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Original Research Article

Histologic grade and surgical margin status as prognostic factors in chondrosarcoma: a retrospective single-center study

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ABSTRACT

Background: Chondrosarcoma is a malignant cartilage-producing bone tumor in which prognosis is influenced by tumor biology and adequacy of surgical treatment. Histologic grade and surgical margin status are considered major prognostic factors. This study evaluated their impact in a retrospective institutional series.
Methods: Patients diagnosed with and treated for chondrosarcoma at a tertiary referral centre between 1986 and 2008 were retrospectively reviewed. Clinical, radiologic, pathologic, treatment, and follow-up data were analysed. Variables included tumour origin, location, histologic grade, Enneking stage, pulmonary metastasis at diagnosis, soft-tissue extension, surgical treatment, margin status, local recurrence, and survival. Associations were analysed using chi-square tests.
Results: A total of 144 patients were included (mean age 42.1±15.0 years; 57.6% male). Pulmonary metastasis at diagnosis was present in 10 patients (6.9%), and soft-tissue extension was identified in 61 (42.4%). Soft-tissue extension was significantly associated with pulmonary metastasis at presentation (p=0.002). Histologic grade and stage data were available for 110 patients; 54.5% had grade 1, 32.7% grade 2, and 12.7% grade 3 tumors. Local recurrence developed in 25 patients. Recurrence was observed in 58.8% of patients with positive surgical margins. In tumors with available grading data, recurrence occurred in 10.0% of grade 1, 36.1% of grade 2, and 35.7% of grade 3 lesions (p=0.004). Soft-tissue extension was also associated with recurrence (p=0.009). Overall mortality was 8.3%.
Conclusions: Histologic grade and surgical margin status were the main determinants of outcome in this series. Soft-tissue extension was associated with both recurrence and pulmonary metastasis at diagnosis.

Keywords: Chondrosarcoma, Bone neoplasms, Prognosis, Histological grade, Surgical margins, Local neoplasm recurrence, Neoplasm metastasis

INTRODUCTION

Chondrosarcoma is a heterogeneous group of malignant cartilage-producing bone tumors and remains one of the most common primary malignant bone neoplasms in adults. Conventional chondrosarcoma is the predominant subtype, and its biological behavior ranges from relatively indolent low-grade lesions to highly aggressive high-grade tumors. Recent epidemiologic data suggest that the national incidence of chondrosarcoma of bone is approximately 2–4 per million per year, although reported rates may vary depending on case definition and the classification of low-grade cartilaginous lesions.[1,2] The clinical behavior of chondrosarcoma is strongly influenced by histologic grade, tumor location, and subtype. Low-grade tumors generally show a more favorable course, whereas higher-grade lesions are associated with increased risks of local recurrence, metastasis, and disease-specific mortality. In addition, pelvic and axial lesions are often more difficult to resect adequately and may therefore carry a worse prognosis than appendicular tumors. Because histologic grading can be challenging with limited biopsy

material, treatment planning at specialized sarcoma centers requires careful integration of clinical, radiologic, and pathologic findings.[2-5]

Unlike osteosarcoma and Ewing sarcoma, conventional chondrosarcoma is largely resistant to standard chemotherapy and radiotherapy. Therefore, surgical excision remains the cornerstone of treatment, and achieving an adequate surgical margin is one of the most important modifiable determinants of oncologic outcome. Previous studies have shown that surgical margins significantly affect local recurrence risk across chondrosarcoma grades, whereas the prognostic impact of local recurrence appears particularly relevant for grade 2 and grade 3 tumors. Current sarcoma guidelines also emphasize referral to specialist multidisciplinary centers for diagnosis, biopsy planning, definitive treatment, and follow-up.[3-7]

Despite improvements in imaging, pathology review, and limb-salvage techniques, the relative prognostic contributions of histologic grade, surgical margin status, and other tumor-related factors remain clinically important, particularly in retrospective institutional series reflecting real-world practice. The present study was therefore designed to evaluate the prognostic impact of histologic grade and surgical margin status in patients with chondrosarcoma, with particular emphasis on local recurrence and overall outcome.

METHODS

Patients and study design

This study was a retrospective, single-center observational study. Patients diagnosed with and treated for chondrosarcoma at the Department of Orthopedics and Traumatology, Ankara University Faculty of Medicine, between 1986 and 2008 were retrospectively reviewed. The study was conducted in accordance with the principles of the Declaration of Helsinki. Institutional review board approval was obtained prior to the study, and approval to use retrospective clinical data was granted (Approval date: 15 September 2009, No:172).

Patients were eligible for inclusion if they had a diagnosis of chondrosarcoma confirmed by institutional pathology records and were evaluated and/or treated at our department between 1986 and 2008. Patients with available clinical records, including demographic, diagnostic, treatment, and follow-up data, were included. Patients were excluded if the diagnosis of chondrosarcoma could not be confirmed from the available records, if the medical files were incomplete or inaccessible for evaluation of the main study variables, or if follow-up and outcome data were entirely unavailable.

Data collection

Clinical records were reviewed retrospectively. The variables extracted included age, sex, presenting symptoms, tumor localization, symptom duration, primary or secondary chondrosarcoma status, histologic grade, Enneking stage, biopsy findings, presence of pulmonary metastasis at diagnosis, presence of a soft-tissue component, type of surgical treatment, surgical margin status, postoperative complications, local recurrence, recurrence interval, and survival status.

Tumors were categorized as primary or secondary chondrosarcomas. Histologic grade was recorded as 1, 2, or 3 when available. Histologic grading and final pathological diagnoses were based on the pathology reports available in the institutional records. For staging purposes, tumors were classified according to the Enneking surgical staging system, a widely accepted system in musculoskeletal oncology for surgical planning and prognostic assessment.[8,9]

Surgical treatment was classified according to the terminology used in the institutional records, including intralesional, marginal, wide, and radical resection. Because surgical margin adequacy is a key determinant of local control in chondrosarcoma, special attention was paid to surgical margin status during data extraction and analysis.[2,3]

The main outcome measures were local recurrence, distant metastasis, and mortality. Local recurrence was defined as tumor reappearance at the primary site during follow-up. The recurrence interval was defined as the time from definitive treatment to recurrence detection. Mortality status was determined from the available follow-up data.

Statistical analysis

Statistical analyses were performed using SPSS version 17.0 (SPSS Inc., Chicago, IL, USA). Descriptive statistics were used to summarize the study data. Continuous variables were presented as mean, minimum, and maximum values where appropriate, while categorical variables were expressed as frequencies and percentages. Associations between categorical variables were analyzed using the chi-square test. The relationships among histologic grade, surgical margin status, soft-tissue extension, pulmonary metastasis at diagnosis, and oncologic outcomes, including local recurrence and mortality, were evaluated. A p-value of less than 0.05 was considered statistically significant.

RESULTS

Patient and tumor characteristics

A total of 144 patients were included in the study. The mean age was 42.13±15.01 years (range, 15-78 years), and 57.6% were male. Pain was the most common presenting symptom, and most patients were diagnosed at our institution. Overall, 73 of 144 patients (50.7%) were aged 36-58 years. The detailed demographic and baseline clinicopathological characteristics of the study population

are summarized in Table 1, and the age-group distribution is presented in Figure 1.

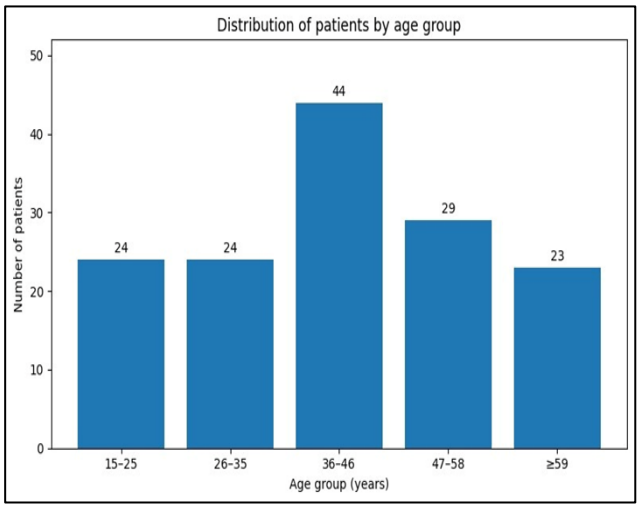

Figure 1: Distribution of patients by age group.

Bar chart showing the age-group distribution of the study population. The largest subgroup was 36–46 years, comprising 44 patients, followed by 47–58 years with 29 patients. The 15–25 and 26–35-year groups each included 24 patients, while 23 patients were aged 59 years or older. Overall, 73 of 144 patients (50.7%) were aged 36-58 years.

Of the 144 tumors, 94 (65.3%) were primary and 50 (34.7%) were secondary chondrosarcomas. Among the secondary chondrosarcomas, 30 (60.0%) were reported to have developed from an enchondroma, whereas the remaining cases were associated with multiple hereditary exostoses, Ollier disease, and Maffucci syndrome. The femur was the most commonly affected site. In the shoulder region, lesions were most frequently located in the proximal humerus and glenoid region, whereas in the pelvis, the iliac wing and acetabulum were the predominant sites.

Sacroiliac involvement was rare. Among the less common sites, the tibia and hand were the most frequently involved, whereas vertebral and foot involvement were uncommon. Notably, three patients had vertebral involvement, and bilateral hand lesions were observed in a 20-year-old patient with Ollier disease. Pulmonary metastasis at diagnosis was present in 10 patients (6.9%), and a soft-tissue component was identified in 61 patients (42.4%). Notably, 9 of the 10 patients (90.0%) with pulmonary metastasis had an accompanying soft-tissue component, and soft-tissue extension was significantly associated with pulmonary metastasis at diagnosis (p=0.002). Needle biopsy was performed in 46 patients (31.9%) and open biopsy in 23 (16.0%). Discordance between the biopsy diagnosis and the final postoperative pathological diagnosis was observed in 21 patients (14.6%). Of these, 19 (90.5%) had received their initial diagnosis at Ankara University Faculty of Medicine.

All discrepant cases were initially interpreted as lower-grade lesions, and 43.0% of these patients subsequently required two or more surgical procedures. Histopathological grade and Enneking stage data were available for 110 patients.

Table 1: Baseline demographic and tumor characteristics.

Variable	Value
Number of patients	144
Age (years) mean±SD (range)	(15-78) 42.13±15.01
Sex N (%)	
Male	83 (57.6)
Female	61 (42.4)
Symptom duration, mean (range), months	19 (1-120)
Diagnosis established at our institution, N (%)	123 (85.4)
Presenting symptom, N (%)	
Pain	99 (68.8)
Swelling	24 (16.7)
Pain + swelling	16 (11.1)
Pathological fracture	5 (3.5)
Tumor origin, N (%)	
Primary chondrosarcoma	94 (65.3)
Secondary chondrosarcoma	50 (34.7)
Tumor location, N (%)	
Femur	43 (29.8)
Pelvis	36 (24.8)
Shoulder region	34 (23.6)
Other sites	31 (21.5)
Pulmonary metastasis at diagnosis, N (%)	10 (6.9)
Soft-tissue component, N (%)	61 (42.4)
Biopsy–final pathology discordance, N (%)	21 (14.6)
Histopathological grade, N (%)*	
Grade 1	60 (54.5)
Grade 2	36 (32.7)
Grade 3	14 (12.7)
Enneking stage, N (%)*	
IA	34 (30.9)
IB	37 (33.6)
IIA	7 (6.4)
IIB	21 (19.1)
III	11 (10.0)

* Available for 110 patients

Treatment and outcomes

Surgical treatment data were available for 116 patients, of whom 100 underwent surgery and 16 did not because of poor general condition, lack of health insurance, or refusal

of treatment by the patient or their relatives. Wide resection was the most frequently performed surgical procedure. Medical treatment was administered to 8 patients, most of whom had advanced disease features, including pulmonary metastasis, soft-tissue extension, or high Enneking stage. No patient underwent radiotherapy or pulmonary metastasectomy. Detailed treatment characteristics and overall oncologic outcomes are summarized in Table 2. The mean follow-up duration was 45 months, and the mean hospital stay was 13.4 days. Complications were recorded in 19 patients (13.1%) and included postoperative femoral fracture, pulmonary embolism, prosthetic dislocation, reversible radial and sural nerve injuries, wound infection, phantom pain, and hematoma. Because some complication records were not fully consistent across the dataset, these findings should be interpreted cautiously. Local recurrence occurred in 25 patients, with a mean time to recurrence of 16 months; grade progression at recurrence was observed in 4 patients (16.0%). Overall mortality was 8.3%. Half of the patients who died were individuals in whom amputation had been planned after recurrence but was not accepted.

Table 2: Treatment characteristics and oncologic outcomes.

Variable	Value
Surgical treatment data available, (N)	116
Underwent surgery, N (%)	100 (86.2 of 116)
No surgery, N (%)	16 (13.8 of 116)
Type of surgery, N (%)	
Intralesional resection	9 (9.0)
Marginal resection	23 (23.0)
Wide resection	47 (47.0)
Radical resection	21 (21.0)
Medical treatment, N (%)	8 (5.6 of 144)
Mean follow-up, months	45
Mean hospital stays, days	13.4
Complications, N (%)	19 (13.1)
Local recurrence, N (%)	25 (17.4)
Time to recurrence, mean (range), months	16 (1-61)
Grade progression at recurrence, N (%)	4 (16.0 of 25)
Mortality, N (%)	12 (8.3)

Table 3: Factors associated with local recurrence.

Variable	Recurrence	No recurrence	P value
Surgical margin, N (%)			0.001
Positive	10/17 (58.8)	7/17 (41.2)	
Negative	15/83 (18.1)	68/83 (81.9)	
Histopathological grade*			0.004
Grade 1	6/60 (10.0)	54/60 (90.0)	
Grade 2	13/36 (36.1)	23/36 (63.9)	
Grade 3	5/14 (35.7)	9/14 (64.3)	
Soft-tissue component			0.009
Present	17/61 (27.9)	44/61 (72.1)	
Absent	8/83 (9.6)	75/83 (90.4)	

* Available for 110 patients.

Factors associated with local recurrence

Among patients with positive surgical margins, recurrence occurred in 58.8% (p=0.001). Local recurrence was significantly associated with histopathological grade (p=0.004) and the presence of a soft-tissue component (p=0.009). Recurrence was observed in 10.0% of grade 1 tumors, 36.1% of grade 2 tumors, and 35.7% of grade 3 tumors. Likewise, recurrence was frequent in patients with a soft-tissue component than in those without (27.9% vs. 9.6%). These associations are detailed in Table 3.

DISCUSSION

The principal finding of this study was that both histopathological grade and surgical margin status substantially affected oncologic outcomes in chondrosarcoma. Local recurrence was observed in 25 patients and was particularly common among those with positive surgical margins, occurring in 58.8% of such cases. Likewise, recurrence was significantly more frequent in grade 2 and grade 3 tumors than in grade 1 tumors. In addition, soft-tissue extension was associated not only with a higher local recurrence rate but also with pulmonary metastasis at presentation. These findings support the concept that prognosis in chondrosarcoma is determined by the combined effect of intrinsic tumor aggressiveness and the ability to achieve adequate surgical clearance.

Our results are in line with previous studies showing that histologic grade and surgical margins are among the most important determinants of local control and survival in chondrosarcoma. In a large retrospective series of pelvic and extremity chondrosarcomas, Stevenson et al demonstrated that surgical margin significantly influenced local recurrence-free survival and that local recurrence adversely affected disease-specific survival, particularly in

higher-grade tumors.[3] More recently, a clinical review by Gazendam et al emphasized that achieving negative surgical margins remains the most important modifiable factor in treating conventional chondrosarcoma, particularly given the limited systemic treatment options and the tumor's resistance to conventional chemotherapy and radiotherapy.[2] In this context, the high recurrence rate observed among our margin-positive cases further underscores the importance of adequate resection for achieving durable local control.

The prognostic importance of histological grade in our series is also strongly supported by the literature. In our cohort, recurrence was substantially lower in grade 1 tumors than in grades 2 and 3, indicating that biologic aggressiveness increases with grade. This observation is consistent with recent reports showing that tumor grade is a key determinant of both recurrence and survival. Kinoshita et al, in a study of high-grade chondrosarcoma, found that tumor grade, surgical margin, and distant metastasis were significant prognostic factors for oncologic outcomes, whereas local recurrence and distant metastasis were closely linked to overall survival.[10] Similarly, registry-based data from Japan showed that distant metastasis at diagnosis was associated with markedly worse disease-specific survival, and that inadequate margins were independently associated with an increased risk of local recurrence in patients without metastasis at presentation.[11] Together, these data support our finding that both tumor biology and adequacy of local treatment are central to prognosis in chondrosarcoma.

Another important finding in the present study was the adverse effect of soft-tissue extension. Patients with a soft-tissue component had a significantly higher recurrence rate, and soft-tissue extension was also significantly associated with pulmonary metastasis at diagnosis. This observation is clinically relevant because extraosseous spread likely reflects both more aggressive tumor behavior and greater difficulty in achieving adequate surgical margins. A recent study of femoral chondrosarcoma demonstrated that the presence of an extraosseous tumor component was associated with poorer local recurrence-free survival and highlighted the technical challenge of achieving adequate margins in these lesions.[12] Recent data on positive-margin cases have also shown that narrow or involved margins, as well as the location of the extraosseous component, can significantly influence recurrence patterns and disease-specific survival.[13] Therefore, our results support the view that a soft-tissue component should not be considered merely a radiologic descriptor, but rather a clinically meaningful marker of aggressive local disease and more complex surgical management. The clinical significance of local recurrence deserves particular emphasis. In our series, recurrence developed after a mean interval of 16 months, suggesting that most recurrences occurred relatively early after index treatment. This pattern is consistent with recent evidence indicating that the prognostic impact of local recurrence is particularly pronounced in grade 2 tumors and that most local recurrences in high-grade lesions occur within the first 5 years after surgery.[5] These findings have practical implications for postoperative surveillance and suggest that patients with grade 2–3 tumors, positive margins, or extraosseous extension may require closer follow-up during the early postoperative period.

Another clinically relevant observation in our study was the biopsy–final pathology discordance observed in a subset of patients, all of whom had initially been reported as lower-grade lesions. This finding is not unexpected in cartilaginous tumors, where sampling limitations and intratumoral heterogeneity may reduce the accuracy of preoperative grading. Current reviews and management guidelines emphasize that biopsy findings in chondrosarcoma should always be interpreted alongside imaging and clinical features, particularly for lesions in which surgical planning depends heavily on grade estimation.[2-4] Our findings, therefore, reinforce the importance of multidisciplinary evaluation and careful surgical planning in specialized sarcoma centers.

This study has several strengths. It presents a relatively large single-center series of patients with chondrosarcoma, a rare primary bone tumor, and provides long-term clinical experience from a tertiary referral institution. The study also simultaneously evaluated several clinically relevant prognostic variables, including histopathological grade, surgical margin status, soft-tissue extension, pulmonary metastasis at presentation, and local recurrence. In addition, the analysis reflects real-world clinical practice and highlights important diagnostic and treatment-related challenges, such as biopsy–final pathology discordance and difficulty in achieving adequate margins in more aggressive tumors. However, the study also has important limitations. First, its retrospective design introduces an inherent risk of selection bias and incomplete data capture. Second, some variables were unavailable for all patients, so several analyses were performed on an available-case basis. Third, the long study period may have been affected by changes in imaging quality, biopsy techniques, pathological interpretation, surgical strategies, and perioperative care over time. Despite these limitations, the study provides clinically meaningful data regarding the prognostic importance of grade, surgical margin status, and soft-tissue extension in chondrosarcoma

CONCLUSION

This study showed that histopathological grade and surgical margin status are the principal determinants of outcome in chondrosarcoma. Higher-grade tumors and positive surgical margins were associated with increased local recurrence, while soft-tissue extension was linked to both recurrence and pulmonary metastasis at diagnosis. These findings reinforce the importance of accurate preoperative assessment, multidisciplinary planning, and adequate oncologic resection in the management of chondrosarcoma. Patients with high-grade disease, positive margins, or extraosseous extension should be

considered a higher-risk subgroup and followed more closely.

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Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Review Board

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