A SINGLE-INSTITUTIONAL, MULTIDISCIPLINARY APPROACH TO PRIMARY SARCOMAS INVOLVING THE CHEST WALL REQUIRING FULL-THICKNESS RESECTIONS

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Objective: Primary sarcomas involving the chest wall requiring full-thickness excision are rare. We reviewed our experience with these lesions in a tertiary referral cancer center by using multidisciplinary approaches.

Methods: A 10-year retrospective study identified 51 patients referred with primary sarcomas of the chest wall: 40 for initial treatment and 11 after previous unsuccessful surgical excisions elsewhere (secondary referral). Presenting symptoms were pain alone in 23 (45%) of 51 patients, pain with an associated mass in 8 (16%) patients, and an asymptomatic mass alone in 13 (25%) patients. Median symptom duration was 241 days in the primary group and 225 days in the recurrent group. Tumor locations were the sternum (n = 11), the rib alone (n = 36), and the posterior rib with extension into vertebral bodies (n = 4). Histologic types included the following: chondrosarcomas (n = 15), malignant fibrous histiocytomas (n = 9), osteosarcomas (n = 4), Ewing sarcomas (n = 3), desmoid tumors (n = 7), and other types (n = 13). The median tumor volume of those referred initially was 311 cm³ compared with 84 cm³ in patients with recurrent lesions.

Results: Twenty-six (51%) of 51 patients received treatment before resection, including chemotherapy alone (n = 22), radiation alone (n = 3), and combined chemotherapy and radiation therapy (n = 1). The complete sternum was removed in 6 of 11 patients, and the average number of ribs requiring resection was 3.8. Four patients had vertebral body resections. Prosthetic meshes alone were required in 16 of 51 patients, and meshes with methylmethacrylate were required in 18 of 51 patients. Muscle flap reconstructions by plastic surgery were required in 24 patients. Negative margins were obtained in 47 of 51 patients. There were no perioperative deaths with morbidities occurring in 12 (24%) of 51 patients (wound [n = 3], prolonged air leak [n = 1], prolonged ventilator requirement [n = 1], arrhythmias [n = 3], doxorubicin (Adriamycin)-induced cardiomyopathy [n = 1], and other [n = 3]). Postoperative treatment was administered to 13 patients (chemotherapy alone, n = 9; chemotherapy with radiation therapy, n = 4). The cumulative 5-year survival of all patients was 64% (initial referral, 61.3%; secondary referral, 72.7%). The average follow-up is 44.7 months.

Conclusions: A combined aggressive multidisciplinary approach to primary sarcomas of the chest wall resulted in no treatment-related deaths and a cumulative 5-year survival of 64% in patients referred to our tertiary care cancer center. (J Thorac Cardiovasc Surg 2001;121:48-60)

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Read at the Eightieth Annual Meeting of The American Association for Thoracic Surgery, Toronto, Ontario, Canada, April 30–May 3, 2000.

Received for publication May 8, 2000; revisions requested Aug 18, 2000; revisions received Aug 28, 2000; accepted for publication Sept 3, 2000.

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0022-5223/2001 \$35.00 + 0 12/6/111381

doi:10.1067/mtc.2001.111381

Primary sarcomas that involve the chest wall are rare.^{1,2} These tumors originate either in the bone or cartilage of the thoracic skeleton or in the surrounding soft tissues with direct invasion into the interspace or bone. Osias Aimar, in 1778, is believed to have performed the first resection of a chest wall tumor. Parham, over a century ago in 1899, was the first to resect a chest wall sarcoma by means of positive-pressure endotracheal ventilation.³ Before this, breaching the integrity of the pleural envelope would result in an immediate ipsilateral pneumothorax and would often prove fatal to the patient. Many advances in oncology, anesthesia, and surgical procedure have improved the operative morbidity and mortality and long-term survival of these patients. Most series in the world literature, however, are small and usually extend over several decades with a variety of approaches to these lesions. We wished to review our recent experience over the past decade with a multidisciplinary approach to bony and soft-tissue sarcomas that involved the chest wall that required full-thickness excision and reconstruction at our tertiary referral cancer center.

Methods

From January 1, 1990, to December 31, 1998, a total of 1222 patients were identified who had a malignant tumor involving their chest wall at the time of their initial referral to The University of Texas M.D. Anderson Cancer Center (MDACC). For this study, we defined "chest wall" as any neoplasm involving the sternum, ribs, costovertebral junction, or vertebral body. Tumors of the scapula and clavicle were excluded from this analysis. The vast majority of patients had nonsarcomatous metastatic lesions to the thoracic skeleton. One hundred sixty-six patients had a sarcoma histology. Eight-seven patients ultimately underwent surgical resection of these neoplasms. Thirty-six patients had sarcomas that were metastatic to the chest wall, and 51 were primary chest wall sarcomas that were either of bone or soft-tissue origin with invasion of the bony thorax. These 51 patients are the focus of this article.

Forty of these 51 patients were referred initially to our tertiary care center for definitive treatment of their malignant disease. However, many had undergone some form of biopsy before transfer. Eleven patients were secondarily referred after previous curative surgical attempts, with local tumor recurrence in the surgical bed.

A retrospective chart review examined the following data elements: patient age; sex; presenting symptoms; symptom duration; history of previous radiation therapy for another malignancy; tumor location; tumor volume; use of excisional, incisional, or needle biopsies to obtain tissue; histologies; and the use of neoadjuvant chemotherapy or radiation therapy before resection. Surgical techniques, morbidity and mortality, pathologic margins, and the use of prosthetic and plastic surgical reconstructive techniques were reviewed.

Postoperative adjuvant therapies were identified. Patients were followed up until March 31, 2000, and patient status (alive or dead) and disease status (free of disease or local-distant tumor recurrence) were recorded.

Statistics. Survival was calculated for two time-dependent end points. The first end point was overall survival, which was defined as the time in months from the date of operation at our institution until the date the patient was last known to be alive. Any death from any cause was considered a failure. Recurrence-free survival was the second time-dependent end point. This was defined from the date of operation at MDACC to the date of the most recent clinic follow-up visit. A failure was defined if a documented sarcoma recurrence occurred during this follow-up period. Two patients (both residing outside of the United States) were excluded from the recurrence-free survival analysis because their disease status in regard to sarcoma recurrence was unknown at the time of their death. For the remaining 49 patients, we have complete follow-up data to March 2000, with a median follow-up of 44.7 months. Distributions of overall survival and recurrence-free survival times were calculated by the Kaplan-Meier method and compared by use of the log-rank test. Factors analyzed for prognostic significance included the following: type of referral (initial vs secondary referral), age (dichotomized into patients < 50 years of age vs those ≥ 50 years of age), sex, tumor location (sternum vs rib with or without vertebrae), symptomatic presentation (pain vs no pain), tumor size in cubic centimeters (dichotomized into <500 cm³ vs ≥500 cm³), tumor histology (desmoid tumors vs chondrosarcomas vs high-grade sarcomas), number of ribs resected (<4 vs ≥4 for tumors involving the ribs), complete versus partial resection of the sternum (for primary sternal lesions), extended resections requiring more than rib and soft-tissue chest wall (ie, lung, diaphragm, pericardium, and thymus), radiation-induced sarcomas versus other high-grade sarcomas, margins (negative vs positive), and use of neoadjuvant or adjuvant therapies, including chemotherapy, radiation therapy, or both compared with patients undergoing an operation alone. A multivariate analysis of these variables was performed by the Cox proportional hazards model. All statistical analyses were performed with SPSS software (SPSS, Inc, Chicago, Ill).

Results

Demographics. Fifty-one patients were referred to our center with primary sarcomas involving the chest wall from 1990 to 1998. There were 23 male and 28 female patients, with a median age of 47 years (range, 10-81 years). Presenting symptoms included pain alone in 23 (45%) of 51 patients, pain with an associated mass in 8 (16%) of 51 patients, and a mass alone in 13 (25%) of 51 patients. Two patients presented with dyspnea, one with generalized fatigue, and one with a radicular paresthesia. Three patients were completely asymptomatic, with the lesion discovered during a rou-

Fig 1. Computed tomographic images and accompanying final pathologic specimen of a grade I chondrosarcoma involving the costal margin and lower portion of the sternum. This tumor slowly progressed over a 10-year period. The patient presented with anterior chest discomfort and the obvious mass. Computed tomographic images demonstrate the classic findings of a chondrosarcoma, and therefore an initial biopsy was not performed.

tine screening chest radiograph. The median duration of symptoms for those in the initial referral group (40 patients) was 241 days (range, 10-3833 days), and that of the secondary referral group (11 patients) was 225 days (range, 46-814 days) from the time they first noticed the symptoms of their tumor recurrence until rediagnosis. The disease-free interval of the 11 patients (date of previous operation until diagnosis of recurrence made at MDACC) was 591 days (range, 138 days to 20.1 years).

Tumor location and volume. Eleven patients had tumors originating in the sternum. Thirty-six patients had rib tumors only (23 anterior, 2 lateral, and 11 pos-

terior). Four patients had tumors that involved the vertebral bodies, each extending over multiple levels, including one T3-5, one T2-6, one T5-7, and one T1-5. The median volume of tumors for the initial referrals was 311 cm³ (range, 6-1200 cm³; Fig 1) and a somewhat smaller volume in the secondary referral group of 84 cm³ (range, 9-776 cm³). Of the 51 patients, 8 patients underwent definitive operations without an initial biopsy. Nine patients had an excisional biopsy, and 7 patients had an incisional biopsy. Twenty-seven had the initial tissue procurement through fine-needle aspiration or core needle aspiration. A definitive diagnosis was made by our cytopathologist in 24 (89%) of 27

Fig 2. Method of histologic diagnosis of sarcoma in the 51 patients. All incisional and excisional biopsies were performed at outside institutions. Fine-needle aspirates (FNA) and biopsy specimens obtained with a Tru-Cut biopsy needle (Allegiance Healthcare Corporation, McGaw Park, Ill) are the preferred methods for diagnosis at our institution. Eight patients were taken directly to the operating room without a biopsy solely on the basis of the radiologic appearance of the tumor.

patients and correlated in each case with the final surgical pathology. Three patients required more tissue after fine-needle aspiration or core needle biopsy: two had incisional biopsies, and one underwent an excisional biopsy (Fig 2).

Histologies. There were a variety of histologies both of bone and soft-tissue origin. Overall, there were 15 chondrosarcomas, 4 osteosarcomas, 3 Ewing sarcomas, 9 malignant fibrous histiocytomas, 7 desmoid tumors, and 13 others. These are divided up by location and type of referral, as shown in Table I. We have included desmoid tumors in this article because of their aggressive local behavior and tendency to recur and the fact that extensive resections are often required.⁴ Many pathologists and surgical and medical oncologists truly consider these lesions as low-grade sarcomas. We have therefore separately analyzed the survival and recurrence data for desmoid tumors and chondrosarcomas (typically a low-grade sarcoma) from the rest of the other sarcomas in our patient population, which are of higher grades.

Radiation-associated sarcomas. Eight patients had received radiation therapy for a metachronous malignancy, including Hodgkin lymphoma in 2 patients, breast cancer in 4 patients, large cell carcinoma of the lung in 1 patient, and a Wilms tumor in 1 patient. Their sarcomas had occurred in the previous radiation portals and included 1 spindle cell sarcoma, 2 neurogenic sarcomas, 1 osteosarcoma, 1 malignant fibrous histiocytoma, 1 peripheral nerve sheath sarcoma, and 2

Table I. Tumor histology

	Initial referral	Secondary referral
Rib (n = 36) and vertebrae (n = 4); total, n = 40		
Malignant fibrous histiocytoma	6	2
Ewing sarcoma	3	0
Osteosarcoma	4	0
Chondrosarcoma	3	3
Desmoid tumor	5	2
Synovial cell sarcoma	1	0
Neurogenic spindle cell sarcoma	2	0
Poorly differentiated-unclassified or anaplastic sarcomas	6	1
Angiosarcoma	0	2
Sternum (n = 11)		
Chondrosarcoma	8	1
Malignant fibrous histiocytoma	1	0
Spindle cell sarcoma	1	0

angiosarcomas. The median time interval from previous radiation therapy until the development of the sarcoma was 9 years (range, 6-26 years). In the 4 patients in whom the previous radiation dosage was known, the average dose was 48 Gy (range, 42-60 Gy).

Use of neoadjuvant therapy. Multiple different drug regimens and combinations were used to treat these patients. Basic regimens used in our institution for osteosarcoma include doxorubicin (75-90 mg/m²) and cisplatin (120 mg/m²), high-dose methotrexate (8-12 g/m²), or standard ifosfamide (10 g/m²) or high-dose

ifosfamide (14 g/m²). Ewing sarcomas are radiation sensitive. Chemotherapy choices for Ewing sarcoma include single agents proven in phase II trials, including cyclophosphamide (50% response), doxorubicin (40% response), ifosfamide (32%), vincristine (30%), and etoposide (30%) with a less than 7% response to single-agent cisplatin. Combinations of the above (CyVADIC: cyclophosphamide, vincristine, Adriamycin, dacarbazine [DTIC]) are often tried. Chondrosarcomas are both radiation and chemotherapy insensitive, although higher grade chondrosarcomas and dedifferentiated chondrosarcomas are treated with similar agents, as described above. For soft-tissue sarcomas, doxorubicin is one of the most active single agents (15%-45% response rate). Ifosfamide has a similar response rate and is often given with doxorubicin for a synergistic response. Advanced desmoid tumors, which often are technically difficult to resect with clear margins, can be treated with radiation therapy postoperatively. They are also hormonally responsive and have been treated at our institution with tamoxifen. Twenty-six of the 51 patients in this review received some form of neoadjuvant treatment.

Chemotherapy alone. Twenty-two patients received a variety of neoadjuvant chemotherapy regimens. The tumor histologies included malignant fibrous histiocytoma in 7 patients, osteosarcomas in 4 patients, Ewing sarcomas in 3 patients, poorly differentiated sarcomas in 3 patients, an angiosarcoma in 1 patient, desmoid tumors in 2 patients, and chondrosarcomas in 2 patients.

Combination chemotherapy and radiation therapy. Combination therapy was used in 1 patient with a monophasic spindle cell sarcoma. A low preoperative dose of 18 Gy was used.

Radiation alone. Radiation alone was used in 3 patients (2 patients with malignant fibrous histiocytomas [50 Gy each] and 1 patient with a malignant peripheral nerve sheath tumor [10 Gy]).

Operations

Sternum. Six total sternectomies and 5 partial sternectomies were performed for those patients with tumors involving the sternum. Six patients had extended resections (adjacent thoracic structures other than chest wall and soft tissues), including 2 (18%) of 11 lung resections and 4 (36%) of 11 thymus resections. Reconstruction involved the use of prosthetics in 10 of the 11 patients. One patient with an isolated resection of the manubrium had the defect closed with bilateral rotational pectoralis major flaps without synthetic support. Mesh and methylmethacrylate were used in 9 patients, and 1 patient had Prolene mesh (Ethicon, Inc, Somerville, NJ) only without cement.

Rib. Thirty-six patients had primary rib resections. The average number of ribs removed was 3.8 (range, 1-9 ribs). Twenty of the 36 patients had extended tissue resections, including lung in 14 (39%) patients, diaphragm in 4 (11%) patients, thymus in 1 patient, and a forequarter amputation in 1 patient. Fourteen (39%) of the 36 patients required Marlex (Bard Implants, Billerica, Mass), Prolene, or polytetrafluoroethylene* alone, and 8 (22%) of the 36 patients used mesh and methylmethacrylate. Of the 22 patients requiring prosthetic reconstruction, 15 required reconstruction for anterolateral defects and 7 for posterior defects. This represents 60% of the anterolateral tumors and 64% of the posterior tumors that required prosthetics.

Vertebrae. A total of 4 combined rib and vertebral body resections were performed, with 1 patient requiring vertebral body reconstruction. The 3 remaining patients had subtotal resections of the vertebrae that were not believed to compromise the structural stability of the vertebral spinal column. The average number of ribs removed in addition to the vertebral resection was 5 (range, 3-8). Pulmonary resections were required in 2 of the vertebral resections (50%). Only 1 of the 4 patients required prosthetic mesh reconstruction and muscle flap coverage. The 3 remaining patients had the defect adequately protected and covered by the scapula and posterior chest wall musculature.

Plastics flaps. A total of 24 pedicled muscular or myocutaneous flaps were used for soft-tissue coverage, including 8 pectoralis major, 6 rectus abdominis, and 8 latissimus dorsi flaps. Eight of the 11 sternal resections required muscle flaps (2 latissimus and 6 pectoralis flaps). Sixteen of the 40 rib and vertebral body resections required muscle flaps (7 latissimus, 5 rectus abdominis, 1 reverse abdominoplasty, 1 deltopectoral flap; 1 multiple flap of the rectus, latissimus, and pectoralis; and 1 bilateral pectoralis advancement flap). There were no flap failures; however, 3 partial skin-flap dehiscences required additional wound care.

Surgical morbidity and mortality. Negative final pathologic margins were obtained in 47 of 51 patients. Incomplete margins occurred in 4 patients: 1 grossly positive margin because of extensive vertebral body involvement, 1 microscopic positive soft-tissue mediastinal margin during a sternal resection, and 2 rib resections that had microscopic soft-tissue margins positive on final pathologic review but negative during frozen section. Additional resections could not be per-

*Gore-Tex mesh, a registered trademark of W. L. Gore & Associates, Inc, Flagstaff, Ariz.

Table IIA. Prognostic factors for overall 5-year survival

Variable	Overall 5-year survival (n = 51)	P value
Total population	63.7%	
Type of referral (initial vs secondary)	Initial (n = 40) 61.3% Secondary (n = 11) 72.7%	.87
Age (<50 vs ≥50 y)	<50 (n = 28) 67.8% ≥50 (n = 23) 58.3%	.47
Sex	Male (n = 23) 54.4% Female (n = 28) 71.3%	.30
Tumor location (sternum vs rib ± vertebrae)	Sternum (n = 11) 90.0% Rib ± vertebrae (n = 40) 55.3%	.08
Symptomatic presentation (pain vs no pain)	Yes (n = 31) 65.2% No (n = 20) 64.5%	.86
Tumor size (<500 vs ≥500 cm ³)	<500 (n = 23) 74.6% ≥500 (n = 13) 40.0%	.05
Histology (desmoid tumors vs chondrosarcomas vs high-grade sarcomas)	Desmoid tumors (n = 7) 100.0% Chondrosarcomas (n = 15) 90.0% High-grade sarcomas (n = 29) 42.9%	.001
No. of ribs resected (<4 vs ≥4)	<4 (n = 20) 53.4% ≥4 (n = 20) 56.7%	.65
Extent of sternal resection (complete vs partial)	Complete (n = 6) 83.3% Partial (n = 5) 100%	.41
Extended resection of adjacent structures	Yes (n = 24) 57.0% No (n = 27) 69.9%	.24
Radiation-induced sarcomas (radiation-induced vs other high-grade sarcoma)	High grade (n = 21) 53.3% Radiation-induced sarcoma (n = 8) 6.5 mo (median)	.11
Margins (negative vs positive)	Negative (n = 47) 67.2% Positive (n = 4) 25.0%	.02
Use of perioperative chemotherapy, radiation therapy, or both	Yes (n = 29) 58.3% No (n = 22) 70.5%	.29

formed. The 30-day perioperative mortality was zero. The median ventilator requirement was 1 day (range, 0-194 days). Median surgical intensive care unit stay was 2 days (range, 0-194 days).

Complications occurred in 12 (24%) of 51 patients and included 3 arrhythmias, 1 congestive heart failure caused by doxorubicin cardiotoxicity, and 4 respiratory complications, including prolonged respiratory failure in 1 patient who required transfer to a chronic rehabilitation facility 194 days after a complex chest wall and vertebral body resection and bilobectomy for osteosarcoma. There were 3 wound complications, 2 necessitating subsequent removal of the prosthetic mesh. Median hospital stay was 7 days (range, 2-194 days).

When we exclude the 1 patient with prolonged ventilatory failure, the average ventilatory requirements of patients with a prosthesis (n = 33) was 2.8 days compared with 1.4 days for those without prostheses (n =

17; $P = .325$, t test). Similarly, there was no significant difference between the group for the average surgical intensive care unit stay (3.4 days compared with 2.1 days, $P = .37$) and the average length of hospital stay (9.5 days with a prosthesis compared with 8.5 days without a prosthesis, $P = .60$). For patients requiring muscle flaps (n = 24), the average ventilator days were 3.8 days compared with 0.9 days for patients without muscle flaps (n = 26, $P = .04$). The surgical intensive care unit days were 4.4 days versus 1.6 days ($P = .05$). The average hospital length of stay was 11.4 days versus 7.0 days for patients not requiring muscle flaps ($P = .01$). These statistics likely reflect the greater magnitude of the operations that required prosthetics and autologous muscle flaps.

Adjuvant therapy. Thirteen patients received additional therapy after resection, including 2 of the 4 patients with microscopic positive margins. Ten

Table IIB. Prognostic factors for overall recurrence-free 5-year survival

Variable	Recurrence-free 5-year survival (n = 49)	P value
Total population	53.5%	
Type of referral (initial vs secondary)	Initial (n = 38) 50.5% Secondary (n = 11) 60.6%	.85
Age (<50 vs ≥50 y)	<50 (n = 27) 52.7% ≥50 (n = 22) 53.1%	.60
Sex	Male (n = 21) 47.9% Female (n = 28) 57.9%	.51
Tumor location (sternum vs rib ± vertebrae)	Sternum (n = 11) 90.0% Rib ± vertebrae (n = 38) 42.6%	.04
Symptomatic presentation (pain vs no pain)	Yes (n = 29) 41.7% No (n = 20) 69.3%	.28
Tumor size (<500 vs ≥500 cm ³)	<500 (n = 23) 46.7% ≥500 (n = 12) 20.0%	.43
Histology (desmoid tumors vs chondrosarcomas vs high-grade sarcomas)	Desmoid tumors (n = 7) 66.7% Chondrosarcomas (n = 15) 92.3% High-grade sarcomas (n = 27) 30.3%	.002
No. of ribs resected (<4 vs ≥4)	<4 (n = 20) 40.9% ≥4 (n = 18) 45.7%	.47
Extent of sternal resection (complete vs partial)	Complete (n = 6) 83.3% Partial (n = 5) 100%	.41
Extended resection of adjacent structures	Yes (n = 22) 50.1% No (n = 27) 56.4%	.51
Radiation-induced sarcomas (radiation-induced vs other high-grade sarcoma)	High-grade sarcoma (n = 21) 26.4% Radiation-induced sarcomas (n = 8) 4.8 mo (median)	.20
Margins (negative vs positive)	Negative (n = 45) 56.0% Positive (n = 4) 25.0%	.10
Use of perioperative chemotherapy, radiation therapy, or both	Yes (n = 29) 36.6% No (n = 20) 81.4%	.05

patients received chemotherapy alone, 2 received combination chemotherapy and radiation therapy, and 1 received radiation therapy alone.

Prognostic factors for survival. Univariate analyses were performed to determine which factors influenced overall 5-year survival and 5-year disease-free survival (Tables IIA and IIB). The overall 5-year survival of our patient population was 63.7% (Fig 3). Patients who were referred for local tumor recurrence after previous curative surgical attempts interestingly fared no worse than those presenting for their initial treatment (Fig 4). Recurrence of sarcomas after resection is, in most series, known to be a poor prognosticator and is usually associated with metastatic disease. There was a tendency for female patients to have improved survival. This could not be explained through cross tabulation

analysis by age and histology of female patients compared with male patients. Female patients had a tendency to have a greater proportion of high-grade sarcomas and were of the same age as our male patients. Patients undergoing sternal resections survived longer, likely because of a higher proportion of chondrosarcomas (81% of the sternal histologies). Pain is recognized to be a poor predictor of malignancy in patients presenting with undiagnosed chest wall masses and it also did not affect long-term survival in our patients with proven cancer. A large tumor tended to do worse in our patient population, although in some studies this was not consistently demonstrated. Histology, as expected, is the most significant predictor of survival (Fig 5). Radiation-induced sarcomas had the worst survival of the group but not statistically worse than that of other

Fig 3. Overall 5-year survival of our patient population was 64%.

Fig 5. Five-year overall survival by histology.

Fig 4. Overall 5-year survival for those patients initially referred for management and those referred after previous surgical resections with recurrence of their tumors (secondary referrals).

Fig 6. Five-year overall survival of radiation-induced sarcomas compared with other high-grade sarcomas in our patient population.

high-grade sarcomas (Fig 6). The magnitude of the resections, including complete sternums or a greater number of ribs or extended resections that required involved intrathoracic organs, did not significantly affect long-term survival or predict recurrence. Our data clearly indicate that it is the pathologic completeness of resection rather than the extent of resection that is one of the most important factors in the surgical management of these malignant tumors. Patients with positive margins (gross or microscopic) had a median survival of less than 5 months ($P = .02$, Fig 7).

In the recurrence-free survival analyses, 53.5% of the patients survived without disease at 5 years. Nine

patients had locoregional recurrences, and 12 had distant recurrences. Histology was again statistically significant at predicting recurrence ($P = .002$, Fig 8). This histologic influence is reflected in tumor location as a positive predictor of disease-free survival because the sternal location had a higher proportion of chondrosarcomas. Although the use of perioperative chemotherapy or radiation therapy appears to negatively affect survival and tumor recurrence, this is likely a reflection of the severity and grade of the sarcoma for which these therapies are used.

Multivariate analyses were performed to identify predictors of long-term survival and long-term disease-

Fig 7. Overall 5-year survival by final pathology margin status.

Fig 8. Overall disease-free 5-year survival by histology.

Table III. Multivariate analysis of overall survival

Variable	Risk ratio	Confidence interval	P value
Tumor location	2.1	0.23–18.7	.51
Histology	23.0	2.1–251.9	.01
Margins	3.7	0.90–15.6	.07
Sex	2.8	0.90–8.4	.08
Age	2.0	0.70–5.7	.19
Radiation-induced sarcoma	2.0	0.59–6.9	.26
Perioperative chemotherapy ± radiation therapy	2.4	0.59–10.2	.22

free survival (Tables III and IV). The greatest predictor of survival was histology for both overall and disease-free survival. The risk ratio confidence interval, however, was large, reflecting the heterogeneity of our population.

Discussion

For the year 2000, The American Cancer Society has estimated an incidence in the United States of 2500 primary bone tumors and approximately 8100 new cases of soft-tissue malignant tumors. This represents 0.2% and 0.7%, respectively, of the total expected 1,220,100 new cancer cases for all sites. The chest wall is a rare site for primary sarcomas and represents 6% to 7% of the total. Often, chest wall sarcomas present as slowly growing masses that are clinically misinterpreted as benign, which results in a long delay in diagnosis.⁵ We have seen, in our patient population, delays in diagnosis of over 10 years from the initial discovery of a mass. Although these lesions are rare, they can represent, in children under 15 years of age, one of the top five malignant tumors responsible for cancer deaths.⁶ Because of their rarity and lethality, referral to a ter-

tiary referral center with a multidisciplinary approach to these malignant tumors is usually of paramount importance.

A plain chest radiograph, posteroanterior, and lateral radiograph with focused rib or sternal views are initially performed. Lesions are examined for lytic and blastic components and for any associated periosteal reaction. A computed tomographic review of the chest is mandatory, with special attention to bone views. The computed tomographic scan permits assessment of both the extrathoracic and intrathoracic tumor extension, as well as the direct extension into the lung, diaphragm, thymus, or pericardium and is usually sufficient for resectional planning of most tumors. Magnetic resonance imaging evaluations are useful in assessing lesions involving the costovertebral junction and vertebral body proper, and permit a detailed evaluation of involvement of the vertebral bodies, disc space, and extension through the neural foramina toward the dural sac.

Consultation with a bone radiologist is often important. Many lesions, especially cartilaginous tumors, can be reliably diagnosed by their radiographic presentation alone, obviating the need for any biopsy. If the

Table IV. Multivariate analysis of recurrence-free 5-year survival

Variable	Risk ratio	Confidence interval	P value
Tumor location	2.3	0.25-21.3	.46
Histology	26.4	2.2-321.9	.01
Margins	3.3	0.79-14.1	.10
Sex	2.8	0.53-15.2	.23
Age	2.8	0.90-8.6	.08
Radiation-induced sarcoma	2.2	0.68-7.0	.19
Perioperative chemotherapy $\pm$ radiation therapy	1.9	0.55-6.78	.30

diagnosis is still in question, two treatment options are possible. First, if the lesion is less than 2 to 3 cm in size involving one rib, then an excisional biopsy can be the next step. If a malignant neoplasm is diagnosed, then a wider excision can be performed. A minimum of a 2-cm margin is required for low-grade tumors, and a 4-cm margin with a rib above and below the tumor is required for high-grade sarcomas.

For large tumors of borderline resectability or a lesion that is suspected of being a sarcoma that is known to respond to neoadjuvant therapy (Ewing sarcoma, osteosarcoma, or malignant fibrous histiocytoma), then a preoperative histologic assessment is required. Many clinicians typically advocate performing a well-placed incisional biopsy, planned in such a manner to minimize tumor spillage, avoiding hematomas and sewing up the capsule of the tumor and obtaining at least 1 cm³ of tissue. We have found, however, that skilled cytopathologists, through the use of fine-needle aspirations or trephine core needle biopsies, can make a diagnosis in nearly 90% of our patients.⁷ Even if the exact subtyping of the tumor is not possible, sufficient material can usually be obtained to guide preoperative chemotherapy or radiation therapy planning. The volume of tissue required to make a diagnosis is often inversely related to the experience of the pathologist in dealing with sarcomas.⁸ As a tertiary referral center, we often have to contend with many complications in the management of both chest wall sarcomas and extremity sarcomas from incisional biopsies that were either not needed, ill placed, or poorly performed, resulting in local tissue tumor contamination. What may have been a relatively straightforward chest wall resection may now require a greater sacrifice of bone and soft tissues, necessitating prosthetic stabilization and plastic reconstruction.

Therefore, our general approach is to avoid incisional and excisional biopsies and proceed initially to fine-needle aspiration or core needle biopsy or directly to the formal planned operation if the radiographic diagnosis is clear. We have not performed an incisional

biopsy of a chest wall lesion for nearly 15 years at our hospital.^{9,10} If a preoperative histologic diagnosis is made, those lesions that have known responses to chemotherapy are usually treated for 2 to 3 cycles with up-front chemotherapy. This permits an in vivo assessment of chemosensitivity, theoretically treats occult metastasis at a subclinical and subradiologic stage, and may facilitate future surgical dissections and the ability to obtain clean surgical margins if the tumor shrinks with treatment. Because chest wall sarcomas are rare, many of the treatment strategies have been extrapolated from experience with extremity sarcomas and applied to the chest wall lesions. Although similar chemotherapy and radiation sensitivity is frequently noted, this is not always the case.

Surgical planning requires a team approach that always includes a thoracic surgeon and thoracic anesthesiologist and may involve plastic surgeons or spine surgeons for lesions requiring extensive soft-tissue resection or vertebral body or dural sac involvement. Wide excision with clear margins is the most important prognosticator for long-term survival. Most structures in proximity to the chest wall and sternum can be sacrificed and reconstructed if necessary.¹¹ Surgical morbidity and mortality in our series and those of others are low.¹²⁻¹⁵

Virtually all chest wall defects can be stabilized and reconstructed if sufficient preoperative planning is done.¹⁶ Although many chest wall defects that are protected by the scapula and posterior musculature do not require reconstruction, lateral chest wall and sternal defects require reconstruction for protection of the underlying viscera, improvement in respiratory mechanics that can significantly shorten ventilator requirements, and overall hospital stay and maintenance of the thorax shape for an improved cosmetic result.¹⁷ Wide margins remain the most important surgical objectives when treating these patients. The ablative surgeon must never compromise his or her resection because of a concern for closing the defect.¹⁸ A separate plastic surgery team must focus on this aspect of the patient's care.

Although the exact role of chemotherapy for the management of these lesions is less well defined than for extremity sarcomas, every effort should be made to consider these patients for combined modality therapy to improve local control and prevent the development of metastatic disease that ultimately is responsible for the death of many of our patients.^{19,20}

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Discussion

Dr Mark S. Allen (Rochester, Minn). The authors have nicely presented their series of patients, which is fairly typical of what a tertiary referral center would see. The wide variety of pathologic cell types and different presentations make me cautious when I try to generalize any conclusions from the data. The distribution of the cell type is fairly typical with what others have reported at other major institutions in that chondrosarcoma is most common, with malignant fibrous histiocytoma and desmoid tumors seen less often. The authors also show that almost half their patients received some sort of preoperative therapy, and a smaller, although still significant, number received postoperative chemotherapy and radiation therapy. It is also of interest that approximately two thirds of their patients received some sort of artificial material for reconstruction, and approximately one half of the patients received some type of muscle flap for reconstruction.

I compliment the authors on their use of the multiple team to take care of these patients. Despite all of these large operations, their mortality rate was zero, and they had a complication rate of only 24%, with wound problems being the most common. The overall survival of 64% is a little bit difficult to interpret because of the different cell types.

I have several questions for the authors. First, I would like to ask Dr Walsh to expound on the preoperative evaluation. It is unclear to me exactly what type of biopsy is required before the initiation of chemotherapy or radiation therapy. In your article you state that you always use a needle biopsy. I was taught as a resident to use a properly placed incisional or excisional biopsy to get adequate tissue to obtain a proper diagnosis. Is this approach outdated now? Do I have to do something different with my cytopathologists or my pathologists to get them to read the needle biopsy results correctly? I think this information would be helpful to pass along, not only for the members of our Association but for other primary care doctors who may see these patients and may read this article in our *Journal*.

What margin did you try to achieve at the time of your surgical resection? In the report from the Mayo Clinic by McAfee and associates in 1985, we found a very good success rate when we enlarged our margins to 4 cm from the tumor in the case of a chondrosarcoma, which led to a cure rate of almost 97%. When the margins were less than that, the cure rates were not as good. In your article you state that complete resection is the goal rather than the margin of resection. What do you believe we should tell people and our residents about this? There seems to be some confusion in the operating room when the residents say, "Well, I heard we should take a rib above and a rib below," or they have some absolute distance from the tumor that we should try to strive for. Can you shed some insight into this question and into what we should use as an acceptable margin?

Finally, do you use any molecular markers or genetic markers to help you decide what kind of preoperative or postoperative therapy to give these patients? What does this new

world of molecular biology have in store for us in the future to help us care for our patients?

Dr Nasser Altorki (*New York, NY*). I have 3 questions for you. Can you comment on the response rate to the preoperative chemotherapy? How do you deal with the margin or the extent of the resection in tumors that have significantly shrunk like the one you showed? Is that based on the prechemotherapy size? Finally, would you expound a bit more on those tumors that are in close proximity to the vertebral bodies? How were those managed?

Dr Timothy M. Anderson (*Buffalo, NY*). I noticed that you had 6 patients who underwent complete sternal resections, yet you only commented on 1 patient with prolonged ventilatory dependency. In a previous study at Emory University (*Ann Thorac Surg* 1993;55:838-43), Mansour and associates showed complete resection as opposed to a partial resection as causing a longer time until extubation. Can you comment on whether complete sternal resection resulted in a longer ventilation time?

Dr Joseph I. Miller, Jr (*Atlanta, Ga*). I would like to ask you 1 question from the moderator's standpoint. In your group of high-grade sarcomas, if a patient comes in tomorrow and you choose to administer preoperative neoadjuvant therapy, how many cycles of chemotherapy would you give preoperatively, what drugs would you use, and would you add radiation to that patient in the group with primary high-grade sarcoma of the chest wall?

Dr Peter Goldstraw (*London, England*). I am intrigued by desmoid tumors because my general surgical colleagues tell me that they get a very high success rate with complete excision of abdominal desmoid tumors and very good long-term results. Like you, I get good clearance of desmoid tumors. They do not die, but they keep recurring. They keep coming back for 5 and 10 years and have a very protracted and miserable life course. Negative margins do not seem to have any effect on the recurrence rate. Have you found anything that you can do to improve the results with thoracic desmoid tumors?

Dr Walsh. I would like to thank all of the discussers for their excellent questions and will respond in order.

First, Dr Allen, after reviewing our recent experience, I feel the use of incisional biopsies in the evaluation of chest wall masses should be abandoned. This is one of the major points that we wish to emphasize with this paper. Incisional biopsies can significantly compromise a future en bloc, oncologic resection and reconstruction of the resulting chest wall defect. A preoperative consultation with a bone radiologist and the selective use of fine needle or trephine biopsies interpreted by a skilled cytopathologist should be adequate to plan future treatment options. Low-grade, cartilaginous lesions can be resected solely on the basis of their radiographic appearance, without the need even for needle biopsies.

In regard to margins, we concur with the published reports from your center and we would strive to obtain at least a 4-cm chest wall margin for high-grade tumors and would resect en bloc any contiguous structure that is clinically involved, including the vertebral body, lung, diaphragm, thymus, or pericardium.

The morbidity of the more extended resections is low. Long-term survival, as we have both demonstrated, is often predicated on the surgeon's ability to obtain clear margins. Frozen section, soft tissue margins are performed intraoperatively. We would accept a 2- to 3-cm margin for lower-grade tumors.

As far as genetic markers, to date we have not used them to guide perioperative chemotherapies but would anticipate that specific sarcoma genetic markers will play a vital role in selecting patients who are to receive neoadjuvant or adjuvant therapies in the near future as we learn more about the prognostic significance of these markers.

Dr Altorki, univariate analysis did not demonstrate an improved 5-year survival when chemotherapy and/or radiation therapy was used. The 5-year recurrence-free survival was, in fact, worse. The two groups, however, are not comparable as chemotherapy was generally reserved for patients with higher-grade sarcomas. Chemotherapy is used for two purposes. One is to deal with the lesion itself in an effort to shrink it down to make the resection perhaps technically easier to obtain clear margins. The second is to treat subclinical, micrometastatic disease that often results in the death of the patient years later. In patients with limb osteosarcoma and Ewing sarcomas, we have seen the dramatic improvement in survival when chemotherapy is employed. We have applied this important management strategy to patients with chest wall sarcomas.

As far as the extent of resection, we will try again to look at the preoperative CT scans and try to resect back to the initial radiographic presentation of the lesion. Frozen section analysis in the operating room is used to guide the extent of resection. As far as vertebral body resections, we have had an extensive combined experience with our neurosurgeons at M.D. Anderson with over 300 patients requiring anterior vertebral body resections and reconstructions for a variety of primary and metastatic tumors involving the spinal column. In the patient population of this study, 1 patient required a complete vertebrectomy with reconstruction and the 3 others required only partial vertebrectomy with formal spinal stabilization.

Dr Anderson, the median ventilator requirement for the 6 patients in our study who had total sternectomies was 3 days as compared with 1 day for the 5 patients with partial sternal resections. This was not a significant difference. In a previous report from our institution reviewing our experience from 1984 to 1990 with Marlex mesh used in chest wall resections for a wide variety of chest wall pathologies, we noticed a significant decrease in the ventilator requirements and hospital length of stay when the defect was supported with prosthetics without any increased risk of wound infection. In this report pertaining to chest wall sarcomas only, there was no significant difference in ventilator requirements, intensive care, or hospital lengths of stay. Patients who required muscle flaps, however, had significantly longer ventilator requirements and intensive care unit and hospital stays in this patient population.

Dr Miller, as far as the high-grade sarcomas, we present all of these more complex cases at our weekly joint Thoracic Surgery/Sarcoma multidisciplinary conference to discuss treat-

ment options. Our sarcoma medical oncologists would usually administer 2 or more cycles of chemotherapy, and the timing of surgery would be based on the ongoing response of the lesion. Over 25 different drug regimens were used in this study. Many of the combinations were chosen on the basis of our experience with similar tumor histologies, often at other tumor locations.

The final question from Dr Goldstraw regarding desmoid tumors—our experience would be more in line with yours than with your general surgical colleagues. These are very difficult tumors to control long term and, as such, we felt they warranted inclusion in this manuscript on chest wall sarco-

mas. I feel, as many of our pathologists do, that they are low-grade sarcomas because of their invasiveness into structures and the difficulty that they pose for us as thoracic surgeons.

Interestingly, they are radiation-sensitive, so the margins can be improved through the use of radiation therapy. We have also seen some fairly dramatic responses in some large, technically unresectable desmoids to combination doxorubicin and dacarbazine chemotherapy. We have also seen responses to low-dose methotrexate and vinblastine. These tumors are also hormonally sensitive and can respond both radiographically and symptomatically to tamoxifen.