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Surgical Management of Conventional Grade I Chondrosarcoma of Long Bones

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We retrospectively reviewed 70 patients with low-grade (Grade I) chondrosarcoma of the appendicular skeleton treated at the Mayo Clinic from 1980 to 2001. Fifty-four patients underwent wide resections and three patients underwent marginal excision for radiographically aggressive lesions. Thirteen patients were treated with intralesional curettage for more indolent lesions. The mean age of the patients was 43 years (range, 5–85 years) and the minimum followup was 0.2 year (mean, 8.5 years; range, 0.2–22.8 years). Of the patients who had wide resection, one experienced local recurrence and one had metastasis develop. One patient in the group treated with intralesional curettage had local recurrence and metastasis. We observed no difference in overall survival rate between the intralesional curettage group and the wide resection group. Although there was no difference in the treatment outcome between the two groups, patients with more radiographically aggressive lesions underwent more extensive surgery. The data suggest in selected patients less radiographically aggressive Grade I chondrosarcoma can be safely treated with intralesional curettage without compromising patient outcome.

Level of Evidence: Level IV, prognostic study. See the Guidelines for Authors for a complete description of levels of evidence.

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Each author certifies that his or her institution has approved the reporting of these cases, that all investigations were conducted in conformity with ethical principles of research, and that informed consent for participating in the study was obtained.
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Chondrosarcoma is defined as a malignant tumor characterized by the formation of cartilage by the tumor cells.[3] Chondrosarcoma is the second most common primary malignancy of bone after osteosarcoma and has a slight male predominance.[3,12,13,24] Chondrosarcomas represented 9.2% of the malignant tumors in patients at our institution and approximately 86% of these were primary chondrosarcoma.[24] The age distribution of patients with chondrosarcoma shows a gradual age-related increase, with the peak incidence occurring during the sixth and seventh decades of life. The majority of patients are older than 50 years.[5] Chondrosarcoma has a predilection for the trunk bones and the upper end of long bones, particularly the humerus and femur. Clinical symptoms are pain and tenderness with or without a mass. Some patients are asymptomatic, as the lesion is discovered incidentally on radiographs.[24]

The behavior of these lesions varies from slowly growing, nonmetastasizing tumors to highly aggressive metastasizing sarcomas. The prognostic factors that determine the outcome are related to the histologic grade, anatomic site, tumor size, and the adequacy of treatment.[1,3,8–10,16] Surgery is the preferred procedure for chondrosarcoma because irradiation and chemotherapy are ineffective.[8,12] The adequacy of treatment (defined as the complete removal of the neoplasm and biopsy site without entering the tumor) is one of the most important factors in determining the incidence of recurrence and survival. The standard of surgical treatment is wide resection, but depending on the location, this may cause increased morbidity or require complex reconstruction.[6,7]

There is evidence Grade I chondrosarcomas may not all behave in the same way clinically or radiographically.[13,16] The local recurrence rate and potential for metastasis are low, so limited surgery (intralesional resection) with adjuvant therapy (cryosurgery, phenolization) has been advocated for less aggressive-appearing lesions.[1,15,21] However, in some studies, the outcome when treated with intralesional surgery has been associated with increased incidence of local recurrence and subsequent disease pro-

gression.[2,18,20,23] We believe less extensive surgery may be indicated in less aggressive chondrosarcoma of long bones. If suitable criteria can identify less aggressive-behaving lesions, then the extent of surgery can be reduced without compromising clinical outcome. This would avoid the need for complex reconstruction necessitated by en bloc resection and minimize morbidity.

We therefore asked whether local recurrence and metastasis of Grade I chondrosarcoma of long bones would be influenced by two different treatment approaches, intralesional curettage with or without adjuvant treatment versus en bloc resection.

MATERIALS AND METHODS

We retrospectively reviewed 70 patients treated for Grade I chondrosarcoma of the long bones from January 1980 through December 2001 with either intralesional curettage (13 patients) or wide resection (57 patients). The timeframe was chosen to allow incorporation of modern surgical treatment and the use of computed tomography (CT) and MRI. This will better reflect the information available to the modern orthopaedic surgeon with modern imaging tools. The primary end points of our study were local recurrence, metastases, and the survival rate of the patients. The power of the study was 0.3 because the number of the events (local recurrence, metastasis, survival rate) was small.

We included in the study only chondrosarcomas that met the following inclusion criteria: (1) intramedullary lesion of the appendicular extremity and (2) definite histologic diagnosis of Grade I chondrosarcoma. Of the 423 cases of chondrosarcoma analyzed, there were 304 Grade I chondrosarcomas. These were classified histologically by a growth pattern of permeation with infiltration and entrapment of normal trabecular bone. Enchondromas were distinguished by a pattern of benign islands of cartilage encased in lamellar bone. We excluded variants of chondrosarcoma, including secondary peripheral chondrosarcoma, dedifferentiated chondrosarcoma, soft tissue chondrosarcoma, clear cell chondrosarcoma, synovial chondrosarcoma, and mesenchymal chondrosarcoma. We excluded patients with tumors in the axial skeleton, pelvis, spine, foot, and hand because of differences in their biologic behaviors and prognoses.[3,8,11,14,17,19,20,22] We also excluded patients who had local recurrence of chondrosarcoma and those with active enchondroma (previously referred to as Grade I/II chondrosarcoma). These exclusions left 116 cases of Grade I chondrosarcoma of the long bone, of which 46 borderline lesions were further excluded. Thus, 70 Grade I chondrosarcomas of the long bone met the inclusion criteria.

The 70 patients with Grade I chondrosarcoma underwent either intralesional excision (13 patients) or wide excision (57 patients). Age and gender were similar in the treatment groups (Table 1). Fifty-seven (88%) patients had pain of a mean duration of 6 months (range, 1–40 months). Eight lesions (12%) were discovered incidentally from plain radiographs or bone scans. The affected sites were the femur (28 patients [39%]), humerus (24 patients [34%]), tibia (11 patients [15.7%]), fibula (four patients [5%]), and radius (three patients [4%]) (Table 1).

Histologic slides prepared from the biopsy specimen and the surgical specimens were reviewed to verify the diagnosis.[16] The pathologist (CYI) was blind to the patient's clinical history, functional outcome, and survival experience. Tumors were scrutinized using plain radiography, CT (when available), and MRI (when available). The surgical margin was considered positive for disease if remaining tumor was found at the margin microscopically in en bloc resection cases. Radiographic data were used in conjunction with the histologic appearance to identify the tumor stage according to a modified Enneking staging system.[6] Low-grade lesions that were locally destructive but associated with a low risk of distant metastasis were Stage IA or IB.

Patients in the group with wide resection had more ($p < 0.001$) cortical disruption and soft tissue extension: none of the 13 patients selected for intralesional curettage had cortical disruption, whereas among 57 patients selected for wide resection 60% had cortical disruption and 23% had soft tissue extension. Thirty-five patients had Stage IA and 35 had Stage IB lesions. All patients with Stage IB lesions underwent wide resection ($p = 0.001$).

Thirteen patients had intralesional curettage and phenolization supplemented with either bone graft (12 patients) or acrylic cementation (one patient). Fifty-seven patients were treated with the intention to obtain wide resection, but marginal margins were obtained in three. In three patients treated with marginal resection, the lesions were in the proximal femur (femoral neck or intertrochanteric region). In two cases, the lesions were in the fibula. We performed wide resection for all tumors located in the fibula and radius, for patients who presented with pathologic fracture, and for patients whose radiographs showed cortical disruption and soft tissue mass.

We used Mayo Clinic medical records and Mayo Tumor Registry records to obtain all data. In each group, we compared the results of treatment between intralesional curettage and wide excision in terms of disease-free survival, local recurrence, and metastasis. The disease-free survival was defined by the period from tumor resection to local recurrence, metastasis, or death from disease. Observation time was the interval between diagnosis and last contact (death or last followup). Data were censored at the last followup for patients without recurrence, metastasis, or death. The minimum censoring time for those who did not experience any event was 4 months (mean, 7.6 years; range, 4 months–22.8 years).

We estimated the local recurrence rate, metastasis rate, disease-free survival, and overall survival rates using the Kaplan-Meier method. Tests of the difference between or among survival curves were performed using log rank tests. Comparison of proportions between the groups of treatment was performed using chi square analysis for categorical variables and one-way analysis of variance for continuous variables. Significance was set at $p < 0.05$.

RESULTS

The overall 5-year disease-free survival rate for both treatment groups, as assessed by the Kaplan-Meier method, was 89% (Fig 1). In each group, the 5-year disease-free

TABLE 1. Baseline Characteristics of Patients at Study Entry

Characteristic	Type of Surgical Treatment		p Value
	Intralesional (n = 13)	*Wide (n = 54) and Marginal (n = 3) (n = 57)*	
Gender			
Male	7	20	0.3
Female	6	37	
Age (years)	36.8 ± 19.3	43.3 ± 18.4	0.87
Location			
Femur	6	22	0.08
Humerus	2	22	
Tibia	5	6	
Fibula	0	4	
Radius	0	3	
Symptoms	6		
Pain	2		0.16
Incidental findings	10	47	
Pathologic fractures	3	5	
Radiology	0	5	
No cortical disruption	13	22	< 0.001*
Cortical disruption	0	35	
Soft tissue extension	0	13	
Staging			0.0001*
IA	13	22	
IB	0	35	
Median length of followup (years)	10.7 (0.2–22.8)	7 (0.2–19.9)	
Number of local recurrence (cases)	1	1	
Number of metastasis (cases)	1	2	
Number of deaths	2	9	
Cause of death			
From disease	1	1	
Other disease	1	8	

*The difference between groups was significant ($p < 0.05$)

survival rate was 79% for intralesional excision and 91% for wide resection (Fig 2).

We observed no difference in the overall disease-free survival rates, local recurrence, or metastasis between patients treated with intralesional resection or wide resection (Figs 3 and 4). One patient in each treatment group died from metastasizing chondrosarcoma.

Two local recurrences occurred during the followup period. One recurrent chondrosarcoma occurred in a 51-year-old woman with a lesion of the distal femur. She was treated with intralesional curettage, phenolization, and bone grafting. The lesion recurred as a dedifferentiated chondrosarcoma 4 months after the initial surgery. Lung metastasis then developed and she underwent pulmonary metastasectomy. She eventually died from lung metastasis 9 months later. The second case of local recurrence involved a 58-year-old man (Fig 5) with an osteolytic lesion at the medial femoral condyle and soft tissue extension (Stage IB). This patient was treated with wide resection and reconstruction with an osteochondral allograft. The

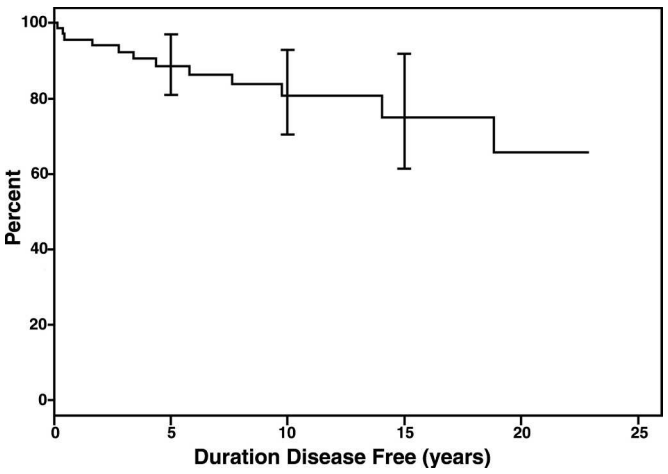

Fig 1. A Kaplan-Meier survival analysis shows patients' overall disease-free survival rate of patients with Grade I chondrosarcoma. There was no difference between the 5- and 10-year disease-free survival rates (89% and 79%, respectively).

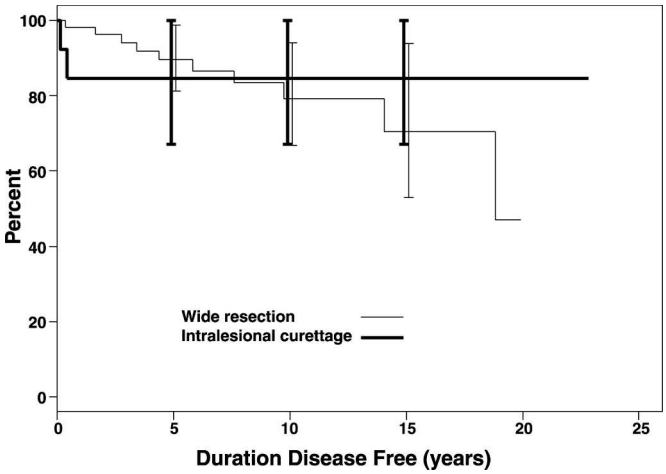

Fig 2. A Kaplan-Meier survival analysis shows patients' overall disease-free survival rate based on type of treatment. There was no difference in the overall disease-free survival rate between patients treated with intralesional resection versus those treated with wide resection.

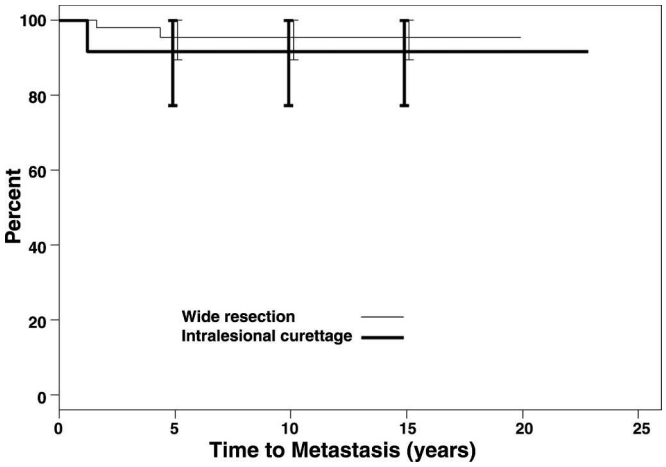

Fig 4. A Kaplan-Meier survival analysis shows the results for metastasis development between treatment groups. There was no difference in the metastasis between patients treated with intralesional resection versus those treated with wide resection.

lesion recurred after 9 years and was treated with wide resection and reconstruction with an endoprosthesis at that time. Followup at 2 years after the second procedure revealed no recurrence. However, the patient subsequently died of primary lung cancer. The pathologist compared tissue from the femoral condyle and from the lung and found different origins.

Two metastases occurred in the group of patients who were treated with wide resection. The first patient with metastasis (Fig 6) had a Stage IB lesion of the left femoral condyle treated with wide resection and reconstruction with a rotating hinge knee replacement. The patient had metastatic lesions develop in the lung, deltoid muscle, and abdomen at 3 years 6 months. In this patient, the histology upgraded to Grade II chondrosarcoma, and he subse-

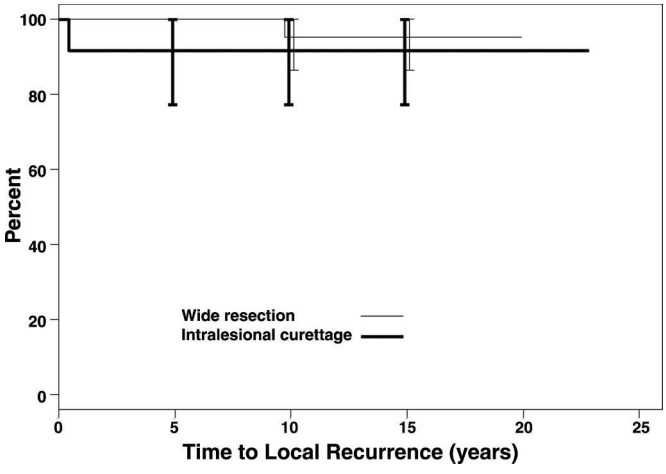

Fig 3. A Kaplan-Meier survival analysis shows the results for local recurrence between treatment types. There was no difference in the local recurrence between patients treated with intralesional resection versus those treated with wide resection.

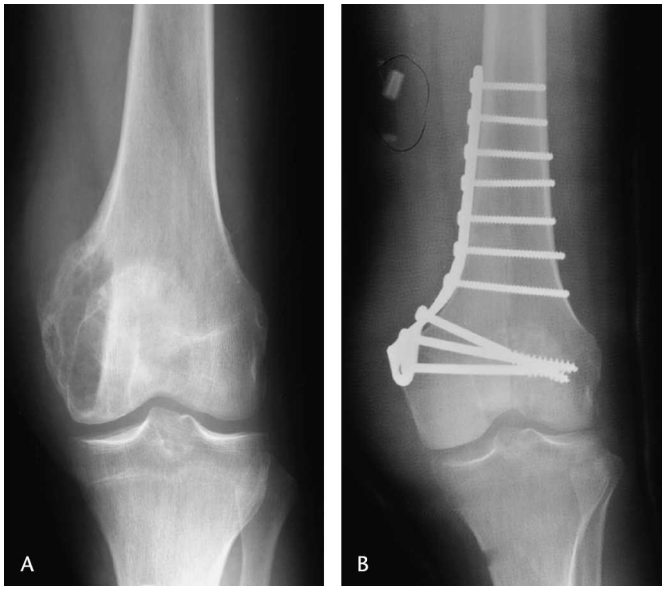

Fig 5A–B. (A) A preoperative plain radiograph shows an osteolytic lesion at the medial aspect of the distal femur. (B) A postoperative radiograph shows the patient after being treated with wide excision and reconstruction with an allograft.

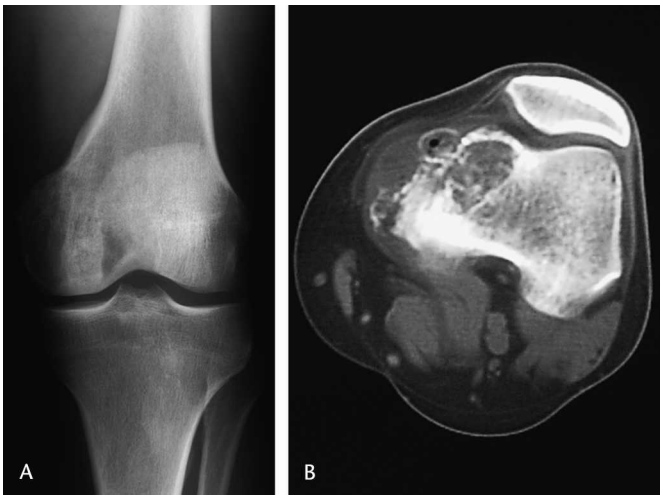

Fig 6A–B. (A) A plain radiograph and (B) CT scan show an osteolytic lesion and cortical disruption of the medial aspect of the distal femur (Stage IB lesion).

quently died 1 year after the metastasis developed. The second patient was the one previously mentioned in whom locally recurrent dedifferentiated chondrosarcoma of the distal femur developed. Another patient was noted to have a multicentric chondrosarcoma develop.[4] This patient with a lesion in the proximal femur (Stage IA lesion) (Fig 7) treated with marginal resection was noted to have another lesion in the ipsilateral tibia 6 years after the first resection. The second lesion was treated with intralesional excision, phenolization, and allogenic bone grafting. The patient has been disease free for 3 years.

DISCUSSION

Local recurrence and metastases are rare in low-grade chondrosarcoma of the long bones. This is true whether the lesion is treated with wide resection or with intralesional curettage. We asked whether local recurrence and metastasis of Grade I chondrosarcoma of long bones would be influenced by two different treatment approaches, intralesional curettage with or without adjuvant treatment versus en bloc resection. We observed only one local recurrence and metastasis in our intralesional curettage group. The overall disease-free survival rates were similar between patients treated with intralesional curettage and those treated with wide resection. Therefore, less extensive surgery such as intralesional curettage can be used with less aggressive chondrosarcoma of the long bones with no cortical destruction and soft tissue extension.

We note several limitations to our study. We acknowledge the treatment bias between the two groups: the surgeon (FHS) preferred performing wide resection in all tumors located in the fibula and radius, and in patients who presented with a pathologic fracture or those whose radiographs showed cortical disruption and a soft tissue mass. Twenty-two patients with less aggressive Stage IA lesions were treated with en bloc resection if marked thinning of the cortex was present or if the lesions were located in the proximal femur or in expendable bones and could be excised without compromising functional outcome. We also recognize the disparity in the number of patients treated with wide excision versus those treated with curettage. This potentially could have skewed the curettage recurrence/metastases data, as not enough of these cases may have been collected to reveal the true recurrence and/or metastases rate, which would be predictably higher in patients treated in this marginal fashion. It may be better to collect additional curettage cases as time goes on and revisit this issue in a followup article when more comparable numbers are achieved. Chondrosarcoma, especially Grade I chondrosarcoma, has a long natural history with rare events; because of this and its relative rarity, it is difficult to get enough power to distinguish between treatment alternatives.

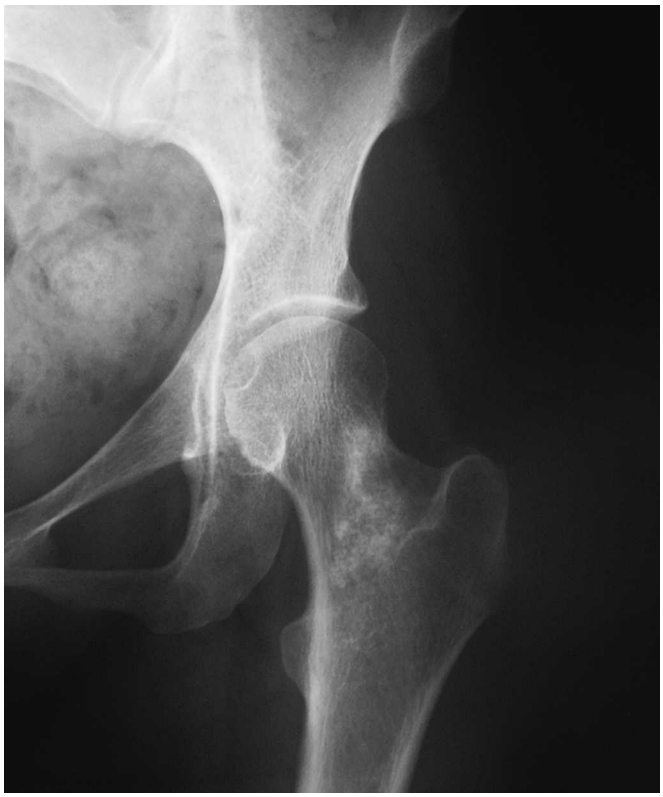

Fig 7. A plain radiograph shows Grade I chondrosarcoma at the proximal femur (Stage IA lesion).

Bauer et al[1] reviewed 23 patients with chondrosarcoma who were treated by intralesional curettage. Two patients had local recurrences, both Stage IA lesions at the proximal tibia and calcaneus. None had metastasis or died of tumor-related causes during a minimum followup of 2 years (mean, 7 years; range, 2–25 years). Schreuder et al[21] treated nine patients with Grade I chondrosarcoma with curettage, cryosurgery, and bone grafting. There was no recurrence after a mean followup of 26 months.

In contrast, some studies have reported poor outcome after intralesional resection.[18,23] Tsuchiya et al[23] treated six cases of borderline chondrosarcoma. Two patients with lesions in the pelvis had local recurrence. In a study of 26 patients with lesions of all grades in the axial skeleton, Ozaki et al[18] reported a high incidence of local recurrence. Both studies recommended wide resection for treatment of chondrosarcoma. The results from these studies were high local recurrence and poor outcome because the study design included lesions in the axial skeleton, which have the worse prognosis,[19] and included all grades of chondrosarcoma.

The differences between institutional experiences may be the result of several factors. There is some variability among pathologists in the grading schemes used to classify the tumors. In addition, some studies include so-called Grade I/II chondrosarcomas, or active enchondroma. We were especially careful to exclude all tumors that were not clearly Grade I chondrosarcoma. We also excluded lesions of the central skeleton because these historically behave differently from long bone lesions.[19]

With appropriate selection, it appears less radiographically aggressive Grade I chondrosarcoma can be treated effectively with intralesional curettage and adjuvant treatment. Tumors that had no associated cortical perforation or soft tissue mass did well with intralesional curettage. Patients with more aggressive lesions (eg, cortical disruption, Stage IB) were selected for en bloc resection and had excellent local control. However, 22 patients with less aggressive Stage IA lesions were treated by en bloc resection. It is difficult to know whether wide resection was necessary. It may reflect the bias of the surgeon during the time of the study. We hope to better classify these lesions so surgical management can be tailored to the aggressiveness of the lesion to enhance local control and minimize morbidity.

Grade I chondrosarcoma can manifest a broad spectrum of biologic behaviors. The diagnosis and treatment of cartilaginous lesions vary with the radiographic manifestation and histologic grading. A multidisciplinary team that consists of experts in radiology, pathology, and orthopaedic oncology is mandatory for effective treatment. Local recurrence and potential metastasis are low after appropriate treatment.

Our goal was to determine if, using radiographic criteria, a less aggressive surgical procedure could be used in selected less aggressive-appearing lesions without compromising outcome. Although there was a substantial treatment bias between the two groups, patients with tumors that did not erode the cortex or have associated soft tissue masses did as well with intralesional surgery. This should help to minimize the surgical morbidity associated with treatment of less aggressive lesions. If the Stage IB lesions had been treated exactly the same as their Stage IA counterparts based on pathology alone rather than in combination with their radiographic appearance, recurrences might have been higher for this group because of the nature of curettage, which leaves microscopic disease; thus, we believe an adjuvant therapy such as phenolization or cryosurgery is required, but it only works well in confined bony defects. Again, it usually is up to the surgeon's judgment, in addition to a pathology diagnosis of low-grade cartilaginous neoplasm, if a soft tissue extension wide resection is performed. Such cases demand respect to avoid local recurrence, which may have an adverse effect on survival.

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References

1. Bauer HC, Brosjo O, Kreicbergs A, Lindholm J. Low risk of recurrence of enchondroma and low-grade chondrosarcoma in extremities: 80 patients followed for 2–25 years. *Acta Orthop Scand*. 1995; 66:283–288.
2. Bjornsson J, McLeod RA, Unni KK, Ilstrup DM, Pritchard DJ. Primary chondrosarcoma of long bones and limb girdles. *Cancer*. 1998;83:2105–2119.
3. Dahlin DC, Henderson ED. Chondrosarcoma, a surgical and pathological problem; review of 212 cases. *J Bone Joint Surg Am*. 1956; 38:1025–1038.
4. Damron TA. Sim FH, Unni KK. Multicentric chondrosarcomas. *Clin Orthop Relat Res*. 1996;328:211–219.
5. Dorfman HD, Czerniak B. Bone cancers. *Cancer*. 1995;75: 203–210.
6. Enneking WF. A system of staging musculoskeletal neoplasms. *Clin Orthop Relat Res*. 1986;204:9–24.
7. Enneking WF, Spanier SS, Goodman MA. A system for the surgical staging of musculoskeletal sarcoma. *Clin Orthop Relat Res*. 1980; 153:106–120.
8. Eriksson AI, Schiller A, Mankin HJ. The management of chondrosarcoma of bone. *Clin Orthop Relat Res*. 1980;153:44–66.
9. Erlandson RA, Huvos AG. Chondrosarcoma: a light and electron microscopic study. *Cancer*. 1974;34:1642–1652.
10. Evans HL, Ayala AG, Romsdahl MM. Prognostic factors in chondrosarcoma of bone: a clinicopathologic analysis with emphasis on histologic grading. *Cancer*. 1977;40:818–831.
11. Gitelis S, Bertoni F, Picci P, Campanacci M. Chondrosarcoma of bone: the experience at the Istituto Ortopedico Rizzoli. *J Bone Joint Surg Am*. 1981;63:1248–1257.

12. Healey JH, Lane JM. Chondrosarcoma. *Clin Orthop Relat Res*. 1986;204:119–129.
13. Inwards CY, Unni KK. Classification and grading of bone sarcomas. *Hematol Oncol Clin North Am*. 1995;9:545–569.
14. Kahn LB. Chondrosarcoma with dedifferentiated foci: a comparative and ultrastructural study. *Cancer*. 1976;37:1365–1375.
15. Marcove RC, Stovell PB, Huvos AG, Bullough PG. The use of cryosurgery in the treatment of low and medium grade chondrosarcoma: a preliminary report. *Clin Orthop Relat Res*. 1977;122: 147–156.
16. Mirra JM, Gold R, Downs J, Eckardt JJ. A new histologic approach to the differentiation of enchondroma and chondrosarcoma of the bones: a clinicopathologic analysis of 51 cases. *Clin Orthop Relat Res*. 1985;201:214–237.
17. Ozaki T, Hillmann A, Lindner N, Blasius S, Winkelmann W. Chondrosarcoma of the pelvis. *Clin Orthop Relat Res*. 1997;337: 226–239.
18. Ozaki T, Lindner N, Hillmann A, Rodl R, Blasius S, Winkelmann W. Influence of intralesional surgery on treatment outcome of chondrosarcoma. *Cancer*. 1996;77:1292–1297.
19. Pring ME, Weber KL, Unni KK, Sim FH. Chondrosarcoma of the pelvis: a review of sixty-four cases. *J Bone Joint Surg Am*. 2001; 83:1630–1642.
20. Pritchard DJ, Lunke RJ, Taylor WF, Dahlin DC, Medley BE. Chondrosarcoma: a clinicopathologic and statistical analysis. *Cancer*. 1980;45:149–157.
21. Schreuder HW, Pruszczynski M, Veth RP, Lemmens JA. Treatment of benign and low-grade malignant intramedullary chondroid tumours with curettage and cryosurgery. *Eur J Surg Oncol*. 1998;24: 120–126.
22. Sheth DS, Yasko AW, Johnson ME, Ayala AG, Murray JA, Romsdahl MM. Chondrosarcoma of the pelvis: prognostic factors for 67 patients treated with definitive surgery. *Cancer*. 1996;78: 745–750.
23. Tsuchiya H, Ueda Y, Morishita H, Nonomura A, Kawashima A, Fellinger EJ, Tomita K. Borderline chondrosarcoma of long and flat bones. *J Cancer Res Clin Oncol*. 1993;119:363–368.
24. Unni KK. Bone tumors: general aspects and data on 11,087 cases. *Dahlin's Bone Tumors: General Aspects and Data on 11,087 Cases.* Philadelphia, PA: Lippincott-Raven; 1996:71–72.