Surgical treatment is decisive for outcome in chondrosarcoma of the chest wall: A population-based Scandinavian Sarcoma Group study of 106 patients

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Objectives: Chondrosarcoma of the chest wall is the most frequent primary malignant chest wall tumor. Surgery remains the only effective treatment. Sarcoma treatment in Sweden is centralized to sarcoma centers; however, sarcomas of the chest wall have also been handled by thoracic and general surgeons.

Methods: One hundred six consecutive reports of chondrosarcomas of the rib and sternum over a 22-year period (1980 to 2002) were studied, with a median of 9 (4 to 23) years of follow-up for survivors. Clinical files were gathered and pathologic specimens reviewed and graded 1 to 4 by the Scandinavian sarcoma pathology group. Surgical margins were defined as wide, marginal, or intralesional.

Results: Ninety-seven patients were treated with a curative intent. Patients operated with wide surgical margins had a 10-year survival of 92% compared with 47% for those with intralesional resections. The 10-year survival was 75% for patients treated at sarcoma centers and 59% for those treated by thoracic or general surgeons. Local recurrence rate was highly dependent of the surgical margins—4% after wide resections and 73% after intralesional resections. The proportion of intralesional resections was higher outside sarcoma centers. Prognostic factors (multivariate analysis) for local recurrence included surgical margin and histological grade; for metastases, prognostic factors included histologic grade, tumor size, and local recurrence. Metastases occurred in 21 of the patients and only 2 were cured.

Conclusions: Patients operated with wide surgical margins resulted in fewer local recurrences and better overall survival. Patients with chest wall tumors should be referred to sarcoma centers and not to general thoracic surgery clinics for diagnosis and treatment.

Chondrosarcoma is the commonest primary bone malignancy in adults.¹ Fifteen percent of chondrosarcomas are located in the thoracic cage, making it to the most frequent primary malignant chest wall tumor with an annual incidence of less than 0.5 per million and year.² There are few reports on chondrosarcoma of the thorax and none have been population based.^{2,3}

Compared to osteosarcoma and Ewing's sarcoma, chondrosarcoma has drawn less research attention. There is no effective chemotherapy, and chondrosarcomas are relatively radio insensitive. Hence, surgery remains the only treatment.

In Sweden, the diagnosis and treatment of patients with primary bone tumor are referred to orthopedic sarcoma centers. This is strictly adhered to for sarcomas of long bones. However, many patients with chest wall tumors are treated by surgeons without experience of sarcomas.

We have reviewed treatment of patients with chondrosarcoma of the chest wall based on a population-based series

from the Swedish Cancer Registry. Our aim was to identify clinical risk factors for local recurrence and metastases and specifically to evaluate the importance of centralized treatment for outcome.

METHODS

All patients with chondrosarcoma of the chest wall diagnosed in Sweden from 1980 to 2002 were identified from the National Swedish Cancer Register and the Scandinavian Sarcoma Group (SSG) Register. One hundred twenty-three patients with ICD-10 location code C413 (rib, sternum, and clavicle) were identified. After exclusion of 9 patients with chondrosarcoma of the clavicle, 3 patients with misclassified tumor location (2 scapulae and 1 spine), and 1 patient with radiation-induced chondrosarcoma, 110 patients remained. Chondrosarcoma of the clavicle was excluded as it is not a flat bone and thereby differs from rib and sternum. Clinical files were collected for each patient from the diagnosing and treating hospitals. Pathologic specimens were reviewed by the SSG Pathology Board (blinded to outcome) and classified as grade 1 to 4, where grade 4 represents dedifferentiated chondrosarcoma.⁴ Tumor size was designated by the greatest dimension as measured from the surgical specimens. After exclusion of 4 cases because the diagnosis of chondrosarcoma was not supported by the Pathology Board, 106 patients remained for analysis.

The following data were registered: sex, age at diagnosis, localization, tumor size, histologic grade, surgical margin, radiotherapy, and chemotherapy, treatment at a sarcoma center, recurrence, and survival.

Surgical margins were classified into wide, marginal, and intralesional according to Enneking.⁵ Applied to chest wall chondrosarcoma, a wide surgical margin required intact pleura internally, intact muscle fascia externally, and transverse rib resection > 2 cm from the tumor on both sides. Marginal surgical margin was defined as macroscopic and microscopic free from tumor, but < 2 cm distance, and intralesional was defined as

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Abbreviation and Acronym

SSG = Scandinavian Sarcoma Group

when the lesion was macroscopically taken out in pieces or there was a microscopic positive margin.

There was a complete follow-up of median 9 (4-23) years for survivors.

Statistical analysis was performed with Statistica, statsoft; chi-square test, Kaplan-Meier survival curve Mann-Whitney *U* test, Kruskal-Wallis test, and Cox-Mantel test. Proportional hazard Cox ratio was used for multivariate analysis.

RESULTS

There were 59 male and 47 female patients, and the mean age was 57 (13 to 85) years, equal in both sexes. Eighty-nine of the tumors were located in the ribs and 17 in the sternum (Figure 1). All except 3 patients had primary chondrosarcoma (2 patients had multiple hereditary exostosis disease and 1 had Ollier's disease).

Treatment

Surgery was performed in 97 patients in a curative intent. Of those one had preoperative and 6 postoperative radiotherapy.

The remaining 9 patients were not treated with a curative intent; 4 had radio- and chemotherapy, 1 was operated to reduce tumor bulk, and 4 had no treatment. The reasons for abstaining from curative surgery were high age, poor general condition, and/or a tumor considered too large.

Surgeries were conducted at 3 orthopedic sarcoma centers (55 patients) or at 16 different thoracic surgery or general surgery departments in Sweden (42 patients). At the sarcoma centers, 25 patients were treated by orthopedic surgeons and the remaining 30 in collaboration between orthopedic and thoracic surgeon. At the nonspecialty center, 29 patients were operated by a thoracic surgeon and 13 by a general surgeon.

The median tumor size was 8 (2 to 23) cm. There were no differences in tumor size between patients treated at sarcoma centers and those treated at nonspecialty centers.

At sarcoma centers, a median of 3 (1 to 6) ribs were resected compared with 2 (0 to 4) ribs at nonspecialty centers ($P = .002$, Mann-Whitney *U* test). In 60 of 97 operations, the defect was replaced by a net, mesh, or polytetrafluoroethylene. There were no peri- or postoperative deaths. Eighty-three percent of the sarcoma center patients had graft prostheses compared with 41% of the patients treated at nonspecialty centers.

Surgical margins were wide in 28% (27/97) of tumors, marginal in 45% (44/97) (46/97), and intralesional in 27% (26/97). Patients treated at a sarcoma center were more often operated with wide surgical margin ($P < .001$, Table 1).

FIGURE 1. Distribution of 106 chondrosarcomas of the chest wall.

Survival

The estimated 10-year survival for the whole series of 106 chondrosarcoma patients was 0.64. Among the 10 non-treated patients, all except 1 died of the chondrosarcoma. Six died within 1 year of diagnosis, but 4 patients lived for 3 to 10 years. Many of these patients had severe difficulties with an enormous mass causing pain, weightiness, and social distress. Several tumors ulcerated, and it was difficult for the patients to cover the mass with ordinary clothes.

The 10-year survival for the 97 treated patients was 0.67. The surgical margin was an independent factor in predicting outcome (Figure 2). It was 0.75 for patients treated at a sarcoma center and 0.59 for those treated outside ($P = .04$, Cox-Mantel test; Figure 3). Patients who developed local recurrence and/or metastases had poor outcome (Figure 4). However, of the 97 treated patients who did not develop local recurrence or metastases, none died of the tumor.

There appeared to be no improvement in survival over time. Hence, the 10-year survival for the 44 patients operated from 1980 to 1991 was 0.63, and for those 53 patients treated from 1992 to 2002, it was 0.66.

Local Recurrence

Thirty-three of the 97 treated patients had local recurrence of the chondrosarcoma. Hence, the local control rate for the thoracic wall was 66%. Mean time to local recurrence was 3.5 years (0.1 to 14 years), but 4 occurred after 10 years. Recurrence was more frequent in high-grade chondrosarcoma, after intralesional surgical margin and treatment nonspecialty centers (Tables 2 and 3). One of 27 patients operated with a wide surgical margin had local recurrence compared with 19/26 after an intralesional margin. Treatment at a sarcoma

TABLE 1. Surgical margins

	Wide	Marginal	Intralesional
Sarcoma center	25	26	4
Nonspecialty center	2	18	22

center resulted in 9/55 recurrences compared with 24/42 in those treated at nonspecialty centers. Eight of the 20 patients who had local recurrence but no metastases died of the tumor.

Among the 33 patients with local recurrence, 3 were not treated and 7 had palliative radiotherapy only. Twenty-five patients were operated for local recurrence, and 15 of these had further local recurrences.

Metastases

None of the patients had metastases at diagnosis. However, metastatic disease was diagnosed during follow-up in 21 of the 106 patients. Pulmonary metastases were found in all expect for 1; other metastatic locations were bone, brain, lymph node, and liver.

Tumor grade, surgical margin, tumor size, and local recurrence were related to development of metastases (Tables 2 and 4). Notably, 16 of the patients with metastases had also recurrence. None of the 19 patients with grade I chondrosarcoma developed metastases, whereas 7 of 8 grade IV (dedifferentiated) tumors metastasized. The metastasis rate was 0.42 in patients with local recurrence compared with 0.08 in patients without a local recurrence ($P = .001$).

DISCUSSION

Chondrosarcoma of the chest wall is the most frequent malignant tumor of the thoracic cage. This report is the first population-based study and included more than 100 patients with chondrosarcoma of the chest wall. Our findings clearly demonstrate the importance of a wide surgical margin in the treatment of chest wall chondrosarcomas.

FIGURE 2. Kaplan-Meier analysis of surgical margins and survival.

FIGURE 3. Kaplan-Meier analysis of where surgery was performed and survival.

Previous studies^{2,3,6-8} on chest wall chondrosarcoma have been center-based and often included a small number of patients. Many studies have included chondrosarcoma of the scapula and clavicle as well, but these were excluded in our study because they are not intrinsic parts of the thoracic cage.

Our report is based on all chondrosarcoma patients in Sweden over a 22-year period (8 to 9 million inhabitants). As opposed to most cancer forms, the result of treatment has not improved over time. In a study of chondrosarcoma of all sites from Finland from 1970 to 1990, there was no change in outcome over time.⁹ Neither we could find any difference in outcome between those diagnosed early or

FIGURE 4. Kaplan-Meier analysis of local recurrence and metastasis and survival.

TABLE 2. Prognostic factors for local recurrence and metastasis, multivariate analysis

	Hazard ratio (95% confidence)	P value
Local recurrence		
Surgical margin		
Wide	1	
Marginal	12.2 (10.2-14.2)	< 0.02
Intralesional	28.1 (26.1-30.1)	< 0.001
Histological grade		
Low grade (grade 1 and 2)	1	
High grade (grade 3 and 4)	2.8 (2.2-3.5)	< 0.01
Metastasis		
Histological grade		
Low grade (grade 1 and 2)	1	
High grade (grade 3 and 4)	3.4 (2.3-4.5)	< 0.05
Local recurrence	24.1 (22.6 - 25.7)	< 0.001
Tumor size (per cm increment)	1.1 (1.0 - 1.2)	< 0.05

late in the study period. There is still no effective adjuvant therapy for chondrosarcoma; surgery remains the only effective treatment today as it was in 1980.

We classified the surgical treatment into 3 categories: wide, marginal, and intralesional. The 10-year survival after wide resections was 0.92 compared with 0.47 after intralesional resections. Most previous studies reported more wide and less intralesional margins; however, the local recurrence rates are similar.^{1,2,10} This discrepancy may be explained by our strict definition of surgical margins.

The treatment at the 3 sarcoma centers (55 patients) gave dramatically higher survival and local recurrence rates than those achieved nonspecialty centers (42 patients at 16 hospitals). The outcome was better at sarcoma centers because the surgical margin was better.

Resection of a large chest wall chondrosarcoma is a major procedure in an elderly patient. This is why 9 patients were not operated with a curative intent. These patients with large tumors lived for a long time without treatment. However, their life situation was difficult due to the chondrosarcoma. The mass resulted in an abnormal thoracic structure and it was troublesome to find ordinary clothes. The chondrosarcoma ulcerated and brought a tremendous smell. Hence, these patients were socially isolated in their last period of their life. Because there were no peri- or postoperative deaths in this series, maybe some of the nonoperated patients would have survived and benefited from an operation.

The local recurrence rate was highly dependent of the surgical margins. It was 0.04 after wide resections and 0.73 after intralesional resections. This confirms that our classification of surgical margins was valid. High malignancy grade, but not tumor size, was also an independent risk factor for local recurrence. Fiorenza and colleagues¹¹ reported that local recurrence in chondrosarcoma in general (all locations) is only relevant to survival if the patient has metastases at the time of detection of local recurrence. However, we found

TABLE 3. Univariate analysis of clinical factors and local recurrence

Factor	Recurrence/number of patients	P value
Surgical margin		<.001
Wide	1/27	
Marginal	13/44	
Intralesional	19/26	
Histologic grade		.03
1	2/19	
2	15/39	
3	11/31	
4	5/8	
Tumor size (cm)*		0.7
≤7	15/49	
>7	14/41	
Treatment center		<.001
Sarcoma center	9/55	
Nonspecialty center	24/42	

*Missing 7 where the size was not measured.

that in chondrosarcoma of the chest wall, local recurrence per se reduces survival even without distant metastasis. Progression of chest wall chondrosarcoma leads to respiratory insufficiency and death; nearly half of the patients in our series who had local recurrence but no metastases died of locally progressive disease. The prognosis in patients with metastases alone or combined with a local recurrence was dismal. Only 2 of 19 survived in our study.

In our series, 20% of the patients developed metastasis. Chondrosarcoma of the pelvis is associated with a higher metastasis rate and chondrosarcoma of long bones with a lower rate. We found 3 independent factors related to metastases; first and most important was the histologic grade and second, local recurrence. The metastasis rate was 0.42 in patients with local recurrence compared with 0.08 in patients without a local recurrence ($P = .001$). The third factor related to metastases was tumor size. Difference in tumor size is probably

TABLE 4. Univariate analysis of clinical factors and metastasis

Factor	Metastasis/number of patients	P value
Surgical margin		0.16
Wide	2/27	
Marginal	10/44	
Intralesional	7/26	
Histologic grade		<.001
1	0/19	
2	5/39	
3	7/31	
4	7/8	
Tumor size (cm)*		0.08
≤7	7/49	
>7	12/41	
Treatment center		.05
Sarcoma center	12/55	
Nonspecialty center	7/42	

*Missing 7 where the size was not measured.

why pelvic chondrosarcoma has a higher rate of metastases and extremity chondrosarcoma a lower rate (ie, pelvic chondrosarcomas are larger and extremity smaller than those of the chest wall). Surgical margin was not an independent risk factor for metastases, which is in line with current views on local recurrence and metastases in sarcoma. However, poor surgical margin was a risk factor for tumor-related death caused by untreatable local recurrence.

Primary bone malignancies are generally handled by orthopedic surgeons specializing in orthopedic oncology. The important point is that patients with chondrosarcoma of the chest wall need to be treated by a multidisciplinary team dedicated to sarcoma care—whether a thoracic tumor surgeon or an orthopedic tumor surgeon performs the procedure is irrelevant. Centralization of treatment of chondrosarcoma of the chest wall will improve outcome.

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