the study population (48%) had at least one comorbidity. Patient demographics and comorbidities are outlined in detail in Table 1.

The majority of tumours were located in the lower limbs (62%), with the remainder in the upper limbs (29%) and trunk (9%). Two thirds of tumours were categorized as deep (66%) indicating that they were deep to or involved the deep fascia. A large tumour resection was considered as a tumour resection diameter ≥ 10 cm, which was present in 75% of cases. Neoadjuvant radiotherapy was administered in most cases (74%) to a total dose of 50 Gy given in 25 daily fractions of 2 Gy over 5 weeks, with surgical resection planned 4-6 weeks after the completion of preoperative radiation. Conversely relatively few patients (6%) had preoperative chemotherapy. The vast majority of soft tissue reconstructions (96%) were performed immediately after tumour resection as part of the same operation. Tumour and treatment details are outlined in Table 1. Two hundred and fifteen patients (73%) had pedicled flaps while free flaps were performed in 79 cases (27%). The flaps performed in the study group are described in Table 2.

One hundred and thirteen patients (38%) developed a postoperative complication in this series. Of these, 11 patients experienced more than one complication. The majority of the complications included minor issues which were treated conservatively, such as a wound infection, dehiscence or delayed wound healing (Clavien–Dindo grade ≤ 2 ; 22.5%), and 20 percent were major complications (Clavien–Dindo grade ≥ 2). Forty-five patients (15% of cases) required a return to the operating room for secondary surgical intervention. Total or partial flap loss occurred in 2.4% (n = 7) and 2.7% (n = 8) of patients, respectively. Medical complications were relatively rare, occurring in

Table 1				
Patient, tumour and	treatment details	and bivariate	analyses for	complications.

		n = 294	%	Complication		p Value
				No	Yes	
				n = 181 (62%)	n = 113 (38%)	
Patient characteristic						
Age (years)	Mean \pm SD	58.9 ± 18.3		57.3 (±17.9)	61.4 (±18.7)	0.02*
	≥ 65	116	39.5	63	53	
	<65	178	60.5	118	60	0.04*
BMI $(kg/m^2)#$	Mean \pm SD	26.9 ± 6.6		26.3 (±6.8)	27.9 (±6.3)	0.006*
	≥ 30	65	22.1	36	29	
	<30	229	77.9	145	84	0.25
Sex	Female	130	44.2	80	50	
	Male	164	55.8	101	63	0.99
Pre-op haemoglobin	Low	101	34.4	49	52	
1 0	Normal	183	62.2	125	58	0.001^{*a}
ASA class	1 or 2	130	44.2	86	44	
	3 or 4	164	55.8	95	69	0.15
Active smoking <30 days	No	241	82	151	90	0110
	Yes	53	18	30	23	0.41
Anticoagulants	No	239	81.3	155	84	0.11
Anticoaguiants	Ves	55	18.7	26	20	0.02*
Pain modication	No	226	76.0	142	23	0.02
Fain medication	NO Vas	220	70.9	145	85 20	0.27
T 1 1 1	ies N-	08	25.1	50 174	50	0.27
	No	285	90.9	1/4	111	0.40
	Yes	9	3.1	1	/	0.49
Any comorbidity	No	153	52	106	47	
	Yes	141	48	75	66	0.005*
Diabetes	No	258	87.8	164	94	
	Yes	36	12.2	17	19	0.059
Hypertension	No	186	63.3	124	62	
Cardiovascular disease	Yes	108	36.7	57	51	0.02*
	No	249	84.7	163	86	
	Yes	45	15.3	18	27	0.001*
Cerebrovascular disease	No	280	95.2	178	102	
	Yes	14	4.8	3	11	0.003*
Congestive heart failure < 30 days	No	286	97.3	179	107	
	Yes	8	2.7	2	6	0.058
COPD history	No	284	96.6	176	108	
-	Yes	10	3.4	5	5	0.51
Thyroid disease	No	272	92.5	170	102	
	Yes	22	7.5	11	11	0.25
Vascular disease	No	288	97.9	178	110	
	Yes	6	2.1	3	3	0.68
Other comorbidities	No	281	95.5	177	104	
	Yes	13	4.5	4	9	0.04*
Tumour/treatment details					ŕ	
Total duration operation (hours)	Mean + SD	669(+332)		631(+317)	730(+348)	0.014*
Total days in hospital	Mean \pm SD	$11.8 (\pm 9.2)$		$10.1 (\pm 7)$	$14.4 (\pm 11.5)$	<0.001*
Diameter of resection	>10 cm	220	74.8	129	91	<0.001
Diameter of resection	$\leq 10 \text{ cm}$	64	21.8	12)	17	0.032* ^b
Presenting status	L ocal recurrence	24	21.0 8 1	13	17	0.032
Tresenting status	Brimary tumour	270	01.9	15	102	0.44
Drien autocart	No.	210	91.0 71.0	108	102	0.44
Prior surgery	NO No.	211	/1.0	127	04 20	0.44
The state of the s	res	83	28.2	54 102	29	0.44
Tumour site	Lower limb	181	61.6	103	/8	
	Upper limb	85	28.9	58	27	0.14
	Trunk	28	9.5	20	8	0.11
Tumour depth	Deep	193	65.7	114	/9	
	Superficial	101	34.3	67	34	0.22
Tumour grade	1/2	110	37.4	80	30	
	3	180	61.2	100	80	0.003* ^c
Tumour stage	1/2	171	58.2	116	55	
	3/4	120	40.8	62	58	0.005* ^c

Table 1 (continued)

		n = 294 %		Complication	Complication		
				No n = 181 (62%)	Yes n = 113 (38%)		
Surgical resection margin	Positive	45	15.3	29	16		
	Negative	248	84.4	151	97	0.65 [°]	
Residual	No prior surgery	216	73.5	131	85		
	No	21	7.1	12	9		
	Yes	56	19.1	38	18	0.55 ^d	
Pre-operative radiotherapy	No	77	26.2	50	27		
	Yes	217	73.8	131	86	0.48	
Pre-operative chemotherapy	No	276	93.9	167	109		
	Yes	18	6.1	14	4	0.21	
Immediate reconstruction	No	12	4	6	6		
	Yes	282	96	175	107	0.40	
Flap characteristics	Fasciocutaneous	103	35	69	34		
-	Muscle	191	65	112	79	0.16	
	Free flap	79	26.9	45	34		
	Pedicled flap	215	73.1	136	79	0.33	
Total number of tissue removed	0-2	198	67.3	129	69		
(skin, muscle/tendon, bone, nerve, vessel)	3-5	90	30.6	50	40	0.12 ^e	
Additional reconstructive procedures	No	179	60.9	120	59		
	Yes	115	39.1	61	54	0.02*	
Vascular repair	No	284	60.9	177	107		
	Yes	10	39.1	4	6	0.19	
Bone/joint repair	No	276	96.6	174	102		
	Yes	18	3.4	7	11	0.04*	
Tendon/joint repair	No	213	93.9	135	78		
	Yes	81	6.1	46	35	0.30	
Abdominal repair	No	280	72.5	174	106		
	Yes	14	27.5	7	7	0.36	

*Denotes statistical significance (p < 0.05).

#BMI = body mass index.

^a Excluding missing values of 10 patients.

^b Excluding patients undergoing delayed reconstruction.

^c Excluding cases where stage/grade/margin could not be determined.

^d Excluding cases that did not have prior surgeries.

^e Excluding patients undergoing delayed reconstruction.

8.5% of cases. Details of the complications are listed in Table 3. Patients who developed any complication had significantly longer operative procedures (p = 0.01) and hospital length of stay (p < 0.001).

A variety of patient factors were found to be associated with complications including age ≥ 65 years, high BMI, low pre-operative haemoglobin, use of anticoagulants and comorbidities (Table 1). Similarly tumour and treatment factors including diameter of resection, need for additional reconstructive procedures (including bone, nerve, tendon and/or major blood vessel repair) as well as high tumour grade (defined as grade 3) and stage (defined as stage 3/ 4) were found to be significantly associated with the risk of developing complications (Table 1). Neither preoperative radiation nor chemotherapy were found to be associated with complication rates in this series. The location of the tumour and the type of flap used for reconstruction did not influence the development of complications.

Variables identified as being significant in univariate analysis were selected for inclusion in the multivariate assessment model (Table 4). A history of cerebrovascular events (defined as stroke or transient ischaemic attacks) or cardiac disease (defined as myocardial infarction, coronary artery disease, valvular disease or arrhythmias) were found to be the strongest independent predictors of post-operative complications (OR 14.84, p = 0.003 and OR 5.71, p = 0.001, respectively). Overall complication rates were high in patients with cardiovascular or cerebrovascular histories (60% and 79%, respectively compared to 38% in the study group in general, p = 0.012 and p = 0.008, respectively). As might be expected the majority of major medical complications occurred in these groups (36% and 16%, respectively). Major wound complication rates were also increased in patients with cardiovascular disease (25% compared to 15% in the study group in general, p = 0.032). The tumour factors high grade and large tumour resection as well as the treatment factor need for additional reconstructive procedures were also found to be important independent predictors of complications (OR 1.91, p = 0.038, OR 1.04, p = 0.035 and OR 2.78, p = 0.001, respectively).

We then examined whether important patient-related (BMI \geq 30 and comorbidities), tumour-related (large

Table 2Overview of pedicled and free flaps performed.

	n (% of total)
Pedicled flaps (n = $215, 73\%$)	
Gastrocnemius	62 (21)
Latissimus dorsi	43 (15)
Radial forearm	26 (9)
Sartorius	23 (8)
Rectus abdominus	17 (6)
Anterolateral thigh	16 (5)
Perforator	7 (2)
Gluteus maximus	5 (1.8)
Soleus	3 (1)
Pectoralis	3 (1)
Gracilis	3 (1)
Tensor fascia lata	2 (0.7)
Vastus lateralis	1 (0.3)
Rectus femoris	1 (0.3)
Semimembranosus	1 (0.3)
Paraspinal	1 (0.3)
Trapezius	1 (0.3)
Free flaps (n=79, 27%)	
Anterolateral thigh	46 (16)
Latissimus dorsi	16 (5)
Rectus abdominus	8 (3)
Radial forearm	6 (2)
Gracilis	2 (0.7)
Parascapular	1 (0.3)

resection diameter, high tumour grade) and treatmentrelated (need for additional reconstructive procedures) risk factors might have a synergistic interaction and increase the chance of developing complications. In the presence of obesity the risk of developing complications increased for all 3 tumour risk factors. Patients with large tumour resections had a greater risk of developing complications if they also had comorbidities (Table 5). We then determined the extent to which these findings were due to interaction rather than simply a sum of the individual risks (Table 5). This confirmed that obesity had significant interaction with large tumour resections (RERI 1.1, SI 1.99, p = 0.02) and high tumour grade (RERI 0.86, SI 1.52, p = 0.01). Comorbidities showed significant synergistic interaction with large tumour resections (RERI 0.91, SI 1.83, p = 0.02).

Discussion

This study examined predictors of post-operative complications in patients undergoing reconstruction of soft tissue sarcoma defects in a large series at a tertiary cancer centre. Patient, tumour and treatment related variables were all found to contribute to increased risk of complications. In addition tumour and patient variables showed evidence of synergistic interaction further increasing the risk of complications in the presence of more than one risk factor.

We identified a number of variables that can significantly impact the development of both medical and surgical

Table	3
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Post-operative complications in the	he study	group.
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Complications classified according to	n	%
the Clavien–Dindo system*		
Grade I	16	5.4
Dehiscence	7	2.4
Delayed wound healing	7	2.4
Infection	1	0.3
Haematoma	1	0.3
Grade II	50	17.0
Wound related	28	9.5
Infection needing abs p.o.	9	3.1
Infection needing abs i.v.	9	3.1
Dehiscence	6	2.0
Delayed wound healing	3	1.0
Partial necrosis	1	0.3
Medical	22	7.5
Delirium	7	2.4
Arrhythmia	4	1.4
\geq 3 Transfusions	3	1.0
Deep vein thrombosis	3	1.0
Pneumonia	2	0.7
Urinary tract infection	1	0.3
Endocarditis	1	0.3
Pulmonary embolism	1	0.3
Grade 3	56	19.0
Grade 3a	11	3.7
Infection	3	1.0
Seroma	2	0.7
Delayed wound healing	1	0.3
Partial necrosis	5	1.7
Grade 3b	45	15.3
Infection	13	4.4
Dehiscence	6	2.0
Haematoma	3	1.0
Delayed wound healing	4	1.4
Flap compromise	4	1.4
Partial flap loss	8	2.7
Total flap loss	7	2.4
Grade IV	2	0.7
Myocardial infarction	1	0.3
Systemic sepsis	1	0.3
Total complications	124	42.2
Total patients developing a complication ^a	113	38.4

* Clavien—Dindo classification: Grade I: Any deviation from the normal postoperative course without the need for pharmacological treatment or surgical, endoscopic, and radiological interventions. Grade II: Requiring pharmacological treatment with drugs other than such allowed for grade I. Grade III: Requiring surgical, endoscopic or radiological intervention (a: under local anaesthesia; b: under general anaesthesia). Grade IV: Life-threatening complication requiring IC/ICU (a: single organ; b: multiorgan dysfunction). Grade V: death.

^a 11 patients experienced >1 complication, and each was counted as one complication event in the statistical analyses.

post-operative complications in patients with STS undergoing flap reconstruction. Significant patient variables included obesity and prior history of cerebrovascular or cardiovascular disease while the tumour related variable of resection diameter and high grade and the treatment variable need for additional reconstructive procedures were also found to be important. While a high BMI may not be modifiable in the acute cancer setting, patients with cerebrovascular or cardiovascular disease may be amenable to

Table 4 Multivariate assessment of independent risk factors for complications.

Characteristic	OR	95% (p Value	
Age ≥65 years	1.00	0.98	1.01	0.63
Body mass index $\geq 30 \text{ kg/m}^2$	1.06	1.01	1.11	0.012*
Having a comorbidity	1.32	0.65	2.68	0.44
Cardiovascular disease	5.71	2.01	16.22	0.001*
Cerebrovascular disease	14.84	2.46	89.67	0.003*
Use of anticoagulants	0.44	0.17	1.19	0.11
Low preoperative haemoglobin	1.95	1.00	3.80	0.052
Diameter of resection ≥ 10 cm	1.04	1.00	1.09	0.035*
High tumour grade	1.91	1.04	3.51	0.038*
Additional reconstructive procedures	2.78	1.54	5.03	0.001*
Hosmer-Lemmeshow p value	0.86			
C statistic	0.77			

* Denotes statistical significance (p < 0.05).

risk assessment and intervention prior to surgical management. Identification of specific risk factors is essential to pre-operative patient counselling since beyond possible risk modification, the provision of accurate information on the risks and benefits of treatment has been identified as a key target in improving the quality of cancer care.¹⁹

As might be anticipated increased diameter of resected tissue was found to be a significant predictor of postoperative complications as larger soft tissue defects would be more challenging to cover and lead to higher rates of wound complications such that total or partial flap failure might be expected.²⁰⁻²³ While composite resections of multiple tissues did not influence the development of complications, the need for reconstruction of deep structures was found to be a significant risk factor. Previous studies have identified an association between vascular reconstruction and complications²⁴⁻²⁶ but in this study only osseous reconstruction was individually associated with complications (p = 0.04). This may reflect the increased complexity of cases that required use of tumour prostheses or bone allografts and the associated risk of infection with use of alloplastic materials.

Although preoperative radiation is considered a risk factor for post-operative complications, we did not find this to be the case in this series. Previous studies have reported higher wound complication rates in sarcoma patients who have received radiation but in many cases the wounds were closed primarily and their findings may not apply to flap reconstructions.^{20,21,27} As pedicled and free flaps import well-vascularized tissue that has not been exposed to radiation it is possible that they mitigate the effects of radiation on wound healing. Preoperative radiation is the standard protocol at our centre and we therefore have significant experience performing complex reconstructions in recently radiated fields and our flap success rate is unaffected by prior radiation.²⁸ Accordingly, we may have a lower threshold for performing flap reconstruction compared to other institutions where patients have not received preoperative radiation. We acknowledge that our findings may not be applicable to other centres. Tumour location has also been reported to influence the development of complications but this study found no significant difference between complication rates in tumours of the upper or lower limbs.^{29–31} Similarly others have shown increased wound problems when tumours are located close to the skin^{32,33} but this was not the case in our study where deep rather than superficial lesions were found to be more predictive of post-operative complications.

Flap coverage facilitates tension free closure that does not rely on compromised native skin flaps for healing. These benefits may help mitigate the effects of risk factors that have been identified as significant for complications in cases where flaps are not used.

The findings of this study support the theory that immediate reconstruction may have favourable effects on postoperative wound healing and also suggest that the effects of risk factors on complications differ when flap reconstruction is included in surgical management.^{2,20,21} This highlights the importance of considering risk factors specific to STS patients undergoing flap reconstruction as they may differ considerably from risk factors in patients undergoing primary wound closure, which have been extensively studied. Similarly patients with STS differ from patients having flap reconstructions for defects at other anatomic

Table 5

Adjusted odds ratios for the	joint effects of tumour,	patient and treatment-related	factors and measures of	their synergistic interaction
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	Tumour and treatment factors														
	Diameter of resection ≥ 10 cm				High tumour grade			Additional reconstructive procedures							
	OR	p Value	RERI	AP	SI	OR	p Value	RERI	AP	SI	OR	p Value	RERI	AP	SI
Obesity alone	1.35	0.70				1.71	0.33				2.15	0.09			
Tumour factor alone	1.76	0.19				1.95	0.06				3.00	< 0.01			
Obesity + tumour/ treatment factor	3.22	0.02*	1.10	0.34	1.99	3.52	0.01*	0.86	0.24	1.52	4.01	0.01	-0.14	-0.04	0.95
Comorbidities alone	1.06	0.94				1.96	0.24				1.85	0.19			
Tumour factor alone	1.68	0.32				2.47	0.04				3.80	< 0.01			
Comorbidities + tumour/ treatment factor	3.18	0.02*	0.91	0.34	1.83	2.78	0.03	-0.65	-0.23	0.73	3.61	0.01	-1.04	-0.29	0.72

RERI = relative excess risk due to interaction; AP = attributable proportion due to interaction; SI = synergy index.

* Denotes statistical significant positive synergistic interaction (p < 0.05).

sites such as the head and neck, breast or extremities secondary to trauma, where other predictors of complications have been identified.

Recognition of possible interactions between risk factors aids the development of a more comprehensive individualized risk profile. Our study demonstrated significant synergistic interactions suggesting that patient variables can further increase the impact of tumour related risk factors. Synergy indicates that the effect of two risk factors in combination exceeds the sum of their individual effects. The combination of obesity and large tumours doubled the effect of these individual risk factors (SI 1.99). Similarly when obesity and high tumour grade occurred simultaneously the effect on complications was increased by a factor of 1.5 (SI 1.52). While comorbidities in general did not increase the risk of complications in our series we noted that when combined with large tumour resection diameter, the combination significantly increased complication rates and the synergistic effect of these variables was almost double the sum of the individual risks (SI 1.83). Although it might be expected that larger and more complex tumours would have higher complication rates in older patients, this was not found to be the case. This result show that the development of complications is multifactorial and that pre-operative assessment must consider risk factors in the context of the presence or absence of other variables.

We previously reported that the American College of Surgeons NSQIP Surgical risk calculator failed to identify patients at risk of complications following flap reconstruction of STS defects.³⁴ We hypothesized that failure to consider tumour-specific factors may have compromised the efficacy of the tool and this is supported by the results of the current study which confirmed that tumour related variables are important predictors of complications and can increase the significance of patient related variables such as obesity and comorbidity that are included in the calculator.

This is, to our knowledge, the most comprehensive study of factors contributing to complications following flap reconstruction of STS defects. We have identified significant patient, treatment and tumour-related risk factors that are specific to this patient population. Accurate risk prediction remains a significant challenge, particularly in complex and diverse procedures such as STS reconstruction. This study is an important step in delineating the relative risk associated with multiple variables and understanding the multifactorial nature of postoperative complications in these patients. There are however, some limitations to our study. We exclusively included patients undergoing flap reconstruction and so no direct comparison can be made to patients undergoing primary closure, making it impossible to determine the contribution of reconstructive surgery to the complications observed. In addition, complications were considered collectively for the purpose of statistical analysis, so specific predictors of individual complications were not identified. With further development, however, this data may form the basis for a disease-specific risk calculator that can improve individualized risk prediction and enhance pre-operative counselling and planning.

Conclusion

This study identifies important risk factors for complications following flap reconstruction of sarcoma defects. The importance of patient, tumour and treatment-related variables is recognized with significant synergistic interaction between patient and tumour variables.

Conflict of interest statement

There is no conflict of interest for any of the authors of this article.

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