Single-Institution, Multidisciplinary Experience of Soft Tissue Sarcomas in the Chest Wall

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Introduction: We report our single-institution, multidisciplinary experience of nearly 20 years of working on chest wall soft tissue sarcoma cases. The aim of this study was to evaluate clinical outcomes in patients with chest wall soft tissue sarcoma.

Materials and Methods: A retrospective review of 49 surgically treated patients with chest wall soft tissue sarcoma was conducted from 1997 to 2015.

Results: The median age of the patients was 57.0 years. There were 19 full-thickness and 30 partial-thickness resections. Reconstruction was warranted in 37 cases. Sarcomas were high grade in 31 (63.3%) and low grade in 18 (36.7%) cases. Local recurrence developed in 8 and metastasis in 9 patients. No 30-day mortality occurred. By the end of the study period, 35 patients were alive and 14 had died. The 1-, 5-, and 10-year survival rates were 93.8%, 76.0%, and 71.6%, whereas the overall recurrence-free rates were 84.4%, 70.7%, and 70.7% respectively. Favorable prognostic variables for survival included age <50 years and radical treatment (resection with wide margin or resection with marginal margin and adjuvant radiotherapy). Patients who had undergone nonradical treatment had a 3.1-fold lower chance of survival than did those who had undergone radical treatment (95% confidence interval, 0.96–10.12; $P = 0.06$).

Conclusions: Our study suggests that surgical resection with wide margins should continue to be the mainstay for patients with chest wall sarcoma. Even extensive chest wall resections and reconstructions are safe. If wide margins are not achieved, (neo)adjuvant radiotherapy should be considered to improve local control.

Key Words: sarcoma, chest wall, soft tissue, plastic surgery, reconstruction

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Soft tissue sarcomas in the chest wall are uncommon malignancies. In 2017, approximately 1.7 million new cases of cancer were diagnosed, of which <1% (12,390) were soft tissue sarcomas in the United States; of these, generally only 10% to 15% were found in the chest wall.[1,2]

Although our previous study demonstrated that chondrosarcoma has a higher 5-year overall survival rate than do soft tissue sarcoma,[3] many publications have analyzed chondrosarcoma, osteosarcoma, and soft tissue sarcoma together,[2,4,5] despite their heterogeneity. Furthermore, the prognosis of soft tissue sarcomas is often dependent on the histological subtype of sarcoma, grade, and location of the tumor[6]; for instance, tumors arising from extremities have better survival rates than do those arising from the retroperitoneum.[7] A study by Gross et al[8] indicated that clinical behavior of chest wall soft tissue sarcomas is similar to that of sarcomas arising in the extremities and that the optimal form of management in these cases is wide surgical resection. More recently, a trend toward improved overall survival and/or reduced recurrence rates has been demonstrated with adjuvant chemotherapy.[9,10]

In the present study, we retrospectively evaluated 49 patients with soft tissue sarcoma located within the chest wall bony structure. The main aims of this study were to evaluate our 20 years of experience with chest wall soft tissue sarcoma, surgical outcome, survival, and disease-free survival and to identify whether there are any independent prognostic factors for survival and survival and recurrence. Furthermore, we aimed to analyze the benefits of adjuvant therapy in our series.

MATERIALS AND METHODS

Patients

Forty-nine patients with primary soft tissue sarcomas of the chest wall were referred to the Department of Plastic Surgery at Helsinki University Hospital in Helsinki, Finland, between 1997 and 2015. A retrospective review of our institutional sarcoma databases was performed to identify appropriate patients. Informed consent was obtained from all patients. Clinical data were obtained from medical records following study approval by the Ethics Committee of Helsinki Central Hospital. The following information was collected for all patients: age, sex, tumor type and location, extent of resection, reconstructive method, metastasis and/or recurrence, and pathologically estimated surgical margin. Preoperatively, plain chest radiography, computed tomography, and magnetic resonance imaging of the thoracic spine were performed for trunk examination, and ultrasonography (ultrasound-guided core needle biopsy) was performed on the tumor. These cases were discussed by the multidisciplinary tumor board.

Regimens

Because of marginal surgical resection and/or histologically aggressive high-grade tumors, patients need adjuvant therapy. Conventionally fractionated radiotherapy doses varied from 42 to 66 Gy. The doxorubicin dosage ranged from 40 to 50 mg/m^2, and the ifosfamide dosage ranged from 4 to 5 g/m^2 per 21-day cycle.

Statistical Analysis

The follow-up period for both overall survival and disease-free survival began from the date of operation and ended on the date of death or the last follow-up. Outcome measures were recurrence and survival, calculated using the Kaplan-Meier method. Differences were determined using log-rank analysis, and independent prognostic factors for survival and disease-free survival were analyzed using Cox proportional hazards regression. The following variables were analyzed for prognostic purposes: sex, age (<50 or ≥50 years), surgical margin (wide resection, marginal resection, or intralesional resection), treatment type (radical or nonradical), tumor grade, and adjuvant therapy (surgical resection only or surgical resection combined with radiotherapy/chemotherapy). Radical treatment was provided using wide surgical margin resection or marginal margin resection

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TABLE 1. Patient Characteristics (n = 49)

Characteristics	Values
Age	
Median, y	57.0
Range, y	17–90
<50 y, n (%)	13 (27)
≧50 y, n (%)	36 (73)
Sex, n (%)	
Male	19 (39)
Female	30 (61)
Oncological history, n (%)	
None	32 (65)
Previous chemotherapy	1 (2)
Previous radiotherapy at site	12 (24)
Previous chemoradiotherapy	4 (8)

with radiotherapy. Desmoid tumor patients were excluded from the latter 4 categories because they only had the local aggressive nature of the disease and because they did not need wide excision and adjuvant therapy.[11] All statistical analyses were conducted using the statistical software NCSS8 (NCSS, East Kaysville, Utah). A P value of ≤0.05 was defined as significant.

RESULTS

Patient Characteristics

Forty-nine patients with soft tissue sarcomas in the chest wall underwent surgical treatment with multidisciplinary decision making. The median age of the patients was 57.0 years (range, 17–90 years), with 19 male patients and 30 female patients. More detailed patient characteristics are listed in Table 1.

Tumor Characteristics

The most common histological type of tumor was malignant fibrous histiocytoma (n = 15; 30.6%), followed by desmoid tumor (n = 11; 22.5%), fibrosarcoma (n = 4; 8.2%), and angiosarcoma (n = 4; 8.2%; Table 2). Thirty-one tumors (63.3%) were high grade, and 18 (36.7%) were low grade. TMN classification of the patients is illustrated in Table 3.

TABLE 3. Operative and Clinical Characteristics

Characteristic	Values
Tumor grade, n (%)	
Low grade	7 (18)
High grade	31 (82)
TMN classification, n (%)	
T1N0M0	14 (36.8)
T2N0M0	14 (36.8)
T3N0M0	6 (15.8)
T4N0M0	1 (2.6)
T2N1M0	1 (2.6)
T1N1M1	1 (2.6)
T3N0M0	1 (2.6)
Chest wall resection	
Partial thickness, n (%)	30 (61)
Full thickness, n (%)	19 (39)
Rib resection, n (%)	24 (49)
No. resected ribs, average	2.58
Sternal resection, n (%)	8 (16)
Lung resection, n (%)	2 (4)
Diaphragmatic resection, n (%)	7 (14)
Clavicle/scapula resection, n (%)	4 (8)
Defect size, cm^2, median (range)	153 (9.9–390)
Adjuvant therapy (without desmoid), n (%)	
Radiotherapy	11 (29)
Chemotherapy	6 (16)
Chemoradiotherapy	1 (3)
None	20 (53)
Margin status, n (%)	
Wide	14 (29)
Marginal	28 (57)
Intralesional	7 (14)

TABLE 2. Histological Subtypes of Soft Tissue Sarcoma of Chest Wall

Histology	Grade 1*	Grade 2*	Grade 3*	Grade 4*	Total No.	%
Malignant fibrous histiocytoma			4	11	15	30.6
Desmoid tumor					11	22.5
Fibrosarcoma		3		1	4	8.2
Angiosarcoma			1	3	4	8.2
Synovial sarcoma				3	3	6.1
Liposarcoma	1		1		2	4.1
Leiomyosarcoma			1	1	2	4.1
Pleomorphic sarcoma				1	1	2.0
Malignant peripheral nerve sheath tumor		1			1	2.0
Cystosarcoma phyllodes			1		1	2.0
Unclassified sarcoma		2	1	2	5	10.2
Total	1	6	9	22	49	100

*Soft tissue sarcoma malignancy grading is based on a 4-tiered grading system used by the Scandinavian Sarcoma Group.[12,13]

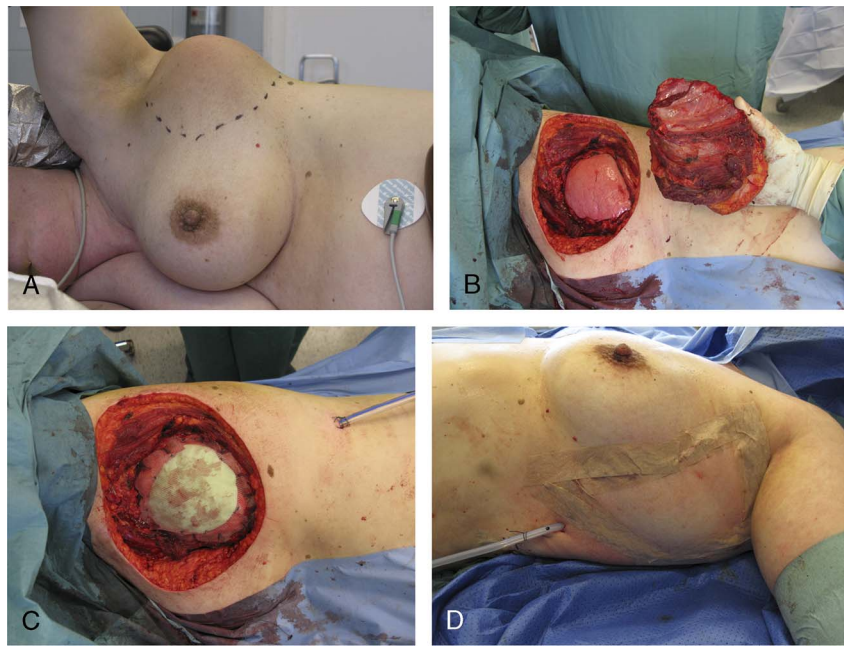

FIGURE 1. A, A soft tissue sarcoma of the anterior chest wall. B, Tumor resection with ribs. C and D, Reconstruction with sandwich mesh method[15] and free tensor fascia lata flap.

Operative Characteristics

After pathological estimation of the surgical margin,[14] a wide surgical resection (>2.5 cm or intact fascia/pleura) was performed in 14 patients, resection margins were proved to be marginal resection (1 mm–2.5 cm) in 28 patients (including 7 desmoid patients), and resection margins were proved to be intralesional in 7 patients (including 4 desmoid patients). Operative characteristics are provided in Table 3.

All patients had one-stage surgery that included tumor removal and defect reconstruction in the same procedure. In only 12 (24%) patients, the chest wall defect could be closed primarily, whereas the remaining 37 (76%) patients all required chest wall reconstruction. Chest wall stabilization was performed in 26 patients, whereas in 11 patients, soft tissue coverage alone with a flap was sufficient and actual chest wall stabilization was unnecessary. In 13 patients undergoing chest wall stabilization, concurrent soft tissue reconstruction with a flap was indicated.

Chest wall stabilization comprised 21 cases using a mesh, 3 cases using a sandwich technique (methyl-methacrylate between 2 meshes),[15] 1 case using free avascular rib grafts and a mesh, and 1 case using Stratos titanium bars (Medxpert, Max-Immelmann-Allee, Eschbach, Germany).

Overall, soft tissue reconstruction with a flap was performed in 24 patients. Microvascular free flap was necessary in 6 patients. Pedicled or local flaps were used in 18 patients (Fig. 1A–D).

Complications

No perioperative mortalities occurred. Most patients (78%; n = 38) had no complications. Complications and Clavien-Dindo classifications are shown in Table 4. The most frequent complication was wound infection (n = 4; 8.2%), followed by artery/vein thrombosis of

TABLE 4. Complications and the CD Classification of Complications

No.	Disease	Reconstruction	Complications	CD
1	Sarcoma	Stabilization (mesh) + pedicled LD flap	Pneumonia	GrII
2	Sarcoma	Stabilization (mesh) + free TFL flap	Artery/vein thrombosis	GrIIIb
3	Sarcoma	Pedicled LD flap	Ileus	GrII
4	Sarcoma	Stabilization (mesh) + pedicled LD flap	Donor site necrosis	GrIIIb
5	Sarcoma	Stabilization (mesh)	Wound infection	GrII
6	Sarcoma	Stabilization (mesh) + free TFL flap	Donor site infection	GrII
7	Sarcoma	Stabilization (mesh +Stratos) + pedicled LD flap	Titanium bars broken	GrIIIb
8	Sarcoma	Stabilization (mesh + cement) + free TFL flap	Artery/vein thrombosis	GrIIIa
9	Sarcoma	Stabilization (mesh + cement) + free ALT flap	Wound infection	GrII
10	Desmoid	Resection only	Wound infection	GrII
11	Desmoid	Stabilization (mesh) + pedicled LD flap	Tip necrosis of flap	GrIIIb

ALT, anterolateral thigh flap; CD, Clavien-Dindo classification; LD, latissimus dorsi; Gr, grade; TFL, tensor fascia lata.

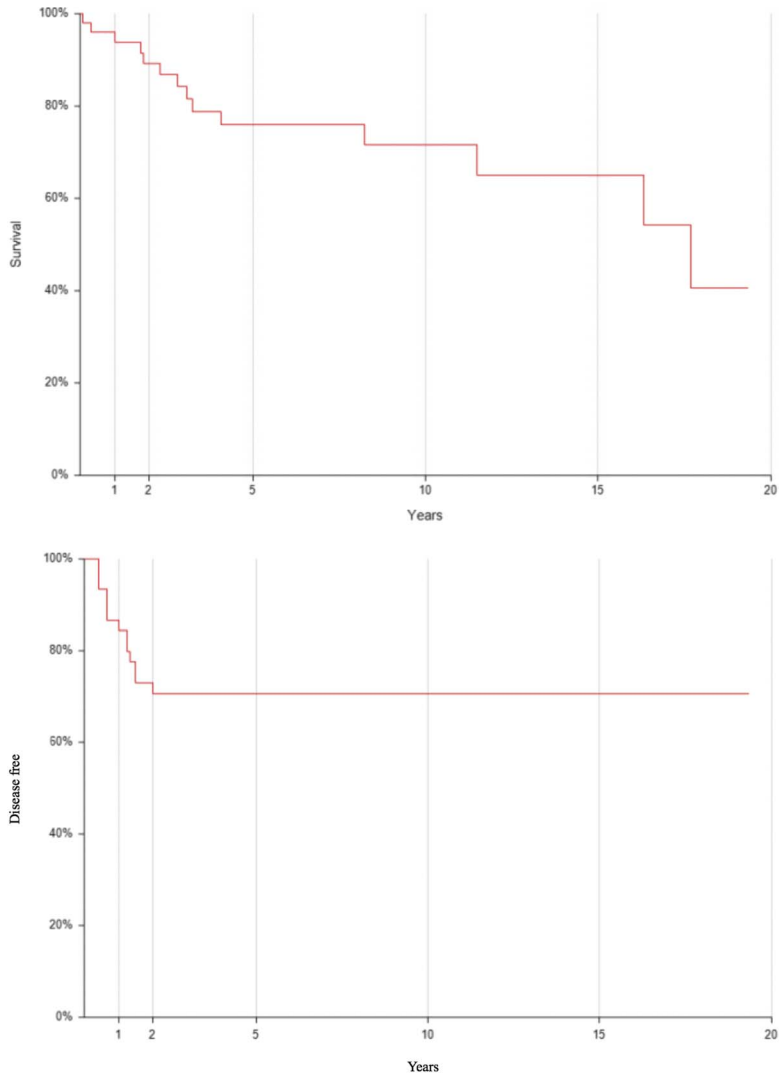

FIGURE 2. Overall survival and disease-free survival. Overall survival (above). Disease-free survival (below).

TABLE 5. Survival and Disease-Free Time (n = 49; Including 11 Desmoid Tumor Patients)

Variable and Categories	No.	5-y OSR, %	*P*	5-y DFSR, %	*P*
All cases	49	76.0		70.7	
Age, y					
<50	13	100	0.02*	69.2	0.93
≧50	36	66.4		71.3	
Sex					
Male	19	69.7	0.45	73.3	0.99
Female	30	80.0		69.8	
Clavien-Dindo classification					
No complications	38	74.5	0.64	70.7	0.71
Grade II	6	62.5		60.0	
Grade III	5	100		80.0	

*$P < 0.05$.

DFSR, disease-free survival rate; OSR, overall survival rate.

the flap (n = 2; 4.1%). A single instance was seen of each of the following: distal tip necrosis of the flap, donor site necrosis, ileus, broken titanium bar (latent), and pneumonia. Six patients who developed complications required antibiotics or ointment, and 5 required further surgery.

Oncological Treatments

Eleven patients received radiotherapy, 6 patients received chemotherapy, and 1 patient received both treatment modalities (Table 3).

Follow-up, Overall Survival, and Disease-Free Survival

The median follow-up time was 7 years and 2 months. No 30-day mortality occurred. By the end of the study period, 35 patients were alive and 14 had died, 9 died of sarcoma and 5 died of other causes. Local recurrence developed in 8 and metastasis in 9 patients. The 1-, 5-, and 10-survival rates were 93.8%, 76.0%, and 71.6%, whereas overall recurrence-free rates were 84.4%, 70.7%, and 70.7%, respectively (Fig. 2). The variables of age, treatment (radical or nonradical), and margin (wide, marginal, or intralesional) correlated with prognosis with a statistically significant difference (Tables 5 and 6; Fig. 3). Patients with high-grade tumors had a lower 5-year overall survival rate (60.8%) than did those with low-grade tumors (100%). However, this difference did not reach statistical significance because of the small sample size.

Patients who underwent nonradical treatment had a 3.1-fold reduction in survival compared with those who underwent radical treatment (95% confidence interval [CI], 0.96–10.12; $P = 0.06$; Table 7). Patients whose surgical margins were marginal or intralesional margin resection had a lower 5-year overall survival rate (61.9% and 0%, respectively) than did those who underwent wide surgical resection (85.1%) Table 6.

DISCUSSION

Soft tissue sarcoma is a rare malignancy that can occur almost anywhere in the human body; the most common sites, however, are the extremities. Sarcoma has an infiltrative growth pattern, and local recurrence of the disease after surgical treatment is common. Soft tissue sarcoma typically disseminates hematogenously, most frequently in the lungs. Although death in patients with soft tissue sarcoma is usually due to distant metastases, local recurrence causes abundant morbidity and may lead to mutilating operations. The prevention and prediction of local recurrence is therefore an important goal in management of these cases.[16]

Here, we present our single-institution, multidisciplinary experience with a long follow-up of working with chest wall soft tissue sarcoma cases comprising an analysis of the fourth largest series of cases of this condition. The largest series of chest wall sarcoma was reported in 1991 by Gordon et al,[17] who examined 149 patients with thoracic wall sarcoma (including 32 desmoid tumors) and identified a 66% 5-year overall survival rate. The second largest series was reported by Burt et al,[18] with a 5-year overall survival rate of 41% and a 5-year disease-free survival rate of 57% in 65 chest wall sarcoma patients. The third was Gross et al,[8] which included 55 patients with a 5-year overall survival rate of 87.3%; indeed, only 42% of tumors were high grade in their series. In our study, the 5-year overall survival rate was 76.0%, and the 5-year disease-free survival rate was 69.6%, which compares well with these previous studies.

Although we attempted to conduct an analysis of recurrence risk in an independent manner, the small sample size precluded a multivariate analysis including all variables. However, we did find that patients who had undergone nonradical treatment had a 3.1-fold higher risk of death compared with patients who had radical treatment (95% CI, 0.96–10.12; $P = 0.06$). We also identified a statistically significant difference in overall survival based on age, treatment, and margin type. In those patients younger than 50 years, radical treatment and wide marginal resection were associated with improved survival. In addition, it was found that in most series of soft tissue sarcomas, age was an important prognostic factor.

Furthermore, we investigated whether the Clavien-Dindo classification correlated with prognosis, as little has been published regarding the efficacy of the Clavien-Dindo classification in soft tissue sarcoma reconstruction. The Clavien-Dindo classification, first developed in 1992,[19] categorized surgical complications according to their severity and has subsequently become standard practice in general surgery.[20,21] In the present study, we did not find a statistically significant association between the Clavien-Dindo classification and patient outcomes. Further research is warranted on the usefulness of the Clavien-Dindo classification for soft tissue sarcoma of the chest wall.

In the present study, the patients with nonradical treatment had a 3.1-fold reduction in survival compared with those who received radical treatment consisting of either wide resection or marginal resection combined with radiotherapy. Surgery alone may be adequate treatment of sarcomas, but the risk of local recurrence remains high if wide margins are not achieved in the procedure. To improve local control rates, the effect of radiotherapy on sarcomas has been investigated. A randomized study by Yang and colleagues[22] demonstrated that postoperative radiotherapy decreased the probability of local recurrence significantly in high-grade sarcomas but had no effect on overall survival. However, a recent database analysis of 3422 patients who underwent resection for large high-grade soft tissue sarcoma between 2004 and 2013 indicated that the hazard ratio for death was 35% less with combined surgery and radiotherapy compared with surgery alone.[12] Six of our patients received adjuvant chemotherapy consisting of doxorubicin and ifosfamide, which are the 2 most active cytostatic drugs in sarcoma. The use of adjuvant chemotherapy in the treatment of soft tissue sarcomas is still controversial, but potential advantages rely on preventing distant metastases. According to the latest updated meta-analysis, both doxorubicin (absolute risk reduction [ARR], 9%) and doxorubicin combined with ifosfamide (ARR, 10%) significantly but modestly

TABLE 6. Survival and Disease-Free Time (n = 38), Without Desmoid Tumor Patients

Variable and Categories	No.	5-y OSR, %	*P*	5-y DFSR, %	*P*
Treatment					
Radical	20	80.3	0.04*	80.7	0.29
Nonradical	18	47.5		64.3	
Margin					
Wide margin	14	85.1	0.02*	84.6	0.05
Marginal margin	21	61.9		70.2	
Intralesional margin	3	0		0	
Grade					
Low grade	7	100	0.05	100	0.09
High grade	31	60.8		67.1	
Adjuvant therapy					
Resection + adjuvant	16	52.5	0.36	58.6	0.10
Resection only	22	79.5		85.0	

Radical treatment: resection with wide margin (>2.5 cm or intact fascia/pleura) or marginal margin resection (1 mm–2.5 cm) with radiotherapy. Resection + adjuvant: patients had tumor resection and adjuvant radiotherapy or/and chemotherapy.

*$P < 0.05$.

DFSR, disease-free survival rate; OSR, overall survival rate.

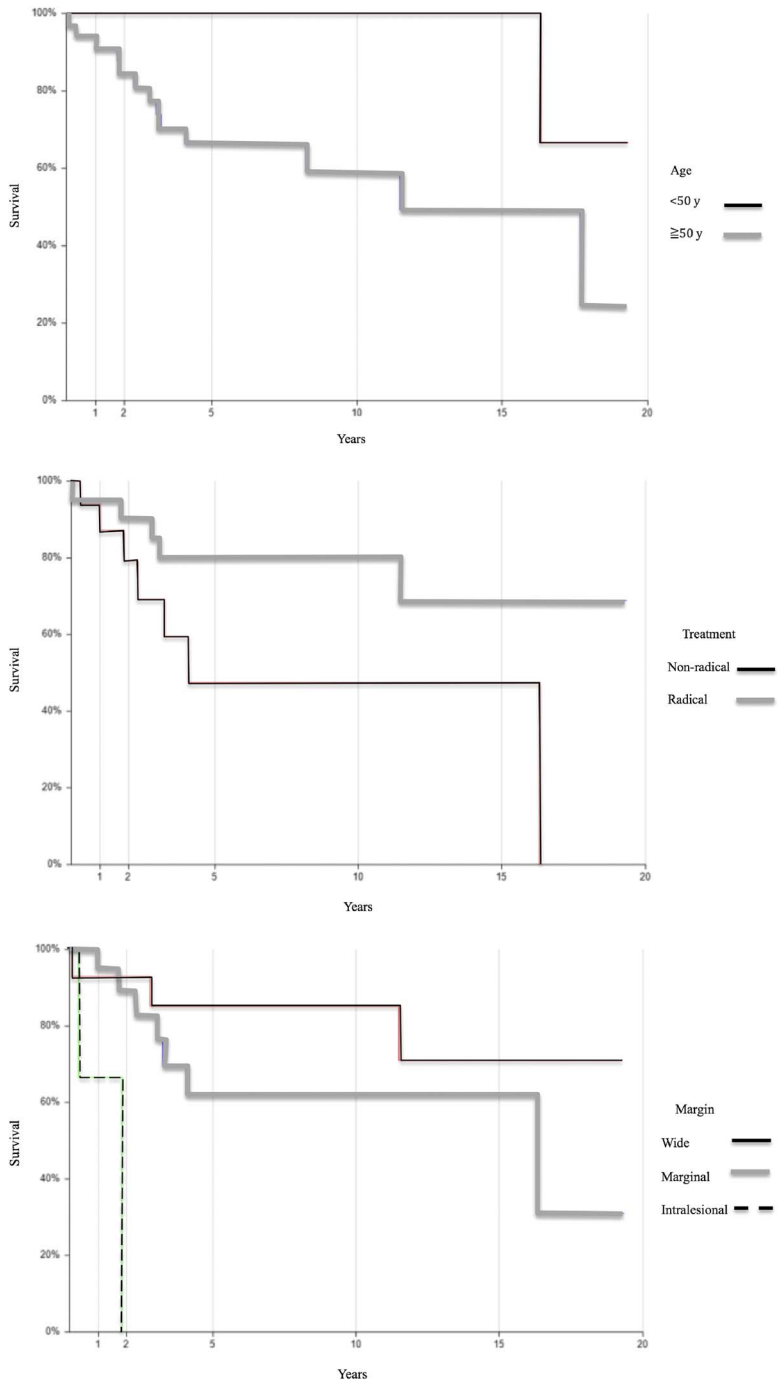

FIGURE 3. Overall survival by age, treatment, and surgical margin. Overall survival by age (thin solid, <50 y; thick solid, ≧50 y; above). Overall survival by treatment (thick solid, radical; thin solid, nonradical; middle). Overall survival by surgical margin (thin solid, wide; thick solid, marginal; dotted line, intralesional; bottom).

decreased distant recurrence rate.[10] The combination of doxorubicin and ifosfamide was also associated with an overall survival benefit and an ARR of 11%.[10]

We acknowledge several limitations to this study. The retrospective reviewing of clinical diagnostic data from the medical records, not initially intended for research work, is prone to bias.

CONCLUSIONS

Our study suggests that surgical resection with wide margins should continue to be the mainstay for patients with chest wall sarcoma. Even extensive chest wall resections and reconstructions are safe. If wide margins are not achieved, (neo)adjuvant radiotherapy should be considered

TABLE 7. Multivariate Analyses of Overall Survival

Variable and Categories	Risk Ratio	95% CI	*P*
Age, y			
<50	1.0		
≧50	1.08	1.02–1.14	0.01*
Treatment			
Radical	1.0		
Nonradical	3.12	0.96–10.12	0.06
Sex			
Male	1.39	0.44–4.44	0.57
Female	1.0		
Adjuvant therapy			
Resection + adjuvant	1.0		
Resection only	0.59	0.19–1.86	0.37
Clavien-Dindo classification			
No complications vs grade II	2.42	0.49–11.72	0.27
No complications vs grade III	1.17	0.25–5.60	0.84

to improve local control. However, because of the heterogeneity of sarcomas, further research is warranted to clarify whether any factors can confer benefits on patients with specific subtypes of sarcoma.

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