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Chondrosarcoma of Bone

THE EXPERIENCE AT THE ISTITUTO ORTOPEDICO RIZZOLI

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ABSTRACT: **We retrospectively reviewed the records of 125 patients with chondrosarcoma seen at the Istituto Ortopedico Rizzoli. All of the patients had been followed for at least five years, and ninety-six patients had been followed for at least ten years. The requirements for the adequacy of treatment were carefully defined.**

Metastasis and survival were related to the histological grade of the tumor. Nine per cent of the grade-1 lesions and 44 per cent of the grade-3 lesions metastasized. Ninety-four per cent of the patients with grade-1 lesions survived for five years, compared with only 44 per cent of patients with grade-3 lesions. The ten-year survival rates were 87 per cent and 27 per cent, respectively.

Adequacy of treatment had an important influence on the incidence of recurrence, length of survival, and length of disease-free survival. The incidence of recurrence in adequately treated patients was 6 per cent, but in inadequately treated patients it was 69 per cent. The five-year survival rates in these two groups were 81 per cent and 53 per cent, respectively. Seventy-eight per cent of the adequately treated patients were disease-free at follow-up (mean, 11.1 years) compared with only 6 per cent of the inadequately treated patients.

We compared the results of this review with those of other reviews of chondrosarcoma.

Chondrosarcoma of bone presents a wide spectrum of clinical behavior and survival, the prognosis being related to the histological grade of the tumor and the adequacy of treatment[1,7,10-12,16,17]. Five-year and ten-year follow-up periods are mandatory to accurately assess the efficacy of treatment and the survival rate. While the histological diagnosis and grading of chondrosarcoma can be difficult at times, especially with low-grade lesions, the tumor grade appears to correlate closely with the incidence of metastasis and the rate of survival. Low-grade lesions tend to be slow-growing, with infrequent metastases that usually occur late[7,10,12,15,17]. Metastasis rates for low-grade tumors have been reported to be between zero and 12 per cent[7,10,17]. High-grade lesions, on the other hand, metastasize early and often, similar to other high-grade sarcomas of bone. Metastasis rates of between 38 and 75 per cent have been reported[7,10,17]. The over-all survival rate for patients with chondrosarcoma has varied from series to series. In 1963, Henderson and Dahlin reported an over-all five-year survival rate of 54 per cent and a ten-year survival rate of 38 per cent in patients with chondrosarcoma. Two more recent reviews have reported a five-year survival rate of better than 75 per cent and a ten-year survival rate as high as 67 per cent[10,17]. Evans et al. stated that this reported improvement in survival may be due to technical advances in surgery in recent years.

Since 1956, the adequacy of treatment has been stressed as an important determinant in the incidence of recurrence and survival in chondrosarcoma[7]. As the tumor is relatively radioresistant, treatment depends solely on the complete surgical removal of the neoplasm. The survival rates for patients with untreated chondrosarcoma have been reported to be as low as zero and 6 per cent[13,16], whereas the survival rates for those with adequately treated chondrosarcoma have ranged from 41 to 84 per cent[7,10,11,17]. In all of these series, adequate treatment was defined as the complete removal of the neoplasm and biopsy site without entering the tumor. However, no distinction was made in these reports between marginal exci-

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sion, wide excision, and radical resection[8,18], which might explain the difference in reported survival rates. Recently a systematic approach to tumor grading and treatment was applied to chondrosarcoma of bone, but the follow-up of the patients in that series was quite short[9]. The purpose of this paper is to review the findings in our group of patients with chondrosarcoma with emphasis on survival rates, especially with respect to the adequacy of treatment. We also attempted to define "adequacy" more accurately in terms of the margin of normal tissue removed with the tumor.

Materials and Methods

Between 1937 and 1980, 287 cases of histologically confirmed chondrosarcoma were seen at the Istituto Ortopedico Rizzoli. As a comparison, between 1959 and 1979, 433 cases of osteosarcoma also were seen, making the incidence of chondrosarcoma approximately one-half that of osteosarcoma[3,5,12]. The present study is a retrospective review of only classic cases of chondrosarcoma. The following variants of chondrosarcoma were not included in this review[4-6,12,19,20]: dedifferentiated chondrosarcoma (at the time of primary diagnosis, twenty-seven patients), soft-tissue chondrosarcoma (three patients), periosteal chondrosarcoma (eleven patients), clear-cell chondrosarcoma (three patients), synovial chondrosarcoma (two patients), and mesenchymal chondrosarcoma (three patients). In addition, the five patients with a second malignant neoplasm aside from chondrosarcoma and the four patients who died immediately after the primary surgical procedure were not included in this review.

Other patients were excluded because it was impossible to determine accurately from the records what the surgical margins of the primary surgical procedure were. This included twenty-two patients who initially were treated at other institutions and forty-nine patients who were seen for consultation only.

Finally, seven patients were lost to follow-up and twenty-six patients had less than the five years of follow-up necessary to study survival rates in chondrosarcoma. Therefore we are reporting on 125 patients, of whom twenty-nine have had at least five years of follow-up and ninety-six have had at least ten years of follow-up. All of these patients received their primary surgical treatment at the Istituto Ortopedico Rizzoli and all had classic chondrosarcoma. Eighty-six patients were male and thirty-nine, female (Fig. 1). It appears that male patients are at increased risk for chondrosarcoma[5,12]. The mean age was 39.0 years (range, fourteen to seventy-eight years). Sixty patients were between thirty and forty-nine years old, twenty were between twenty and twenty-nine, and fourteen were between fourteen and nineteen years old (Fig. 1).

The charts of all 125 patients were examined for pertinent clinical data. Current follow-up was obtained on each patient by a questionnaire sent to the "Ufficiale Sanitario del Commune" (official town physician).

Definition of Surgical Adequacy

For each patient in the series, a detailed technical and anatomical description of the primary surgical procedure was available. The operative procedures were classified using the following standardized criteria of the Musculoskeletal Tumor Society[8,18]. An *intralesional* operation meant that the lesion was invaded during the operative procedure, leaving residual tumor tissue in the tumor bed. In some of these, a portion of the bulk of the tumor was removed. In a *marginal excision* the lesion was removed without a cuff of normal tissue around the tumor. Occasionally a pseudocapsule about a chondrosarcoma provides a plane of dissection which tempts the surgeon to perform a marginal excision. In a *wide excision* the lesion was removed together with a margin of normal tissue completely encircling the tumor. There were some anatomical locations where wide excision was impossible, such as the popliteal fossa, the axilla, and the inguinal region, because these areas are not contained within muscle compartments. In these situations, the excision was classified as marginal. A *radical resection* indicated complete removal of the le-

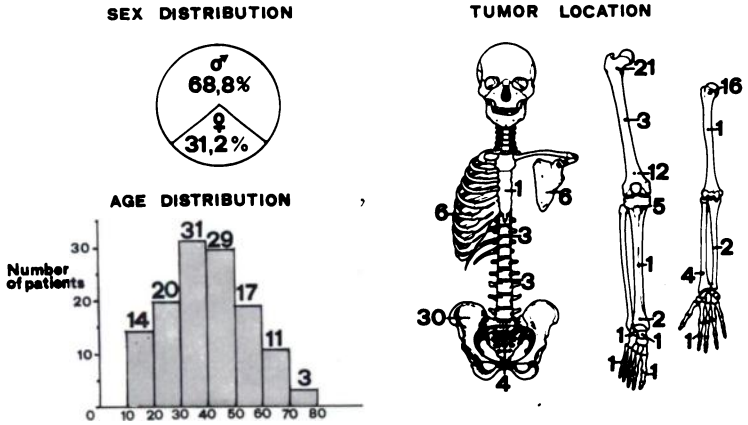

FIG. 1

Age and sex distribution and tumor location.

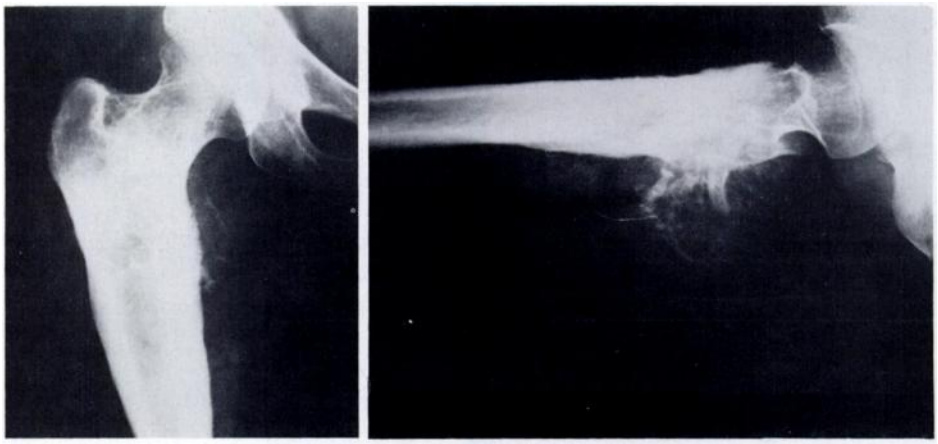

FIG. 2-A FIG. 2-B

Anteroposterior and lateral radiographs of a central chondrosarcoma. Note the large soft-tissue extension of the tumor. This lesion was radiographic grade 3 and histological grade 3.

sion, including all of the involved muscles from their origin to their insertion and all of the involved bone from joint to joint. The ablative surgical procedures also were classified by these requirements. In addition, the surgery was classified as *contaminated* if the tumor was entered during the surgical procedure. By definition, all intralesional procedures were contaminated.

We considered adequate surgery for chondrosarcoma to be a non-contaminated wide excision, wide amputation, radical resection, or radical amputation. Inadequate procedures included intralesional surgery, marginal excision, marginal amputation, and any contaminated procedure. Finally, excision of the biopsy scar was mandatory if the procedure was to be considered adequate.

In an earlier review, Campanacci et al. noted that the grades assigned to the preoperative radiographs of chondrosarcomas correlated well with the ability to perform adequate surgery[2]. This radiographic grading system also was used in the present series, as follows. For central chondrosarcomas: grade 1 — the cortex around the lesion is completely intact; grade 2 — the cortex is invaded with a soft-tissue mass; and grade 3 — there is a large extraosseous development of chondrosarcoma (Figs. 2-A and 2-B). This last grade sometimes is difficult to distinguish from a peripheral chondrosarcoma. The radiographic grading of the peripheral chondrosarcomas was as follows: grade 1 — the tumor is very dense with calcification, its margins are sharp, and it does not invade the cortex of the contiguous bone (Figs. 3-A and 3-B); grade 2 — the tumor margins are somewhat blurred, with radiolucency within the tumor, and the contiguous bone is invaded; and grade 3 — the tumor outline is not visible, there are large areas of radiolucency within the tumor, and there is extensive invasion of the contiguous bone.

Histological Tumor Grading

All tumors were graded by gross and histological evaluation by two of us (F. B. and M. C.), pathologists

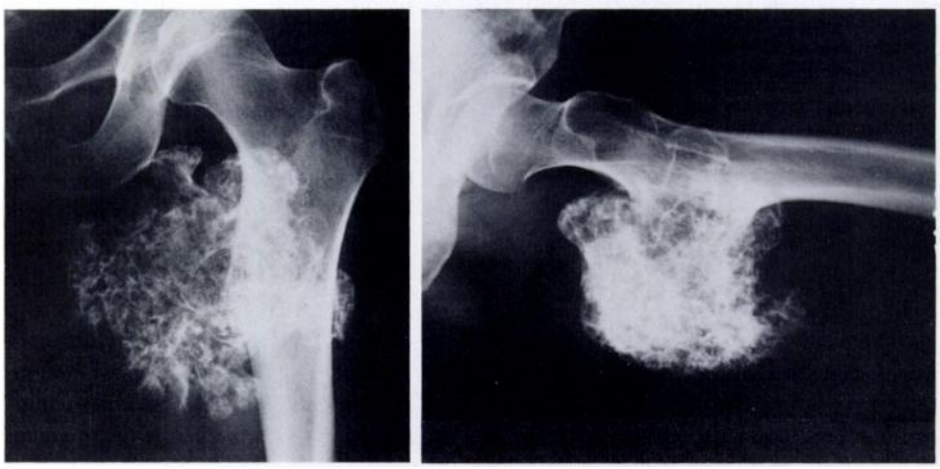

FIG. 3-A FIG. 3-B

Anteroposterior and lateral radiographs of a peripheral chondrosarcoma. The lesion is densely calcified, with well delineated margins. The tumor appears to be extending from the flared base of a pre-existing exostosis. This lesion was radiographic grade 1 and histological grade 1.

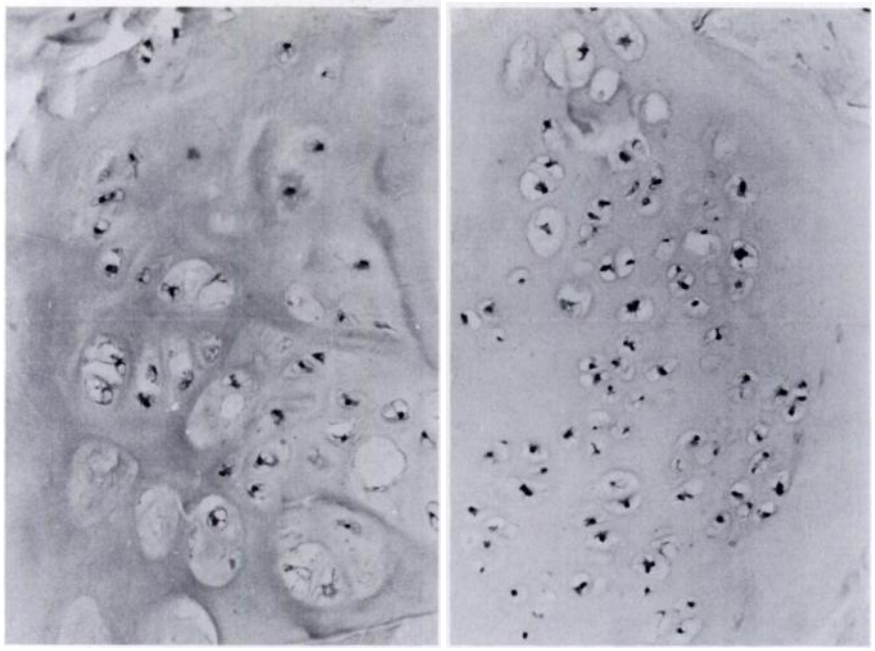

FIG. 4 FIG. 5

Fig. 4: Histological grade 1. It is possible to see cartilage cells with moderately enlarged nuclei and minimum pleomorphism. A binucleate cell is present (hematoxylin and eosin, × 250).

Fig. 5: Histological grade 2. Increasing cellularity and pleomorphism is evident, and more binucleate cells are present (hematoxylin and eosin, × 250).

with considerable experience in the grading of chondrosarcoma. The histological grade assigned depended on both gross and histological examination. Special care was taken to ensure that the biopsy specimen had been obtained from an adequate sample of the tumor. This was especially important in ruling out dedifferentiated chondrosarcoma, which consists of areas of low-grade cartilaginous tumor and of dedifferentiated high-grade sarcoma. In young patients, the tumor was searched particularly carefully for malignant osteoid-forming cells, so that a chondroblastic osteosarcoma would not be mistaken for a chondrosarcoma.

As the histological grade has an important influence on metastasis and survival in chondrosarcoma, it is important to define the grading system clearly. Three histological grades were assigned. In grade 1 (Fig. 4), grossly the lesion is generally lobular and nodular, with margins having a lobular and nodular appearance. The intercellular matrix of the tumor is generally chondroid and only rarely is there myxoid material. The cartilage cells have small, hyperchromatic nuclei that infrequently are enlarged. Because of the nuclear hyperchromasia, there is very little nuclear morphology visible. Generally the cartilage cells are present in lacunae and there also are binucleate cells. Usually grade-1 lesions are calcified, with non-neoplastic bone formation toward the perimeter of the tumor. Usually there is no necrosis.

In grade 2 (Fig. 5), grossly the tumor is generally nodular and lobular, but the margins may have permeating borders. The tumor matrix is chondroid but often there are transitional zones to myxoid material. There are more cells than in grade-1 lesions. In the center of the lobules, the cartilage cells are widely spaced but are more compact toward the periphery. The cells are pleomorphic, with larger nuclei than in grade-1 tumors. The incidence of binucleate cells increases, generally more than one cell occupies a lacuna, and mitosis is rare. As the chromatin is rather granular, nucleoli may be visible. These lesions frequently are calcified, with non-neoplastic bone formation present at the periphery. Necrosis occasionally is present, especially in larger tumors.

In grade 3 (Fig. 6), grossly the tumor is not well marginated. At the periphery of the lobules the cells appear mesenchymal, while toward the center they are more differentiated. This must not be confused with a mesenchymal chondrosarcoma, which is a distinctly different entity. Frequently the intercellular matrix is myxomatous. These tumors are hypercellular, with pleomorphic nuclei. The cartilage cells usually are not located in lacunae, although sometimes they are arranged in cord-like fascicles. The nuclei are hyperchromatic and large nucleoli sometimes are visible. Giant cartilage cells and multinucleate cells are frequent. Many mitotic figures are visible. Evans et al. stated that if more than two mitoses per ten high-power fields are seen, the tumor is most likely grade 3. Calcification and non-neoplastic bone formation are rare, but necrosis is common and extensive.

In addition to the histological grading, the tumors were classified as myxomatous or non-myxomatous, using cytological characteristics and the appearance of the intercellular matrix as criteria (Fig. 7). The matrix in myxomatous tumors stains pale blue with hematoxylin and

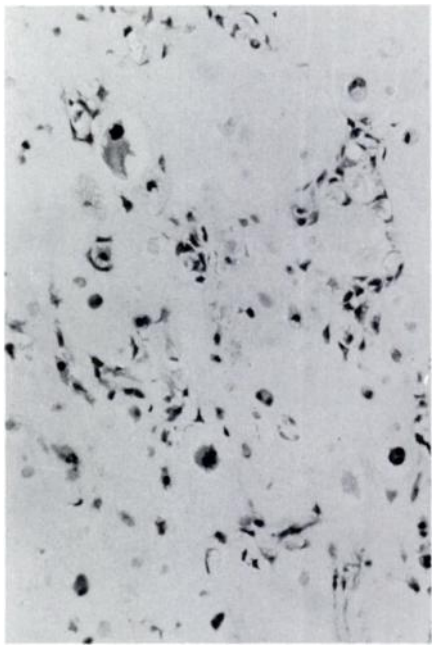

FIG. 6

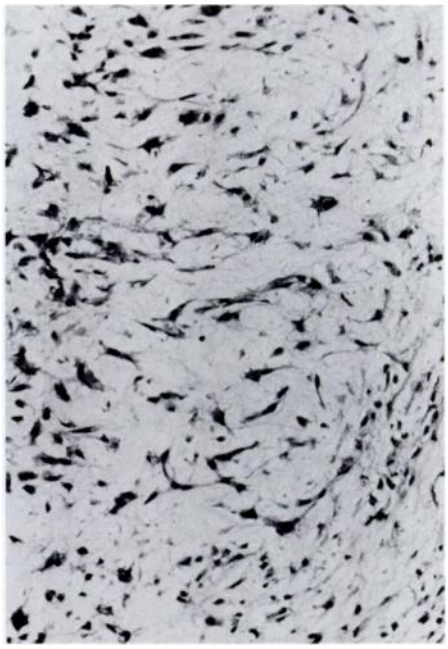

FIG. 7

Fig. 6: Histological grade 3. The cells are very large and pleomorphic, and multinucleate cells are common. The cartilage cells generally are not located in lacunae. A large amount of nuclear chromatin is visible (hematoxylin and eosin, × 250).

Fig. 7: Myxomatous chondrosarcoma, histological grade 3. The cells are stellate, with interconnecting cell processes, and the matrix has a soap-bubble appearance (hematoxylin and eosin, × 250).

eosin and has a soap-bubble type of appearance[15]. The cartilage cells are rather stellate, in a non-lacunar arrangement, with interconnecting cell processes. If the majority of the chondrosarcoma was composed of myxoid tissue, it was classified as myxomatous. The myxomatous tumors also were studied as a group to see if this property had an influence on the rate of metastasis.

In this review, statistical significance was evaluated using the chi square test.

Results

Sixty-nine of the chondrosarcomas were classified as central while fifty-six were peripheral (Table I). At times it was difficult to make this distinction radiographically, and in these cases final classification was postponed until pathological examination of the surgical specimen was possible. The mean age of the patients with peripheral chondrosarcoma was 33.0 years (range, fourteen to fifty-four years) and for those with central chondrosarcoma it was 43.9 years (range, fourteen to seventy-eight years). In this series, we considered definite proof that the chondrosarcoma was not a primary neoplasm to be either radiographic evidence of a pre-existing benign lesion or areas of benign cartilage within the chondrosarcoma. Using these strict criteria, eighteen of the chondrosarcomas were considered to be secondary neoplasms, fourteen being secondary peripheral tumors and four, secondary central tumors. Of the fourteen secondary peripheral tumors, eleven originated from multiple exostoses and three, from a solitary exostosis. All of the four secondary central neoplasms were associated with Ollier's disease. None of the central chondrosarcomas were secondary to an isolated enchondroma, which emphasizes the rarity of this occurrence[5].

Figure 1 shows the skeletal distribution of the chondrosarcomas. Ninety of the chondrosarcomas were located in a proximal limb or in the axial skeleton. Fifty-one were located in the pelvis or proximal part of the femur (thirty and twenty-one, respectively); twenty-two, in the proximal end of the humerus or the scapula; and only one, in

TABLE I

PERIPHERAL AND CENTRAL CHONDROSARCOMAS

	Peripheral	Central	Significance
Number of cases	56	69	
Mean age *(years)*	33.0	43.9	
Male patients *(per cent)*	69.6	68.1	
Axial skeletal or proximal limb site *(per cent)*	84	62	$p < 0.02$
Proved secondary lesions *(number)*	14	4	
Histological grade *(per cent)*			
Grade 1	43	13	$p < 0.001$
Grade 2	53	67	$p < 0.02$
Grade 3	4	20	
Myxoid tumors *(per cent)*	7	35	$p < 0.001$
Adequate treatment *(per cent)*	55	46	
Local recurrence *(per cent)*	38	32	
Metastasis *(per cent)*	16	38	$p < 0.02$
Survivors *(per cent)*			
5 years	89	49	$p < 0.001$
10 years*	77	32	$p < 0.001$
Disease-free at follow-up *(per cent)*	57	30	$p < 0.005$

* Based on ninety-six patients.

TABLE II

HISTOLOGICAL TUMOR GRADES

	Grade 1	Grade 2	Grade 3
Number of cases	33	76	16
Mean age *(years)*	31.1	41.2	44.7
Male patients *(per cent)*	61	74	63
Axial skeletal or proximal limb site *(per cent)*	79	68	75
Myxoid tumors *(per cent)*	9	29	19
Adequate treatment *(per cent)*	64	43	56
Local recurrence *(per cent)*	33	38	19
Metastasis *(per cent)*	9	33	44
Mean time to metastasis *(months)*	112	24.4	6.7
Survivors *(per cent)*			
5 years	94	61	44
10 years*	87	41	27
Disease-free at follow-up *(per cent)*	67	34	31

* Based on ninety-six patients.

the hand. Ten tumors were located in the spine or sacrum, the majority of these being inaccessible for adequate surgical removal.

One hundred and fourteen patients were able to recall the time of onset of their symptoms, the most common of which was pain. Some patients complained of both a mass and pain, most commonly in peripheral chondrosarcomas. In those patients who had been followed for a preexisting benign condition (osteochondroma, multiple osteochondromas, or Ollier's disease), the onset of pain usually signified the development of malignant degeneration[5,12]. The mean length of time from the onset of symptoms until diagnosis was 19.0 months. In most cases, the slowly growing tumor did not cause symptoms during its early development[12]. In this series, the patients with grade-1 and grade-2 tumors did not seek medical attention until a mean of 19.4 months had elapsed after the onset of symptoms. The patients with grade-3 tumors, however, sought medical attention after a shorter interval (mean, 15.5 months), and one patient was seen with a pathological fracture without any prior symptoms. Thirty-three (26 per cent) of the chondrosarcomas were histological grade 1, seventy-six (61 per cent) were grade 2, and sixteen (13 per cent) were grade 3. Twenty-eight (22 per cent) of the 125 chondrosarcomas were predominantly myxomatous. Three of the histological grade-1 tumors, twenty-two of the grade-2, and three of the grade-3 tumors were myxomatous (Table II). Four of the peripheral chondrosarcomas and twenty-four of the central chondrosarcomas were myxomatous ($p < 0.001$).

Treatment

Thirteen patients were treated by biopsy alone (intralesional), as the lesion was inoperable. Ten of these patients received a course of radiation therapy (4000 to 5000 rads). Ten of the thirteen inoperable lesions were central chondrosarcomas in a proximal limb or axial skeletal location, with such a large extra-osseous extension that surgical removal was impossible. Because of their location and extra-osseous extension and the lack of a pathological specimen, it was most difficult to classify these lesions as either central or peripheral chondrosarcomas.

Twenty-eight patients had a marginal excision of the tumor, fifty had a wide excision, and thirty-four had an amputation. There were ten hindquarter amputations and five forequarter amputations. The remaining ablative procedures were either amputations through the bone or joint disarticulations. All of the amputations had at least wide excision margins. In recent years a trend toward limb salvage has evolved at the Rizzoli Institute. With the common use of bone-scanning (technetium-99m methylene diphosphonate), tomography, arteriography, and more recently computerized tomography, a more accurate appraisal of the extent of the lesion can be made. With this information, procedures such as periarticular resection of the shoulder or periacetabular resection of the hip with limb salvage are posssible in some patients. Adequate surgical margins, however, still must be obtained in these more sophisticated limb-salvage procedures.

By the criteria already given, 50 per cent of the aforementioned surgical procedures were thought to be adequate and 50 per cent, inadequate (Table III). Treatment was considered to be inadequate in the thirteen inoperable lesions, in all of the twenty-eight marginal excisions (including contaminated marginal excisions), and in twenty-one contaminated wide excisions. Treatment was adequate in all of the thirty-four amputations and the twenty-nine wide excisions. In Table III we compare those patients who were treated adequately with those who were treated inadequately. More of the inadequately treated patients had lesions in a proximal limb or axial skeletal location (81 per cent compared with 63 per cent, $p = 0.05$). Eighty-six per cent of the adequately treated tumors and 89 per cent of the inadequately treated tumors were in histological grades 1 and 2; the difference was not statistically significant.

TABLE III

ADEQUATE AND INADEQUATE TREATMENT

	Adequate	Inadequate	Significance
Number of cases	63	62	
Mean age *(years)*	39.2	38.9	
Male patients *(per cent)*	68	69	
Axial skeletal or proximal limb site *(per cent)*	63	81	$p = 0.05$
Histological grade *(per cent)*			
Grade 1	33	20	
Grade 2	53	69	
Grade 3	14	11	
Local recurrence *(per cent)*	6	69	$p < 0.001$
Metastasis *(per cent)*	14	42	$p < 0.005$
Survivors *(per cent)*			
5 years	81	53	$p < 0.005$
10 years*	68	38	$p < 0.01$
Disease-free at follow-up *(per cent)*	78	6	$p < 0.001$

* Based on ninety-six patients.

Eighteen per cent of the chondrosarcomas were in radiographic grade 1; 53 per cent, grade 2; and 29 per cent, grade 3. Sixty-four per cent of the twenty-two radiographic grade-1 tumors were treated adequately, compared with 49 per cent of the sixty-six grade-2 and 46 per cent of the thirty-seven grade-3 tumors.

Results of Treatment

At the time of follow-up, fifty-three patients were tumor-free, nineteen patients were alive with a recurrence, thirty-five patients had died from metastases, twelve patients had died from uncontrolled recurrence, and six patients had died from unrelated causes.

Recurrence

Forty-three patients (34 per cent) had a local recurrence of the tumor following primary treatment. The mean length of time from primary treatment until recurrence was 26.8 months (range, two to 168 months). The incidence of recurrence in adequately treated patients was 6 per cent, while patients treated inadequately had a recurrence rate of 69 per cent (Table III). The difference was statistically significant ($p < 0.001$). The incidence of recurrence was 33 per cent in histological grade-1 lesions (at a mean of 36.8 months), 38 per cent in grade-2 lesions (at a mean of 22.9 months), and 19 per cent in grade-3 lesions (at a mean of 29.6 months) (Table II).

Metastases

Thirty-five (28 per cent) of the patients in the series had a known metastasis, thirty-one being pulmonary and four being osseous. The mean length of time from primary treatment until metastasis in these patients was 27.8 months (range, two to 264 months). Two patients with histological grade-3 lesions had a pulmonary metastasis identified two months following primary treatment. Their initial chest radiographs were negative, however, even when reviewed retrospectively. A third patient with a histological grade-3 lesion also had a metastasis identified four months after primary treatment. The patient with the latest appearance of a pulmonary metastasis (twenty-two years) had had a histological grade-1 chondrosarcoma of the sacrum that initially was treated inadequately by a contaminated marginal excision. The tumor had recurred twice within the first five years and again at fifteen years. Twenty-two years after the primary treatment a pulmonary metastasis developed, and three years later the patient died of the chondrosarcoma.

Table II compares the patients with tumors of different histological grades. The incidence of metastasis was 9 per cent in histological grade-1 tumors (at a mean of 112 months after treatment), 33 per cent in histological grade-2 tumors, (at a mean of 24.4 months), and 44 per cent in histological grade-3 tumors (at a mean of 6.7 months). The difference in the metastatic rate between grade-1 lesions and the grade-2 and 3 lesions was statistically significant ($p < 0.001$).

Twenty-eight of the chondrosarcomas were myxomatous. There was a 36 per cent incidence of metastasis in patients with myxomatous chondrosarcoma and a 26 per cent incidence in those with non-myxomatous tumors. This difference was not statistically significant.

Survival Rates

The over-all five-year survival rate was 67 per cent and the ten-year survival rate was 50 per cent. Patients with peripheral chondrosarcoma, as a group, had better survival statistics than did those with central chondrosarcoma (Table I). In fact, the five-year survival rate for the patients with peripheral chondrosarcoma was 89 per cent, while only 49 per cent of the patients with a central chondrosarcoma survived for five years ($p < 0.001$). The ten-year survival rates for these two groups were 77 per cent and 32 per cent, respectively ($p < 0.001$). In Table I we compare the peripheral and central chondrosarcomas. Only 4 per cent of the peripheral chondrosarcomas were histological grade 3, while 20 per cent of the central chondrosarcomas were grade 3. The converse was also true, in that 43 per cent of the peripheral chondrosarcomas were grade 1 while only 13 per cent of the central lesions were grade 1.

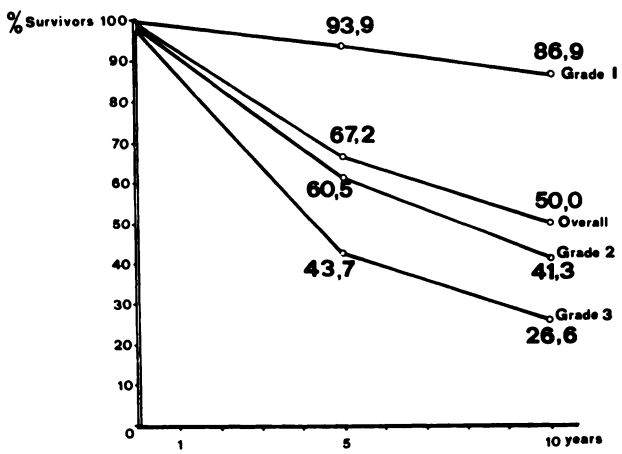

FIG. 8

Survival and histological grade.

The five-year survival rate for patients with histological grade-1 lesions was 94 per cent; for those with grade-2 lesions, 61 per cent; and for those with grade-3 lesions, 44 per cent. The ten-year survival rates diminished somewhat, being 87 per cent in grade-1, 41 per cent in grade-2, and 27 per cent in grade-3 lesions (Table II). The difference in both five and ten-year survival rates between histological grade-1 lesions and grade-2 and 3 lesions was statistically significant ($p < 0.001$) (Fig. 8).

Adequately treated patients had both a lower recurrence rate and better survival statistics (Table III). The five-year survival rate for adequately treated patients was 81 per cent, but decreased to 53 per cent in inadequately treated patients ($p < 0.005$). The figures at ten years were

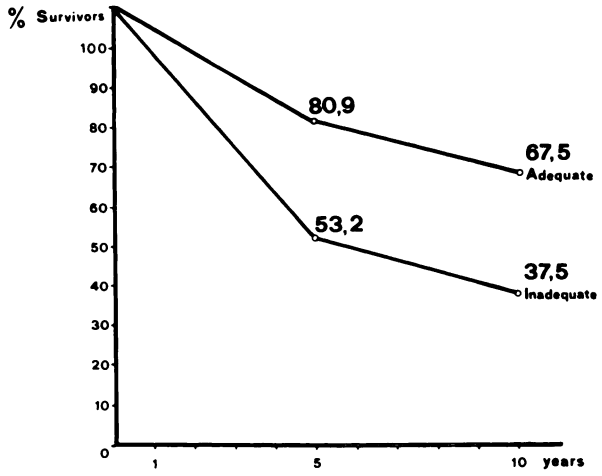

FIG. 9

Survival and adequacy of treatment.

68 per cent and 38 per cent, respectively ($p < 0.01$) (Fig. 9).

At the time of follow-up, fifty-three (43 per cent) of the patients were tumor-free at a mean of 11.1 years (range, five to thirty-eight years) after primary treatment. Ninety-two per cent of these patients were considered to have received adequate treatment. Seventy-eight per cent of the patients who were adequately treated were disease-free at follow-up, compared with 6 per cent of the patients who had received inadequate treatment ($p < 0.001$).

Discussion

In the present series, there were fifty-six peripheral chondrosarcomas and sixty-nine central chondrosarcomas. Fourteen of the peripheral chondrosarcomas were proved to be secondary lesions by rather strict criteria (radiographic evidence of a pre-existing benign lesion or benign cartilage within the chondrosarcoma), and probably more of the remaining lesions were secondary but this was unproved by our criteria. In some of the latter patients, the radiograph at the time when they were seen with a chondrosarcoma revealed what appeared to be remnants of a benign exostosis in the vicinity of the chondrosarcoma. These remnants consisted of the flared base of the previous exostosis, communicating with the medullary canal of the involved bone. Since this proof was suggestive but not conclusive, we did not classify these lesions as secondary.

In Table I we compare the central and peripheral chondrosarcomas. As the data indicate, these two tumors were found to be distinctly different. The patients with a peripheral chondrosarcoma tended to be younger than those with a central tumor, probably because more of the peripheral tumors were secondary[5]. The peripheral chondrosarcomas also had a greater predilection for a proximal limb or axial skeletal location. The central chondrosarcomas tended to be of a higher histological grade. The majority of the myxoid tumors were central lesions. Probably due to these differences in histological characteristics, the patients with peripheral chondrosarcoma had far superior survival statistics and a lower incidence of metastasis. There was no statistical difference between the percentages of adequately treated peripheral tumors and adequately treated central tumors to help to explain this difference in survival. There was a similar incidence of local recurrence for the two groups, probably due to the fact that the two groups had a similar percentage of adequately treated patients. This also shows that the adequacy of treatment has a greater influence on the incidence of local recurrence than does the histological tumor grade.

At the present time, surgery remains the only effective means of treating chondrosarcoma of bone. When the surgery is adequate, not only is the incidence of recurrence less but survival and disease-free survival are improved[7,10-12,16,17]. We have defined adequate treatment in terms of surgical margins[8,18]. Using very rigid requirements of adequacy, only 6 per cent of our adequately treated patients had a local recurrence, compared with 69 per cent of the patients who were inadequately treated ($p < 0.001$). Others have reported significantly higher recurrence rates for adequately treated patients[10,17]. Since adequacy of treatment was not defined in terms of surgical margins in those series, perhaps patients treated by marginal excision were included in the adequate-treatment group. Enneking et al. thought that the plane of dissection in a marginal excision permits residual islands or pseudopods of tumor to be left in the tumor bed. In this series, we considered all marginal excisions of chondrosarcoma to be inadequate procedures. However, at least some of these marginal excisions must have been adequate inadvertently, as our incidence of recurrence (69 per cent) for inadequately treated patients was lower than that reported in the literature. In fact, both Sanerkin and Gallagher and Evans et al. reported a much higher incidence of local recurrence (87 per cent and 93 per cent, respectively) for inadequately treated patients than was seen in our series. Although marginal excision may be adequate in some tumors, the results are unpredictable and wide excision margins or more must be the surgical goal for chondrosarcoma.

Like Sanerkin and Gallagher, we found no significant relationship between the histological tumor grade and the incidence of local recurrence. Although our patients with grade-3 tumors had a lower local recurrence rate than did those with grade-2 tumors (Table II), those with grade-3 tumors also had a higher incidence of adequate treatment than the patients with grade-2 lesions. Thus, it appears that adequacy of treatment was the major influence on the incidence of local recurrence, and not the histological grade of the tumor.

The patients with radiographic grade-1 lesions had the highest percentage of adequate treatment. It is notable that ten of the thirteen inoperable lesions were radiographic grade 2 or 3. The tumor site also plays a major role in determining whether adequate surgery can be performed. Eighty-one per cent of the inadequately treated tumors were in a proximal limb or axial skeletal location,

compared with 63 per cent of the adequately treated tumors ($p = 0.05$). Axial skeletal and proximal limb locations tend to be the most difficult areas in which to obtain adequate surgical margins because of vital neurovascular or visceral structures, or both. Also, because of their association with lesions that extend into the axilla or groin and are not contained within muscle compartments (extracompartmental), it is impossible to obtain wide excision margins in these areas without performing high-level amputation.

Using both gross and histological criteria, 26 per cent of the chondrosarcomas in the present series were considered to be histological grade-1 lesions; 61 per cent, grade-2; and 13 per cent, grade-3 lesions (Table II). Others have reported a higher incidence of grade-1 lesions[7,10,17]. Grade-1 lesions tend to be the most difficult ones to classify, even for pathologists with considerable experience in the grading of chondrosarcoma. Grade-3 lesions, however, are more obvious, which probably explains the relative consistency in their reported incidence in various series[7,10,17]. Twenty-two per cent of the tumors in our series were predominantly myxomatous (Table II). Mankin et al. have reported on biochemical studies of four myxoid tumors[14,15]. While this tumor was uncommon in their series, they concluded that myxoid chondrosarcomas have a greater tendency for recurrence and metastasis. In our series, the myxomatous tumors did have a metastatic rate higher than that of the non-myxomatous tumors (36 per cent compared with 26 per cent), but the difference was not statistically significant.

The incidence of metastasis (28 per cent) in our series was somewhat higher than in other reviews[7,10-12,17] Perhaps this is due to the fact that our tumors tended to be of a higher histological grade than those in other reported series. The incidence of metastasis and rate of occurrence clearly are related to the histological grade of the tumor. While our grade-2 and 3 tumors had similar metastatic rates, the metastases of grade-3 tumors occurred much sooner (6.7 months compared with 24.4 months) (Table II). Only 9 per cent of the histological grade-1 lesions metastasized. Delayed metastasis is not uncommon in chondrosarcoma. Sanerkin and Gallagher reported one patient with a metastasis at fifteen years (after dedifferentiating) and others that occurred between three and eight years. None of the patients in our series survived once metastases developed, although a patient has been reported to have survived for two years after a thoracotomy for removal of a metastasis[17].

The over-all survival rate in our series was higher than that reported by Henderson and Dahlin but lower than other, more recent reports[10,17]. The histological tumor grade had a significant influence on survival. Our 94 per cent five-year survival rate for patients with grade-1 tumors is comparable to that in other reports[10,17]. The survival rate in our patients with higher-grade tumors also is comparable to that in the series already mentioned[10,17].

Adequately treated patients had higher survival rates than inadequately treated patients. Our five-year survival rate of 81 per cent for adequately treated patients is exceeded only by that reported by Evans et al. At the last follow-up, 78 per cent of our patients who were treated adequately were completely disease-free, while only 6 per cent of our inadequately treated patients were without evidence of disease ($p < 0.001$) (Table III). Nineteen of our patients were alive but with a recurrence at follow-up. While these patients qualify as survivors, at least some of them probably will have delayed metastases or will die of uncontrolled local disease. This probably will make the difference in the survival statistics between adequately and inadequately treated patients even greater in the future.

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Ligamentous and Capsular Restraints Preventing Straight Medial and Lateral Laxity in Intact Human Cadaver Knees*†

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ABSTRACT: **In this study, we determined which ligaments and capsular structures resist medial and lateral opening of the joint space in cadaver knees during clinical testing for straight medial and lateral laxity. Restraining function was recorded as the per cent contribution of each structure in resisting the force applied by the examiner. In sixteen cadaver knees tested at 5 and 25 degrees of flexion from full hyperextension, the collateral ligaments provided the primary restraint (greater than one-half of the total) at both flexion angles. At 5 degrees, the posterior part of the capsule and the cruciate ligaments were important secondary restraints. As flexion increased, the posterior part of the capsule became slack, causing a marked decrease in its restraining action. The middle one-third of the medial and lateral halves of the capsule, traditionally considered important, provided little restraining force. The iliotibial tract and the popliteus musculotendinous unit provided little passive restraint. However, a force applied to either the iliotibial band or the biceps tendon, to simulate muscle tension, produced an additional restraint that *in vivo* presumably would protect the lateral ligaments and capsule.**

Using an instrumented kinematic chain to determine the three-dimensional joint motion in six knees during testing for straight varus-valgus laxity by the maneuvers used clinically, we found that axial rotation of the tibia occurred that may be misinterpreted as medial or lateral joint opening. When just the medial or the lateral collateral ligament (the primary restraints) was sectioned, only a three to five-millimeter increase in joint opening occurred. This increase was small because only low forces were applied during the clinical examination and the secondary restraints blocked further opening even though the primary restraint was disrupted. Near full extension, the secondary restraints almost completely blocked opening of the joint after sectioning of the collateral ligaments.

CLINICAL RELEVANCE: **With knowledge of the hierarchy of restraining moments contributed by the medial and lateral ligament and capsular structures and an appreciation of the rotatory movements of the knee that may occur during tests for straight varus-valgus laxity, both diagnosis and treatment can be more precise.**

In the past, most assessments of ligament function have been based on the changes in laxity observed after cutting selected ligaments[3,11,18,32] or else on the injury patterns associated with observed clinical laxities[1,8,13,14,16,20,24,25,28]. As a result, confusion and disagreement persist as to the ligament injuries associated with specific laxities. Often in clinical practice the ligaments that may be involved are just listed. Accurate diagnosis and optimum treatment require that the function of the ligaments in resisting joint opening be understood and ranked in order of importance.

Recently we described a new method for determining the restraining force provided by each ligament and capsular structure[5,6,9]. This method allows the ligaments to be ranked in order of importance based on the per cent of the total restraining force that each provides. In addition, the method yields results that are independent of the order in which the ligaments are cut, and therefore all ligaments can be studied in each knee.

The purpose of this report is to describe how we applied this method to the measurement of the passive restraints to straight medial and lateral opening of human

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