Chondrosarcoma of the Chest Wall

A Single Institution Review of 50 Cases

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Introduction: Chondrosarcoma (CS) is most common primary osseous tumor of the chest wall. The aim of this study was to report results from surgical procedures and evaluate clinical factors predicting survival of patients with chest wall CSs treated in a single tertiary sarcoma center.

Materials and Methods: Fifty patients with primary CS located in the ribs and sternum were included. Details of the clinical data and oncological outcomes, including local recurrence (LR) and disease-specific survival (DSS), were collected.

Results: The tumor was primarily originated in the sternum in 6 patients (12.5%) and in ribs 2 to 11 in the remaining patients. Specimens were histologically graded 1 in 13 patients (26%), 2 in 28 (56%), 3 in 8 (16%), and 1 (2%) as mesenchymal grade 3 CS. R0 margins were obtained in all cases. Reconstruction was warranted in 47 (94%) cases. Local recurrence developed in 3 (6%) patients, and the median time to LR was 17 (range, 16–68) months. Eight (16%) patients developed metastasis. Increasing tumor volume was a statistically significant factor for reduction of DSS.

Conclusions: Chondrosarcoma of the chest wall can be treated effectively with clear margins, resulting in lower LR rate and higher DSS than CS of the extremities and pelvis. Metastasis of the chest wall mostly occurs in high-grade tumors, and the locations of the metastases differ greatly from those observed in CS of the extremities and pelvis. Metastases are commonly extrapulmonary, indicating the need for postoperative follow-up with multiple imaging modalities to monitor recurrence and metastases.

Key Words: chondrosarcoma, ribs, sternum, prognosis

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Chondrosarcomas (CSs) constitute a heterogenous group of tumors, where cartilage matrix is produced by tumor cells. Chondrosarcomas are rather rare tumors that can occur almost anywhere in the human skeleton. However, the most common sites are the extremities, especially the pelvis.[1] Chondrosarcoma is the second most common primary bone tumor in the skeleton and the most common primary osseous tumor of the chest wall, leading to challenging surgical resections and reconstructions.[2,3] As CSs are relatively resistant to radiotherapy and conventional chemotherapy, surgery is the principle method of treatment.[4–7] The majority of tumors grow slowly and rarely metastasize and therefore have a good prognosis after adequate surgery.[4]

Chondrosarcoma is divided into 3 histological grades: grade 1 (low) and grades 2 and 3 (high). In addition, dedifferentiated CS is a highly malignant variant characterized by high-grade, noncartilaginous sarcoma juxtaposed with low-grade CS and a distinct interface between the 2 components.[8] Moreover, according to the latest World Health Organization classification, grade 1 CS in acral and extremity locations should be termed atypical cartilaginous tumor; however, in the pelvis, spine, and chest wall, the term CS grade 1 should be used.[8] The clinical behavior and prognosis of these tumors depend on a number of variables. Of these, grade is one of the most important.[9] In addition to grade, age, sex, and location have all been reported to be significant factors in determining clinical behavior and survival.[1,4–6,9–11] Axial location, that is, pelvis, spine, and chest wall, has been reported to have inferior outcomes compared with appendicular location.[12–14]

Grade 1 CS is classified as a locally aggressive or intermediate tumor, as disease-specific survival (DSS) is reported to be close to 100%. For grade 1 CS in the extremities, intralesional curettage is an accepted method of surgical treatment. However, most authors recommend resection with clear margins for pelvic CS of any grade.[1,15]

In addition to the pelvis, other axial locations, such as the spine and chest wall, are inherently rare entities for primary bone sarcomas. Chondrosarcoma is the most common malignant bone tumor in the chest wall and the third most common tumor after chordoma and osteosarcoma in the spine.[16,17]

The aim of this study was to present results from surgical procedures and evaluate clinical factors predicting the survival of patients with chest wall CS treated at the Helsinki University Hospital.

PATIENTS AND METHODS

Study Design

After institutional ethical review board approval, patients who were diagnosed and surgically treated for CS in the chest wall between May 2001 and June 2019 at the Helsinki University Hospital were identified from retrospectively reviewed and collected data. A total of 50 patients with primary CS located in the ribs and sternum were included in the present study. All patients were diagnosed and treated at the referral hospital; those who were initially treated elsewhere and referred for the management of a recurrence were excluded. Chest wall MRI for local control (Fig. 1) and body computed tomography (CT) to detect distant metastasis were routinely performed as preoperative valuation for all patients. Patients with vertebral tumors and those who had been primarily treated elsewhere and referred for the management of a recurrent tumor were excluded. Data on the clinical and oncological outcomes, including local recurrence-free survival (LRFS) and DSS, were collected.

Resection specimens were evaluated by specialized bone sarcoma pathologists for grade and the involvement of histological margins. Margins were defined in the bony resection area as well as in the soft tissue direction. Histologic grades were determined based on cellularity, nuclear atypia, and the presence of an abundant hyaline cartilage matrix or mucomyxoid matrix and mitosis. The highest grade seen on histology was recorded, even when this higher grade comprised only a small area. The follow-up protocol included a chest x-ray every 3 months and local imaging with MRI or CT every 6 months for the first 2 years, followed by a chest x-ray and local MRI every 6 months for 5 to 10 years. A complete data set was available for all patients included in the final analysis.

Statistical Analysis

Disease-specific survival and LRFS rates including 95% confidence intervals (CIs) were assessed using the Kaplan-Meier method. Survival rates were calculated from the date of the surgery to the most recent follow-up,

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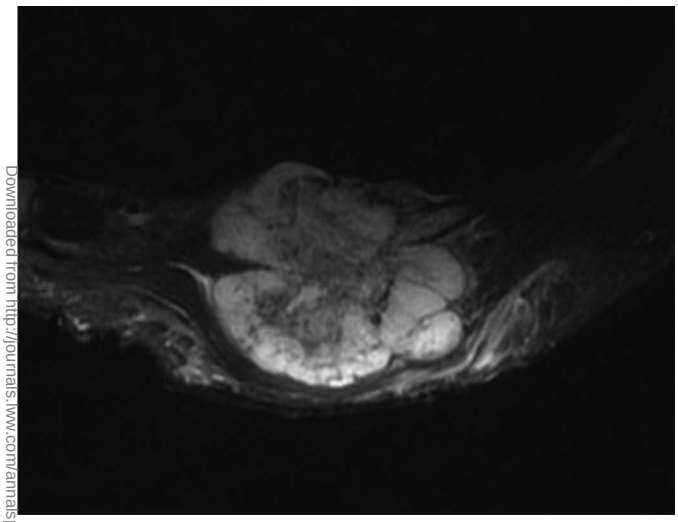

FIGURE 1. A grade 2 chondrosarcoma of the sternum.

confirmation of local recurrence (LR), or death. Between-group comparisons were performed using log-rank test. The Cox regression model was used to identify independent factors affecting DSS and LRFS. Continuous variables were reported as median and interquartile range (IQR). Differences in proportions were assessed using Fisher exact test. All analyses were performed using STATA version 16, and a P value of <0.05 was considered significant.

RESULTS

Patient Characteristics

The final study population included 50 patients with a median age of 59 years (IQR, 50–67 years) and a median follow-up of 61 months (IQR, 20–97 months). In 6 patients (12.5%), the primary tumor originated primarily in the sternum and distributed equally in ribs 2 to 11 in the remaining patients. The histological grading of specimens was grade 1 in 13 (26%) patients, grade 2 in 28 (56%) patients, grade 3 in 8 (16%) patients, and mesenchymal grade 3 CS in 1 (2%) patient.

Reconstruction

The chest wall defect could be closed primarily in only 3/50 patients (6%), whereas the remaining 47/50 (94%) patients required chest wall reconstruction. Of the 47 patients who underwent chest wall stabilization, 38 (76.0%) were treated with artificial mesh and in 9 (18.0%) with the sandwich technique (methyl-methacrylate between 2 meshes). Soft tissue reconstruction with a pedicled latissimus dorsi flap was performed on 12 patients (Fig. 2), and a microvascular free tensor fascia lata (TFL) flap was necessary in 1 patient. The recipient vessels for the free flap were internal thoracic artery and subclavian vein. Additional stabilization with the sandwich technique was used if the resection comprised 3 or more ribs in the anterior or anterolateral area or the defect size was more than 10 × 10 cm. In total, 46/50 patients (92.0%) had no complications requiring revision, but 2/50 (4.0%) had deep infection requiring surgery and the removal of the artificial mesh. One patient with a cement mesh sandwich reconstruction (2.0%) had prolonged pleural effusion, and 1 patient (2.0%) with a similar cement mesh sandwich reconstruction had an aorta perforation from the cement reconstruction 3 years postoperatively. The patient had had 2 primary malignant tumors, which were operated before CS surgery. Previous surgeries had caused deformity in the area of the thoracic wall leading to kyphosis, which endorsed the protrusion of the sandwich reconstruction and the erosion of the aorta. The patient was treated surgically with cement mesh sandwich reconstruction removal and aortoplasty. All patients with LR had direct closure without local or free flaps. There was no 30-day mortality. Detailed patient characteristics are presented in Table 1.

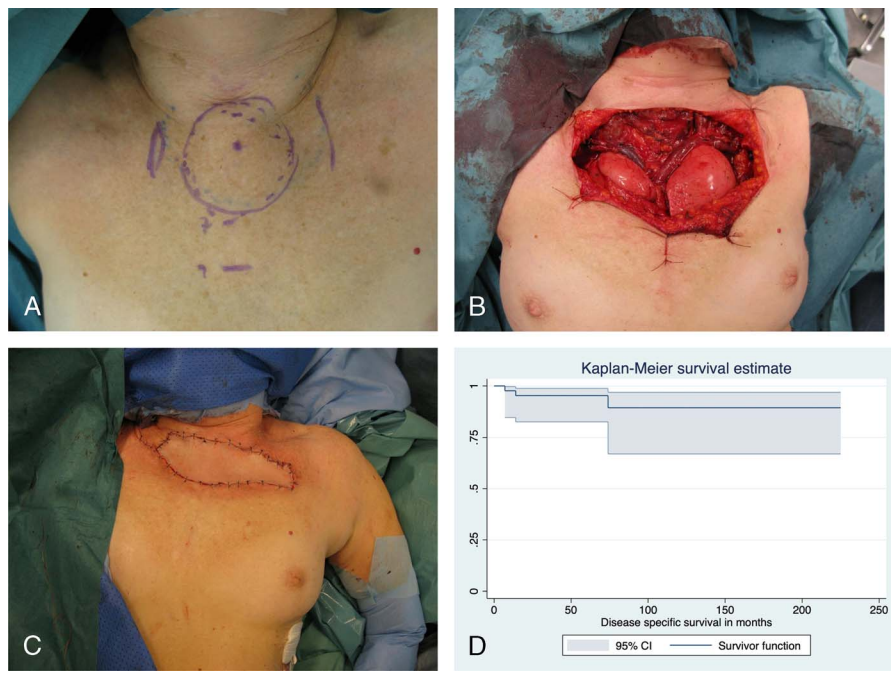

FIGURE 2. A, Chondrosarcoma of the manubrium sterni with planned skin marked. B, Anteriori chest wall tumor resection. C, Reconstruction with artificial mesh and pedicled musculocutaneous latissimus dorsi flap. D, Disease-specific survival with 95% confidence interval for all patients. full color online

TABLE 1. Patient Characteristics

Eligible Patients	
Female	50
Location	19 (38%)
2nd rib	6 (12%)
3rd rib	4 (8%)
4th rib	5 (10%)
5th rib	3 (6%)
6th rib	5 (10%)
7th rib	4 (8%)
8th rib	4 (8%)
9th rib	6 (12%)
10th rib	4 (8%)
11th rib	1 (2%)
Sternum	6 (12%)
Costochondral joint origin	
Yes	20 (40%)
No	24 (48%)
Sternum	6 (12%)
Central CS	42 (84%)
Peripheral ex-osteochondroma CS	8 (16%)
Grade	
Grade 1	13 (26%)
Grade 2	28 (56%)
Grade 3	8 (16%)
Mesenchymal grade 3	1 (2%)
Syndrome	
None	47 (94%)
Multiple hereditary osteochondromas	3 (6%)
Local recurrence	3 (6%)
Site of LR	
Soft tissue	3 (6%)
Metastasis	8 (16%)
Site of metastasis	
Lung and soft tissue	1 (2%)
Lung + soft tissue and brain	1 (2%)
Lung and bone	1 (2%)
Lymph node	1 (2%)
Liver and lymph node	2 (4%)
Missing	2 (4%)
Median age in years (IQR)	59 (50–67)
Median max size in cm (range)	7 (6–9)
Median volume cm^3 (range)	120 (95–1080)
Median maximum size in cm (range)	7 (3–25)

Predictors of Local Recurrence and Local Recurrence-Free Survival

R0 margin was obtained in all cases. Local recurrence developed in 3 (6%) patients, and the median time to LR was 17 months (range, 16–68 months). The LRFS was 100% at 1 year, 95% at 5 years (95% CI, 81–99), and 90% at 10 years (95% CI, 70–97) (Fig. 1). All LRs occurred in the soft tissue of grade 2 tumors. The median soft tissue margin in patients with or without LR was 1.0 mm ($P = 0.967$). In general, the median bony margin was 15 mm. The observed differences in increasing tumor volume (hazards ratio, 1.004; 95% CI, 1.001–1.007; $P = 0.005$) in this study's inferential uncertainty were sufficiently small to include increasing volumes as clinically relevant differences in reduction on LRFS. The median volume of the tumor in patients without LR was 95 cm^3 and 1080 cm^3 in patients with LR ($P = 0.036$, Mann-Whitney U test), and the median maximum size of tumor in patients without LR was 7.0 cm and 12 cm patients with LR ($P = 0.041$, Mann-Whitney U test).

Metastasis and Disease-Specific Survival

Eight (16%) patients developed metastasis. Metastasis occurred in addition to the lung also occurred in the soft tissue, brain, lymph node, and liver; the distribution of metastasis is summarized in Table 1. Disease-specific survival was 98% at 1 year (95% CI, 85–100), 95% at 5 years (82–99), and 89% at 10 years (67–97) (Fig. 2D). The observed difference in grade ($P = 0.125$), different location (sternum vs ribs) ($P = 0.379$), LR ($P = 0.509$), or age ($P = 0.105$) effect on DSS has uncertainty as confidence levels were wide and results insufficient to include them as clinically relevant factors in DSS. However, none of the patients with grade 1 CS have since died of the disease. Furthermore, all 8 patients who died of the disease had metastasis, but only 1 of the 3 patients with LR later developed metastasis. The observed differences in metastasis ($P = 0.000$) (Fig. 3) and increasing tumor volume (hazards ratio, 1.002; 95% CI, 1.001–1.004; $P = 0.005$) in this study's inferential uncertainty were sufficiently small to include them as clinically relevant differences in DSS.

DISCUSSION

In the present study, we present our single-center, multidisciplinary experience and analysis of 50 patients with primary CS of the chest wall.

Wide surgical excision is the criterion standard for the treatment of CS or any other sarcoma. Although we know that it is essential to achieve a "wide" margin to reduce the risk of LR, no clear definition of a wide margin exists. In CS, a 4-mm margin has been shown to decrease the rate of LR.[4] Moreover, the aim of a 4-mm margin in extremity CS is achievable and often does not increase morbidity for the patient. Replicating a 4-mm margin can, however, be difficult in certain locations of the chest wall due to the proximity of the tumor to the thoracic wall. It is, however, recognized that the quality of the margin has possibly even a more important role than the quantity of the margin in the local control.

In the literature, the quality of the margin is rarely reported even though it has been hypothesized that the margin markedly influences survival.[16,18] In our study, we analyzed both the bony and the soft tissue margin and noticed that the quality of the margin had no effect on DSS nor LRFS. In fact, the LR in our series was always detected in soft tissue, although the median soft tissue margin was 2.5 mm in cases of LR compared with 1 mm in cases without LR. Strong natural barriers such as pleura are most likely responsible for the success of small margins. Indeed, the only factor affecting LRFS in our study was the increasing size of the tumor.

In CSs of the extremities, LR in addition to grade has been shown to be one of the most significant factors affecting DSS. Interestingly, in the present study, we found that LR in the chest wall did not lead to worse overall survival. This finding is in accordance with those reported in previous studies.[19] In very large tumors, the removal of the tumor without tumor rupture can be very difficult as the bulky intrathoracic tumor mass might be larger than the thoracic wall aperture needed for resection. However, spilling of the tumor should be avoided by all means, as contamination of the thoracic cavity by malignant CS cells is untreatable and eventually fatal. Therefore, in cases of very large tumors, the spilling of the tumor could be avoided by widening the thoracotomy exposure.

The increased rate of LR in large tumors with direct closure indicates the importance of sufficient soft tissue resection, including subcutaneous tissue, which might reveal resecting the skin and reconstructing with local flap as well. We recommend large soft tissue resections, especially in high-volume tumors, which may result in a defect requiring

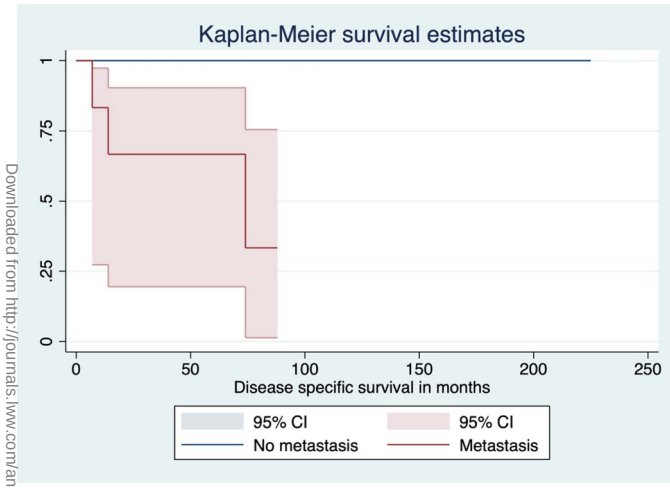

FIGURE 3. Disease-specific survival with 95% confidence interval stratified by distant metastasis. full color online

soft tissue reconstruction with a local/pedicular or a microvascular free flap. Flap reconstructions are commonly used in soft tissue sarcomas of the chest wall and have proved to be safe procedures. Pedicular latissimus dorsi musculocutaneous muscle flap is a workhorse flap for chest wall reconstruction. The latissimus dorsi flap has multiple advantages, including the relative long pedicle allowing a wide arc of rotation, a large size, easy harvesting, and tailoring the flap to the chest wall defect.[3,20]

Tensor fascia lata flap is commonly used for large chest wall defects and carries several strengths. Tensor fascia lata flap allow harvesting and reconstruction of the chest wall in the same position as the tumor resection and using a 2-team approach. Moreover, even a large donor site on the thigh does not impair breathing. Tensor fascia lata flap is a classic flap given the large flap size, whereby large and constant vessels permit safe anastomosis.[3]

The ribs are thought to be more frequently affected than the sternum, which was also confirmed in our study, as only 12% of the cases were located in sternum.[18,21,22] In accordance with the literature, our results revealed that 60% of the tumors in the ribs were actually locating in the costochondral arches of the sternum.[23] However, the location (sternum/rib) of the tumor did not have any effect on LRFS or DSS.

Our results revealed metastatic disease to be strongly correlated with worse possible outcome, a finding which has been reported in the literature. Moreover, disseminated disease is usually the cause of disease-specific death, and the metastatic potential is highly dependent on the grade of the tumor. However, our results show that none of our patients with grade 1 tumor died of their disease. Typically, primary bone sarcomas, including high-grade CS, usually disseminate hematogenously, most frequently into lungs.[6,24] In the present study, however, we observed that the metastatic spread of the disease was most often elsewhere than in the lungs. For example, metastases were seen in the lymph nodes, the soft tissue, the liver, and the brain. This is of particular interest because extrapulmonary metastases of CS or any soft tissue or bone sarcoma is rarely reported in the literature. Extrapulmonary metastases in sarcomas are, however, frequently reported in myxoid liposarcoma,[25,26] but otherwise only in rare cases are reports on extrapulmonary metastases published. Extrapulmonary metastases highlight the need for a more specified postoperative follow-up schedule, especially for high-grade tumors because the most commonly used chest x-ray or low-dose pulmonary CT are unable to detect extrapulmonary metastases located outside the chest area. Other imaging modalities, such as positron emission tomography/CT, might improve the detection of metastases and provide a basis for restaging.

This study has some limitations that should be addressed. This is retrospective study with its inherent limitations. However, the study focuses on histologically verified primary CS and, despite the limited numbers, represents one of the largest cohorts to date. The small numbers presented will undoubtedly result in selection bias. Moreover, the study does not include patient health-related quality of life or functional outcomes.[27]

CONCLUSIONS

In conclusion, we can say that in predicting the local control of the tumor, the current study attempts to provide some answers to the one modifiable factor: the surgical excision margin. The findings of this retrospective study of 50 primary CS of the chest wall demonstrate that chest wall CS can be treated effectively with clear margins, resulting in a lower LR rate and higher DSS than CS of the extremities and pelvis. Metastases mostly occur in high-grade tumors and, more interestingly, the locations of metastases differ greatly from those of CS in the extremities and pelvis. Metastases are commonly extrapulmonary, indicating the need for an important postoperative long follow-up with multiple imaging modalities to monitor recurrence and metastases.

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