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Does Curettage without Adjuvant Therapy Provide Low Recurrence Rates in Giant-Cell Tumors of Bone?

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Adjuvant treatment or filling agents have been recommended for reducing recurrence rates of giant-cell tumors of bone. However, reports of low recurrence rates without either caused us to question this concept. We retrospectively reviewed 193 patients treated during a 27-year period, comparing our results with historic controls. One hundred thirty-seven patients had curettage as a primary treatment, and of these, 26 (19%) had local recurrences. The local recurrence rate of giant-cell tumors confined to bone (Campanacci Grades I and II) was only 7% compared with 29% in tumors with extraosseous extension (Campanacci Grade III). Six patients (4%) had a fracture after curettage. Twenty-nine patients who were referred to us with local recurrences after treatment elsewhere had curettage, and 10 (34%) of these patients had local recurrences develop. Twenty-seven patients had excision as their primary treatment, and two (7%) of these patients had local recurrence develop. We recommend primary curettage for intraosseous giant-cell tumors without adjuvant treatment or filling agents, but tumors with soft tissue extension or with local recurrence require more aggressive treatment.

Level of Evidence: Therapeutic study, Level IV (case series—no, or historical control group). See the Guidelines for Authors for a complete description of levels of evidence.

Although most giant-cell tumors (GCT) of bone are considered benign, they can behave like malignant tumors and metastasize. However, it is their unpredictable tendency to recur locally that makes initial treatment challenging to the orthopaedic oncologist.

Recurrence rates can be low with wide local or radical excision. However, with this type of surgery the patient can have considerable functional loss, and therefore, many surgeons do curettage as a primary method of treatment. When treated this way, the reported recurrence rates in published series range from 0–47% (Table 1). It is debatable whether adjuvant therapies, such as phenol or cement, decrease recurrence rates. Capanna et al[8] reported a recurrence rate of 45% in 280 patients who had curettage alone compared with 18% in 387 patients who also had adjuvant treatment. Gitelis et al[16] reported a recurrence rate of just 5% in 20 patients, and Bini et al[3] reported an 8% recurrence rate in 38 patients when cement was used as an adjuvant. However, there also are reported rates of low recurrence when curettage was done alone with no adjuvant therapy; Blackley et al[4] reported 12% recurrence in 59 patients, and Richardson and Dickinson[24] reported 0% recurrence in 16 patients.

After curettage, filling the cavity with bone graft or cement is a common treatment to provide structural support and prevent collapse.[3,4,15,16,23,24,26] We think that this is unnecessary as the empty cavity gradually fills with new bone that consolidates with time (Figs 1–4), and we know of no study showing that healing in these lesions is any faster when bone graft is used.

Given the controversial evidence provided in the literature and our experience, we questioned whether recurrence rates after curettage would be low without the use of adjuvant therapy, therefore suggesting filling agents are not required.

MATERIALS AND METHODS

We retrospectively reviewed the records of 193 patients treated at our institution between 1970 and 1997. All patients who had a diagnosis of GCT of bone were identified using our bone tumor

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TABLE 1. Reported Rates of Recurrence after Primary Curettage

Authors	Year	Number	Additional Treatments	Recurrence
Turcotte et al[28]	2002	120	None; cement; phenol liquid nitrogen	12%
Ward and Li[29]	2002	24	H_2O_2; phenol; electrocautery; cement	8%
Ghert et al[15]	2002	47	Cement + phenol or electrocautery	13%
Blackley et al[4]	1999	59	Bone graft	12%
Saglik et al[26]	1999	21	Bone graft;	33%
		6	cement	0
Richardson and Dickinson[24]	1998	16	Bone graft	0
Masui et al[20]	1998	17	None	47%
Bini et al[3]	1995	38	Cement	8%
O'Donnell et al[23]	1994	49	Cement;	24%
		11	cement + phenol	27%
Gitelis et al[16]	1993	20	Cement	5%
Capanna et al[8]	1990	280	None;	45%
		187	cement;	19%
		147	phenol;	19%
		20	nitrogen;	19%
		33	cement + phenol	3%
Campanacci et al[6]	1987	106	None;	34%
		16	phenol;	13%
		6	nitrogen;	0
		2	cement	0
McDonald et al[21]	1986	85	80/85 phenol	34%
Sung et al[27]	1982	34	Bone graft	41%

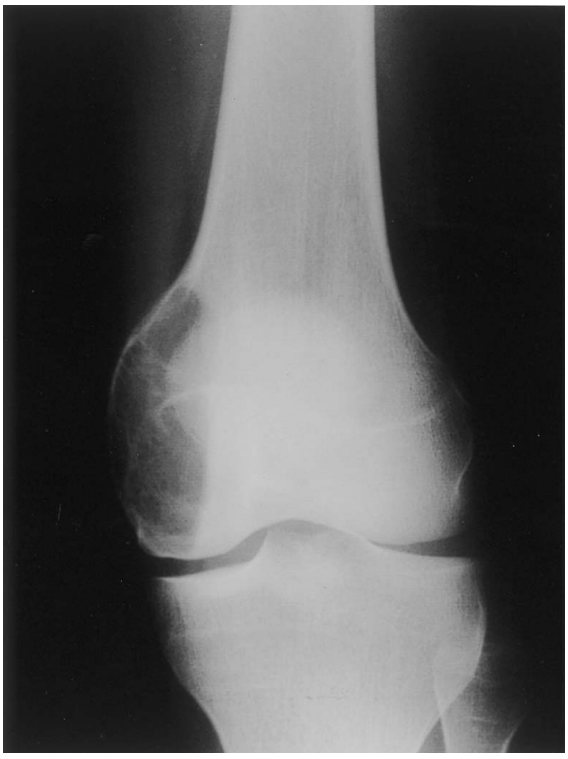

Fig 1. This radiograph shows a giant cell tumor of the distal femur.

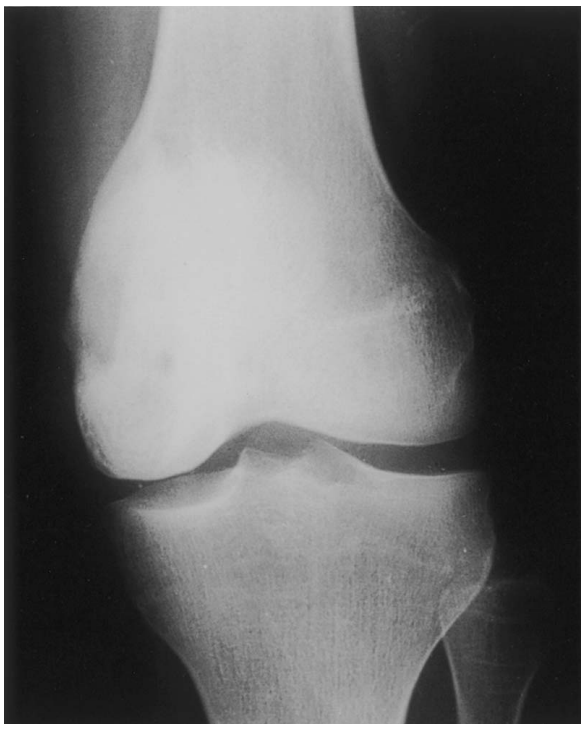

Fig 2. Consolidation of the cavity after curettage of the GCT that is shown in Figure 1, without any adjuvant treatment or filling agents is shown in this radiograph.

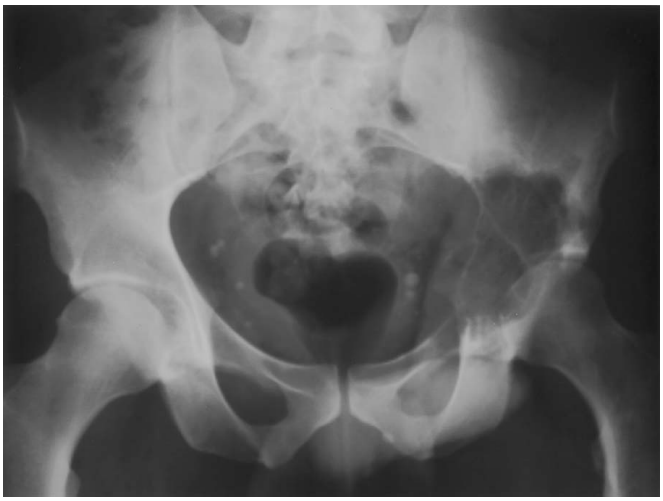

Fig 3. This radiograph shows a giant cell tumor of the pelvis.

database. Patients were included if the histologic diagnosis of GCT was confirmed, the definitive surgery was done at our unit, and there was a minimum followup of 2 years after surgery. We reviewed the complete medical records, radiographs, and computed tomography (CT) and magnetic resonance imaging (MRI) scans (when available).

Twenty-seven patients had excision of GCT, either as the primary treatment or after referral to our unit with local recurrence after treatment elsewhere. Our relative indications for excision rather than curettage included intraarticular fractures, joint invasion, unstable fracture pattern, large soft tissue extension, expendable bone (head of fibula), and multiple recurrences.

The remaining 166 patients were divided into two groups: Group 1 included 137 patients who had curettage as their primary surgery at our unit; Group 2 included 29 patients who were referred to our unit with recurrence, after treatment elsewhere, and had curettage.

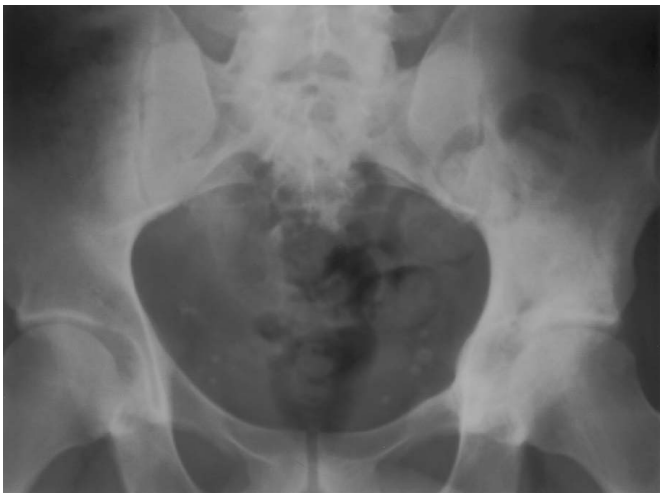

Fig 4. The consolidation of the cavity after curettage of the GCT that is shown in Figure 3, without any adjuvant treatment or filling agents is shown in this radiograph.

The GCTs were graded radiologically using the grading system described by Campanacci et al.[6] A Grade I tumor has well-marginated borders, with the cortex being slightly thinned but intact and not expanded. A Grade II tumor has well-defined margins, the cortex being very thin and expanded but intact. A Grade III tumor has fuzzy borders, the cortex being obliterated with evidence of soft tissue extension. The diameter, the volume, and the distance from the articular surface were measured using CT and MRI scans. The volume was calculated using the formula for a sphere: 0.52 × length × breadth × height. The percentage of bone occupied by tumor was calculated as the proportion of the cross-sectional area of the bone at the widest dimension of the tumor. Local recurrence was diagnosed clinically, radiologically, and pathologically.

Curettage was done through a large cortical window (> 50% tumor length) using a series of curettes of different size and shape to remove all visible tumor. The cavity then was burred with a high-speed burr, washed, and brushed until all abnormal bone was removed and only normal bone was visible. Throughout the procedure a dental mirror was used to see obscured areas of the cavity. More recently, a high-speed pulse lavage system has been used to wash out the cavity. We did not use any adjuvant therapy, and the cavity was left empty. Any soft tissue extension was excised. Postoperatively, the patient remained nonweightbearing for as few as 6 weeks, and regular radiographs were taken to confirm consolidation of the cavity (Figs 2, 4). If there was an associated fracture, this was stabilized with osteosynthesis and the limb was immobilized in a cast. The patients were examined regularly in our clinic with radiographs taken every 3 months for 2 years, and then every 6 months for 5 years.

There were two observers of the clinical and radiologic data. Neither was the operating surgeon. Function was assessed according to the scoring system of the Musculoskeletal Tumor Society.[12]

Statistical significance of the factors influencing recurrence was determined using unpaired t tests, chi square tests, and Fisher's exact tests. A p value < 0.05 was considered significant.

RESULTS

The majority (137 of 193 patients, or 71%) of the patients had primary curettage (Fig 5). Giant-cell tumors occurred most commonly during the third decade in the 193 patients (Fig 6). The most common site was about the knee, with 53.9% occurring in that location (Fig 7).

The mean followup for 137 patients who had primary curettage at our institution was 70.3 months (range, 24–214 months). There were 78 males and 59 females with a mean age of 33.1 years. Initial radiographs were available for 113 patients. The Campanacci grades were I in 14 patients, II in 47 patients, and III in 52 patients. The mean volume of tumors was 95 cm^3, and the mean proportion of bone occupied by the tumor was 82%. Twenty-nine pa-

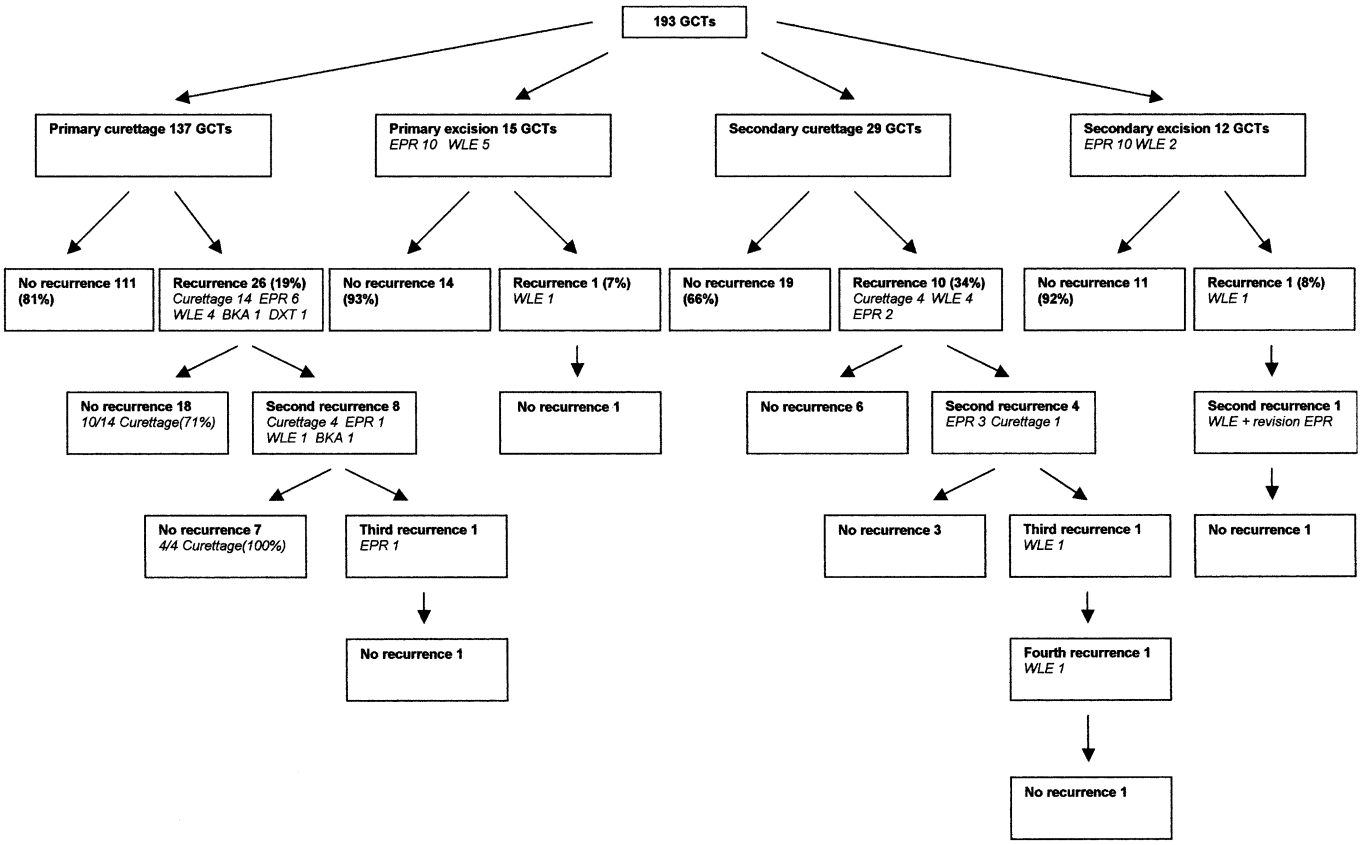

Fig 5. This flowchart summarizes the results of treatment of all 193 patients with giant cell tumors in this series. WLE = wide local excision; EPR = endoprosthesis; BKA = below-knee amputation; DXT = radiotherapy

tients (21.2%) presented with pathologic fractures, four of whom had internal fixation of the fractures. The remaining 25 patients had the fractures treated nonoperatively.

For the 137 patients who had curettage alone, the overall rate of local recurrence was 19%. This rate varied with Campanacci grade, being only 7% in patients with intraosseous tumors (Grades I and II), but 29% in patients with tumors with extraosseous extension (Grade III) (Table 2). We identified no other significant factor for local recurrence. Eighty percent of local recurrences occurred within 24 months, but the longest took 7 years to develop (Fig 8). Of the 26 patients with local recurrences, 21 had recurrences develop in bone, three had recurrences develop in soft tissue, and two had recurrences develop in bone and soft tissue. Eighteen patients had one local recurrence, seven patients had two local recurrences, and one patient had three local recurrences. Treatment of the first local recurrence was curettage or excision in 18 patients and wide excision and reconstruction with an endoprosthesis in six patients. The success rate of the second curettage was 10 of 14 (79%). The four patients with additional local recurrences had a third curettage and none had an additional recurrence. Therefore, 125 (91%) of 137 patients were treated successfully treated by curettage alone (111 patients after one curettage, 10 patients after two curettages, and four patients after three curettages). Eight patients had wide excision of the recurrence with insertion of an endoprosthesis, and two patients, neither of whom had attended regular followups, had amputation for massive local recurrence.

Seven of the 166 (4.2%) patients who had either primary or secondary curettage had fractures develop at a mean of 4.7 months. Six of these patients had internal fixation, and all seven fractures healed.

One patient with a distal femoral GCT and two local recurrences subsequently had lung metastases develop that were excised 38 months and 44 months after initial curettage. The patient remains free from disease 13 years after first being treated.

Fifteen patients had excision as their primary treatment because of the location or the extent of the local disease (Fig 5). Five GCTs of the fibula head had excision alone,

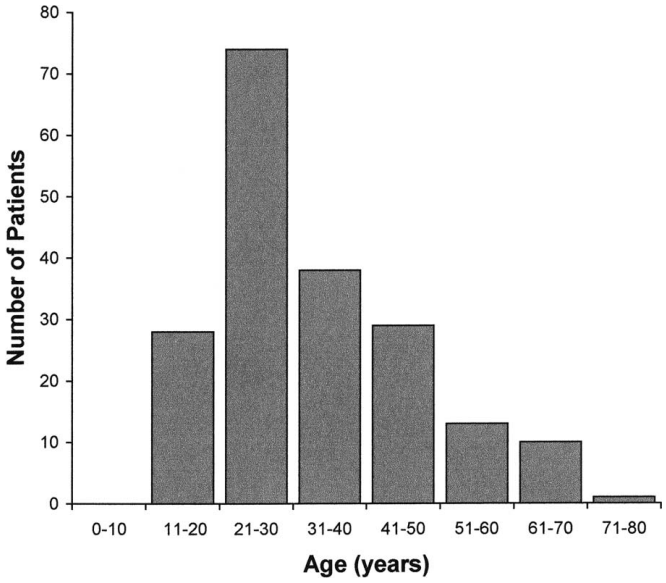

Fig 6. The age distribution of the 193 patients with GCT is shown in this histogram.

and 10 tumors at other sites had resection and endoprosthetic replacement. There was only one local recurrence in this group.

Forty-one patients were referred to our institution with recurrence of GCT after treatment elsewhere (Fig 5). The initial treatment was curettage alone in 10 patients, curettage and bone grafting in 27 patients, and excision in four patients. Twenty-nine of these patients had curettage and 10 patients (34.5%) had local recurrences develop at a mean of 20 months. The remaining 12 patients had wide excision of the GCT, with insertion of an endoprosthesis in 10. One of these 12 patients had local recurrence.

The Enneking functional score[12] was documented in 112 of the 137 patients who had primary curettage at a mean of 55 months followup, with a mean score of 28.6/30 (95.3%) in the lower limb and 27.5/30 (91.7%) in the upper limb. The functional score was documented in all 15 patients who had primary excision at a mean of 122 months followup, with a mean score of 26/30 (86.7%) in the lower limb and 24.5/30 (81.7%) in the upper limb. The functional scores were similar in the curettage group and primary excision groups.

DISCUSSION

Although curettage with the use of adjuvant therapies and filling agents is a popular treatment, we do not think that the case for these has been proven. Our overall recurrence rate of 19% after curettage only is one of the lowest in a large reported series (Table 1). Some series with apparently very low recurrence rates included few patients with Campanacci Grade III tumors, such as that of Gitelis et al[16] (5%) and Bini et al[3] (18%). In our series, the recurrence rate for patients with Grades I and II tumors is 7%, and therefore, any series with a predominance of patients with low-grade tumors might be expected to have good results with any treatment, with or without adjuvant therapies. We agree with others that it is the efficacy of the initial curettage that is the most important factor, regardless of the adjuvant therapy used.[4,24,28] Turcotte et al[28] reported a series of 148 patients who had curettage and could not identify a significant statistical effect on local recurrence by any adjuvant therapy, including phenol, nitrogen, and cement.

The current study is a retrospective review of material from one institution and might be limited by referral bias. It also is limited by the single protocol with no attempt to randomize cases. Patients with extensive disease were treated more aggressively with resection and endoprosthe-

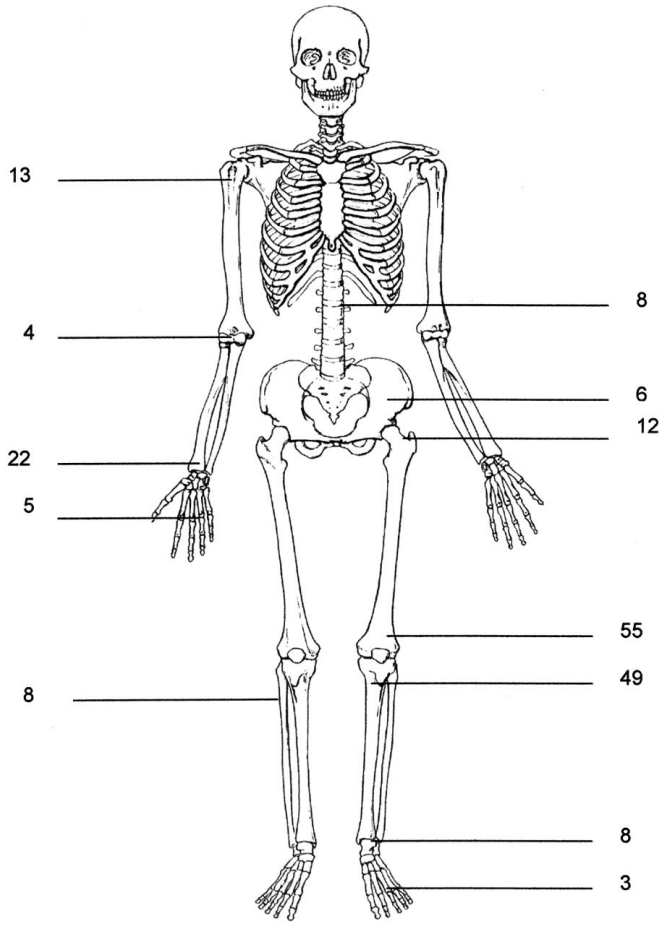

Fig 7. The anatomic sites of the 193 giant cell tumors are shown in this diagram.

TABLE 2. Factors Analyzed for Risk of Recurrence after Primary Curettage

Factor	Recurrence	No Recurrence	Significance
Grade I	1 (7.7%)	13	
Grade II	3 (6.8%)	44	
Grade III	15 (28.8%)	37	p = 0.001
Male	14 (18.7%)	64	
Female	12 (20.3%)	47	p = 0.724
Mean age (years)	32.9	33.1	p = 0.532
Fracture	4 (13.8%)	25	
No fracture	22 (20.4%)	86	p = 0.423
Mean anteroposterior diameter	82.2%	82.4%	p = 0.966
Mean mediolateral diameter	91.5%	84.6%	p = 0.093
Mean volume	142.6 cm^3	166.1 cm^3	p = 0.751
< 1 mm to articular surface	4 (17.4%)	19	
1–5 mm to articular surface	11 (13.9%)	68	
> 5 mm to articular surface	0	4	p = 0.650

sis while those with smaller tumors had curettage. There is no control group, and it is only possible to compare our results with results of other published series. However, it is a relatively large series, with results consistent with those reported in the literature.

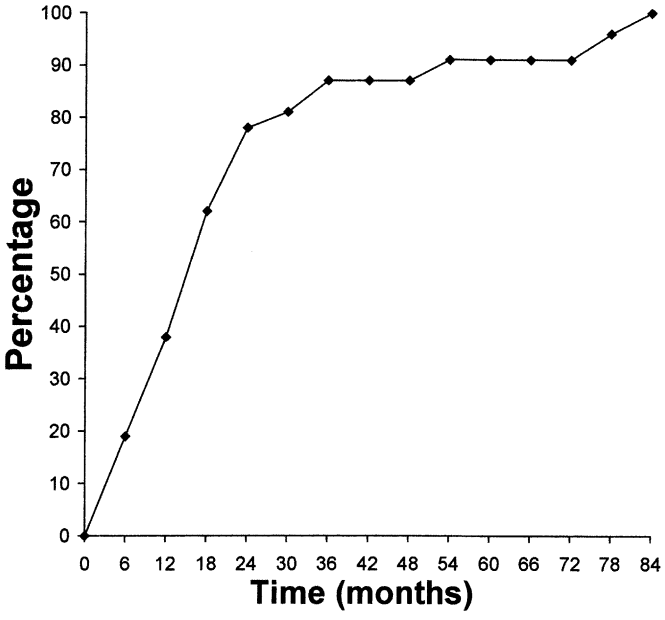

Fig 8. This graph shows the time taken for a recurrence to develop after curettage in 26 patients, expressed as a percentage of the total number of recurrences.

As with other authors, we found the recurrence rate did not correlate with age, gender, tumor size, site, or distance from the articular surface.[21,23,25] The factors reported to influence recurrence rates are the width of the surgical window[8] and adequacy of the surgical margin.[20,21,25] In a large series, Capanna et al[8] reported a recurrence rate of 48% when a small window was used (less than 50% tumor length), and this was reduced to 26% when a large window was used (greater than 50% tumor length). Richardson and Dickinson[24] advocated completely deroofing the tumor and reported no recurrences in 16 patients who had curettage without adjuvant treatment, although these were all Grade I or Grade II tumors. In our series, using a large cortical window, the recurrence rate for Grade I and Grade II tumors was 7%.

We assessed the risk of local recurrences in patients at a minimum followup of 2 years, although not all local recurrences will have become apparent by that time. In our series, 80% of recurrences developed within 2 years, and there were no local recurrences after 7 years.

We found that the risk of recurrence was greater in patients who had intralesional excision (19%) compared with patients who had wide local or radical excision (7%), which was similar to findings by others.[20,21,25] However, Gitelis et al[16] reported that patients who had wide local or radical excision with or without insertion of an endoprosthesis have poorer function and a higher rate of complications than patients who had an intralesional excision. They reported a major complication rate of 33% and a mean functional score of 23/30 (76.7%) in patients who had en bloc excisions, compared with a major complication rate of 10% and a mean functional score of 29/30 (96.7%) in patients who had intralesional excisions. In our series, the deep infection rates were 3% in patients who had curettage and 11% in patients who had excision. The mean functional scores were similar after curettage and primary excision although there were few patients in the excision group.

Cement has been used to provide structural support and to kill residual tumor cells by thermonecrosis, but the value of this has not been proven. Methylmethacrylate monomer has been reported to be highly toxic.[14] It also has been shown to cause thermonecrosis of surrounding cancellous bone[22] and of chondrocytes in subchondral bone.[30] In addition, cement has been shown in a canine model to change the stiffness and shape of the material supporting the articular surface causing degenerative change.[13] Campanacci et al[7] reported a 10-fold increase in joint degeneration if cement was used as a filling agent compared with bone graft. Liquid nitrogen has been used as an adjuvant to curettage, but it can cause osteonecrosis (the depth of which is difficult to control), skin necrosis, pathologic fractures, and degenerative changes in the long

term.[19] Phenol is readily absorbed through the skin, causing local necrosis and systemic toxicity.[2] A recent report regarding the use of zinc chloride is interesting, but again, this has not been tested in a randomized setting.[31]

Others have filled the defect after curettage with bone grafts, autograft, or allograft.[1,4,26,27] Only six patients (3.6%) in our study required additional surgery for fractures after curettage without filling the cavity. It is possible that these fractures could have been prevented if bone grafts had been used, but bone grafts have possible complications such as donor site morbidity, infection, and graft failure. Bone grafts are not initially load-sharing, and we know of no study showing that healing in these lesions is any faster when bone grafts are used. Gitelis et al reported that it is more difficult to see recurrences when a bone graft has been used.[16] We observed that the empty cavity gradually fills with new bone and that this cavity consolidates with time (Figs 1–4). We think that filling agents are unnecessary after curettage, although a randomized controlled trial is needed to support this opinion.

Although Jaffe et al[18] graded these tumors histologically, no correlation has been found between the aggressiveness of the tumor and the histologic grade.[10,17,27] As a result, histologic grading as a predictor of recurrence has been abandoned. Campanacci et al[6] graded these tumors radiologically as Grades I, II, and III. They found no correlation between the risk of recurrence and the radiographic grading of the tumor. However, in our series there was a significantly greater risk of recurrence of Grade III tumors as reported by others.[23,25] The original grading system of Campanacci et al was based only on plain radiographs; therefore, we think it sometimes is difficult to distinguish between a Grade II and a Grade III tumor. Computed tomography or MRI scans are helpful in grading these tumors.

It has been reported that 2–21% of patients will present with a pathologic fracture.[3,6,23,27] The incidence in our series was 22.4%. Although O'Donnell et al[23] reported a high incidence of local recurrence in patients who presented with pathologic fractures, we agree with others that the presence of a fracture does not lead to an increase in the recurrence rate.[11,21,25,28] Of the 34 patients with a fracture, 29 were treated by curettage (four required additional stabilization with osteosynthesis) and five patients had excision. There were five recurrences in four patients. One patient had a nonunion develop that required bone grafting. The remaining fractures healed without problems. Therefore, we agree with Dreinhofer et al[11] that patients who present with pathologic fractures can be treated adequately by curettage without significant complications.

Our results of repeat curettage after local recurrence of GCT show a success rate of 100% in patients who previously had curettage and 79.3% in patients referred from elsewhere. Unless the size of the recurrence or the degree of soft tissue involvement precludes it, recurrence can be treated with curettage with a reasonable chance of success.

Pulmonary metastases are rare in patients with GCT, but it was reported that approximately 2% of these tumors will metastasize (1.6% in our series).[5,9] Locally aggressive disease and multiple recurrences are thought to be risk factors for the development of pulmonary metastasis. Histologic features of the pulmonary metastases seem to be identical to the primary bone lesion.[9] In our series, all three patients who had metastases had previous local recurrences. They all responded to additional excision of the metastases.

Giant-cell tumor of bone is difficult to treat. Detailed and extensive curettage, without adjuvant therapies or filling agents, is effective for Grade I and Grade II lesions. The optimum treatment for Grade III lesions and patients with local recurrence is unclear, and a multinational, randomized, controlled trial to resolve this issue is needed.

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