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RESEARCH ARTICLE

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Curettage and cryosurgery for enchondroma and atypical cartilaginous tumors of the long bones: Oncological results of a large series

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Abstract

Background and Objectives: Intralesional surgical treatment is the preferred therapy for atypical cartilaginous tumors (ACTs) of the long bones in many institutions. However, the literature is still controversial regarding intralesional treatment versus wide resection. Due to the relative rarity of these tumors, studies reporting on the results of intralesional treatment are often small sample studies.

Methods: We retrospectively analyzed the oncological results of 55 enchondromas, 119 ACTs, and 5 chondrosarcomas grade 2 (CS2) treated with curettage and cryosurgery between the years 2004 and 2017 at our institution. The median follow-up period was 53 months (range, 24–169 months).

Results: In total, seven cases (three ACT, four CS2) recurred. Residual tumor was detected in 20 cases. Three cases underwent secondary curettage and cryosurgery due to local recurrence. Four cases underwent wide resection and reconstruction due to local recurrence with aggressive imaging characteristics. In total, 20 postoperative complications were seen.

Conclusion: Curettage and cryosurgery for enchondroma and ACT show very good oncological results with a low recurrence rate and acceptable complication rate. Curettage and cryosurgery is reliable as a surgical treatment for enchondroma and ACT. Further research should define the criteria for determining which specific cartilaginous tumors necessitate surgical treatment.

KEYWORDS

chondrosarcoma, complication, cryosurgery, intralesional curettage, local recurrence

1 | INTRODUCTION

The incidence of cartilaginous tumors located centrally in the long bones increased enormously during the last decade. In the Netherlands, the incidence of chondrosarcoma was 2.88 per million citizens in 1989–1996 compared with 8.78 per million citizens in 2005–2013.[1] This might be explained by the simultaneous increased use of magnetic resonance imaging (MRI) and as a resultant rise in incidental findings.[1–3]

Cartilaginous tumors of the central bone are classified as either benign (enchondroma), locally aggressive (atypical cartilaginous tumor/chondrosarcoma grade 1), intermediate grade malignant (chondrosarcoma grade 2) or high grade malignant (chondrosarcoma grade 3).[4] Prognosis and treatment differ according to their classification.[1,2,4,5] Because chondrosarcomas are resistant to radiotherapy and chemotherapy, surgery remains the only curative treatment option. The most common treatments for cartilaginous tumors are intralesional surgery (extended curettage with local adjuvant) and wide resection. Grade 2 and Grade 3 chondrosarcoma behave aggressively and wide resection with free margins is mandatory.[4] Due to their slow growth and very low metastatic potential, atypical cartilaginous tumors (ACTs), formerly known as chondrosarcoma grade 1, are usually treated with intralesional surgery, because functional results are superior to wide resection.[6] Taken into account the behavior of ACTs and the difficulty in differentiating them from benign enchondromas, wide resection is considered disproportionate.

There is still controversy over the best surgical method in current literature.[6–8] In their systematic review, Dierselhuis et al.[6] found evidence of very low certainty that recurrence-free survival is equal between intralesional treatment and wide resection. They stated that there was very limited and very low-certainty evidence on how to treat central low-grade chondrosarcoma of the long bones. Accordingly, Shemesh et al.[7] addressed the need for methodologically high-quality studies on this topic in their systematic review. Due to the relative rarity of these tumors, studies reporting results on intralesional treatment are often small sample studies, limited by (lack of) meaningful statistics. Local recurrence and complication rates vary widely, respectively, 0%–26.3% and 0%–21%.[6–8]

In our orthopedic oncology center, we have been treating both enchondroma and ACT with curettage and cryosurgery since 1991. In this paper, we describe our oncological results and complications after curettage and cryosurgery of these tumors located in the long bones. In addition, we will discuss our points of view on future treatment of cartilaginous tumors. To the best of our knowledge, this is the largest study describing the results of curettage and cryosurgery for enchondroma and ACT of the long bones.

2 | METHODS

All patients who underwent curettage and cryosurgery for cartilaginous tumors at our institution between 2004 and 2017 were selected from our archives.

Patients were included in this retrospective study if they met the following eligibility criteria: (1) having central cartilaginous tumors treated with curettage and cryosurgery; (2) tumor located in the long bones; (3) at least 2 years follow-up postoperatively; (4) not diagnosed with Ollier or Maffucci disease; (5) no juxtacortical chondroid tumor; (6) no additional treatment (i.e., radiofrequency ablation); (7) no prior treatment at other institutions.

Enchondromas are benign bone tumors and we are aware that surgical treatment is not necessary.[4] Due to difficulty in differentiation enchondroma from ACT on conventional radiographs as well as MRI, especially in the long bones, overtreatment by curettage and cryosurgery is common.[9]

In some early cases, a trocar biopsy was performed as a separate procedure before curettage and cryosurgery. In all patients, the same method of curettage and cryosurgery was used, three cycles of freezing below −50°C and thawing were applied.[10,11] Surrounding soft tissue was protected with gauze and the temperature was monitored during cryosurgery. The cavity was filled either with a bone graft (homologous or autologous) or cement (polymethyl methacrylate [PMMA]). In several cases, prophylactic plating was applied to decrease fracture risk. The decision for prophylactic plating was not standardized during this study period. Growing insights led to more usage of prophylactic plating during ongoing years. Titanium plating was used to minimize interference on MRI studies at follow-up. Postoperative partial weight-bearing mobilization started several days after surgery and was continued for 6–12 weeks, depending on the extent of surgery and anatomical location.

All biopsy and curettage material was reviewed by experienced pathologists and histological diagnosis was made according to established criteria.[4,12]

Postoperative follow-up consisted of regular physical examination and conventional radiology, whereas additional MRI studies were performed in cases of clinical or radiological suspicion of local recurrence. Patients were discharged from follow-up after a disease-free period of at least 2 years. When discharged, patients were instructed to contact our hospital in case of (pain) complaints or other local problems at the surgical site, such as local recurrence.

Data regarding patient and tumor characteristics, operation details, complications due to curettage and cryosurgery, residual tumor, recurrence, metastasis, upgrading after recurrence, and re-operations were collected from clinical charts. To differentiate local recurrence from residual tumor, postoperative imaging was compared with preoperative imaging.

Analysis of the data was performed using IBM SPSS Statistics for Windows (version 25). All continuous variables were visually inspected and tested for normality by the Shapiro–Wilk test.

TABLE 1 Patient demographics

	N (%)
Mean age (range, years)	50 (12–78)
Female	116 (65)
Male	62 (35)
Location	
Proximal humerus	42 (23)
Humerus diaphysis	14 (8)
Ulna diaphysis	1 (<1)
Distal ulna	1 (<1)
Distal Radius	2 (1)
Proximal femur	9 (5)
Femur diaphysis	37 (21)
Distal femur	41 (23)
Proximal tibia	9 (5)
Tibia diaphysis	5 (3)
Distal tibia	3 (2)
Proximal fibula	12 (7)
Fibula diaphysis	2 (1)
Distal fibula	1 (<1)
Tumor size	
Enchondroma	4.5 cm (IQR, 3.0–7.0; range, 1.0–16.8)
ACT	4.4 cm (IQR, 3.0–7.0; range, 1.3–18.0)
Chondrosarcoma grade 2	5.1 cm (IQR, 5.0–7.4; range, 4.5–8.9)

Abbreviations: ACT, atypical cartilaginous tumor; IQR, interquartile range.

The Fisher exact test was used to identify differences between groups. $p < 0.05$ was considered statistically significant.

3 | RESULTS

In total, 179 cases were included in this study, one patient was enrolled with two separate cartilaginous tumors. In 73 cases, a trocar biopsy was performed before curettage and cryosurgery. In 11 out of 73 cases (15%), definite diagnosis after curettage and cryosurgery was higher than biopsy diagnosis (four cases ACT vs. CS2, seven cases enchondroma vs. ACT). After curettage and cryosurgery, 55 cases were histopathologically diagnosed as enchondroma, 119 as ACT (i.e., chondrosarcoma grade 1), and 5 as chondrosarcoma grade 2.

In 113 cases, the defect was filled with cement (PMMA); in 53 cases, a bone graft was used (45 homologous, 8 autologous), and in 13 cases the defect was not filled. In 56 cases, prophylactic plating was applied for tumors located in the femur (35), humerus (17), and tibia (4). Patient demographics can be found in Table 1.

Median follow-up after curettage and cryosurgery was 53 months (IQR, 33–64 months; range, 24–182 months). In 54 cases, MRI was performed for the following reasons: diagnosed with CS2 ($n = 5$), suspicion of residual tumor on radiographs ($n = 17$), persistent pain complaints ($n = 22$), infection ($n = 1$), neuropraxia ($n = 1$), and in two cases other, noncartilaginous, tumors were the reason for MRI. In six cases, the exact reason to perform MRI could not be retrieved. Patients diagnosed with chondrosarcoma grade 2 after curettage and cryosurgery received intensive follow-up. Regular MRI and X-thorax were performed on these patients to screen for recurrence and metastases.

3.1 | Oncological results of curettage and cryosurgery for enchondroma and ACT

Residual tumor was detected in 20 cases (11.5%), with a median size of 2.5 cm (IQR, 1.9–3.6 cm). Two out of 20 cases were re-operated and one case biopsied. No transformation of tumor grade was seen. In the remaining 17 cases, we refrained from surgery and opted for active surveillance. No tumor growth or tumor-related pain was noticed during follow-up (mean, 93 months; range, 32–165 months). Residual tumor was not related to tumor size, tumor location, or tumor grade (p values: $p = 0.572$, $p = 0.914$, $p = 0.203$).

Three cases (2%) underwent secondary curettage and cryosurgery due to local recurrence, with no transformation of tumor grade seen. Two patients were already discharged from regular follow-up but returned, as instructed, due to new pain complaints. All three patients suffered from pain related to the local recurrence. After surgery, the pain complaints were relieved. Currently, all three patients are free of disease.

Two cases (1%) underwent wide resection and reconstruction with tumor prosthesis due to local recurrence with radiologic aggressive characteristics (cortex breakthrough and soft tissue expansion). Both cases were histologically diagnosed with chondrosarcoma grade 2 after resection. In retrospect, areas of grade 2 chondrosarcoma (such as bone entrapment and hypercellularity) were already visible in previous specimens graded as ACT. In addition, characteristics of high-grade chondrosarcoma had been already visible on MRI before curettage and cryosurgery.

3.2 | Oncological results of curettage and cryosurgery for chondrosarcoma grade 2

In two out of the five cases diagnosed as chondrosarcoma grade 2, recurrence occurred after 12 and 28 months, respectively. Both cases underwent wide resection and reconstruction with tumor prosthesis. Pathological diagnoses remained Grade 2 in both cases. In the other three cases, lesions did not recur during follow-up.

TABLE 2 Detailed information of local recurrence and chondrosarcoma grade 2 cases

Patient age	Tumor size (cm)	Location	Preoperative MRI characteristics	Biopsy grade	Grade after curettage and cryosurgery	Time till recurrence (months)	Surgical intervention (PA grade)	Total FU (months)
Residual tumor								
40	2.8	Distal femur	Scalloping	None	ACT	7	ACT	108
60	1.5	Distal femur	No malignant criteria	None	Enchondroma	22	Reactive tissue[a]	100
Recurrence								
17	9.8	Tibia diaphysis	Scalloping and cortical thickening	ACT	ACT	10	Curettage and cryosurgery (ACT)	128
70	5.7	Proximal humerus	Not available	None	ACT	85	Curettage and cryosurgery (ACT)	107
57	3.0	Proximal tibia	Not available	ACT	ACT	117	Curettage and cryosurgery (ACT)	167
78	5.3	Proximal humerus	Extensive scalloping, cortex breakthrough, loss of ring and arc pattern, perilesional edema	ACT	ACT[b]	12	Resection (CS2)	65
63	4.0	Proximal tibia	Cortex breakthrough, loss of ring and arc pattern, perilesional edema	ACT	ACT[b]	19	Resection (CS2)	83
Chondrosarcoma grade 2								
58	4.5	Distal femur	Not available	None	CS2	26	Resection (CS2)	115
56	8.9	Proximal humerus	Extensive scalloping, cortex breakthrough, loss of ring and arc pattern, perilesional edema, periostitis	ACT	CS2	28	Resection (CS2)	88
36	5.1	Tibia diaphysis	Extensive scalloping, loss of ring and arc pattern	ACT	CS2	None	None	94
50	7.4	Tibia diaphysis	Extensive scalloping, focal loss of ring and arc pattern	ACT	CS2	None	None	42
49	5.0	Distal femur	Extensive scalloping, cortex breakthrough, focal loss of ring and arc pattern	ACT	CS2	None	None	39

Abbreviations: ACT, atypical cartilaginous tumor; FU, follow-up; MRI, magnetic resonance imaging; PA, pathology.

[a]Postoperative MRI after secondary curettage cryosurgery showed the residual tumor remained.

[b]Erroneously diagnosed ACT.

TABLE 3 Postoperative surgical intervention

Surgical intervention	N
Biopsy	1
Secondary curettage and cryosurgery	3
Segmental resection	4
Removal of osteosynthesis material	30
Removal of neuroma	1
Fracture treatment	6

No metastatic disease was seen in any of the patients nor did any patients die of the disease.

Detailed information on secondary operated cases and cases of Grade 2 chondrosarcoma can be found in Table 2.

3.3 | Complications

In total, 20 complications (11.1%) occurred due to curettage and cryosurgery, nine fractures, four superficial wound infections, three deep vein thrombosis, two transient peroneal nerve palsy, one reflex sympathetic dystrophy, and one neuroma.

Seven out of nine fractures were related to sufficient trauma. In six out of nine cases, fracture was a reason for reoperation, the other fractures consolidated without surgical intervention. None of the cases with postoperative fractures had residual tumor or recurrence of the tumor.

In total, 43 patients (24%) were reoperated during follow-up, eight of whom underwent multiple surgical interventions. The majority of the patients underwent osteosynthesis removal. Fifty-four percent of the prophylactic plating used was eventually removed due to complaints related to it. All surgical interventions are reported in Table 3.

4 | DISCUSSION

We presented an overview of all cartilaginous tumors in the long bones treated with curettage and cryosurgery between 2004 and 2017 at our institution.

Our oncological results after curettage and cryosurgery of enchondroma and ACT are excellent and comparable with other studies.[13–15] We found a recurrence-free survival of 97% which is in line with the literature (mean recurrence-free survival, 93%; range, 77%–100%).[6]

Two cases initially diagnosed as ACT after biopsy and curettage and cryosurgery recurred with radiologic aggressive characteristics. After wide resection, both lesions were diagnosed histopathologically as Grade 2 chondrosarcoma. We concluded that these cases did not show tumor progression but were erroneously diagnosed as ACT and should have been initially diagnosed as Grade 2 chondrosarcoma. On MRI, before curettage and cryosurgery, characteristics of high-grade chondrosarcoma (e.g., loss of ring and arc pattern, perilesional edema, cortex breakthrough) had been already visible in both cases.[2,16] In retrospect, both cases showed focally histopathological characteristics of Grade 2 chondrosarcoma (e.g., high cellularity, mitoses) in the first specimen. As shown by Laitinen et al.,[17] the prognosis should be based on the highest grade found in the specimen. It is known that histopathological grading of chondrosarcoma is difficult and open to interpretation. The SLICED study estimated interobserver reliability for the grading of cartilaginous neoplasms in long bones to be 0.443 (moderate) for pathologists.[9]

We noted residual tumors in 20 cases (11.5%), of which two cases underwent secondary curettage and cryosurgery. With the current knowledge of residual tumors, we nowadays would not have operated on these two cases. As seen in the remaining cases in which we choose for active surveillance, residual tumor did not cause pain complaints nor showed tumor growth. The current literature remains inconclusive on the frequency and duration of active surveillance. This is a topic of great interest and we are currently working on a natural course study that will aid to answer the question on the duration and frequency of follow-up.

To lower the residual rate, navigated curettage or an intraoperative computed tomography might be used to verify complete tumor removal.[18] Clinical relevance could be questioned due to the benign nature of these residual tumors.[14]

Five cases were diagnosed with chondrosarcoma grade 2 after curettage and cryosurgery. Preoperative MRI already showed signs of high-grade chondrosarcoma in all five cases; however, they were graded as ACT after biopsy. A mismatch between biopsy tumor grade and definitive tumor grade is a known problem caused by tumor heterogeneity.[19,20] For this reason, biopsies are nowadays sparsely performed in our hospital to differentiate between the different grades of cartilaginous tumors. To warrant wide resection, a biopsy is performed to confirm the diagnosis of high-grade chondrosarcoma in the few cases when MRI grading is not conclusive. Our oncological results of chondrosarcoma grade 2 treated with curettage and cryosurgery were poor, with a recurrence-free survival rate of 60%. More importantly, no metastatic disease was seen and all five patients are currently disease-free. Only a few other studies could be found to compare with our oncological results of curettage and cryosurgery of chondrosarcoma grade 2 in the long bones. Ozaki et al.[21] reported recurrences of all three cases of chondrosarcoma grade 2 in the long bones treated intralesionally. No evidence of disease was reported after resection. Cho et al.[22] reported on 15 cases of unexpectedly found chondrosarcoma grade 2 after curettage. Only three cases were not reoperated and underwent radiological follow-up (total follow-up of 67, 111, 119 months). All three cases were continuously disease-free.

Based on our results and the few cases described in the literature, we propose intensive follow-up by MRI and X-thorax of intralesional-treated grade 2 chondrosarcomas and only when recurrence is detected, wide resection should be performed.

Complications occurred in 11% of the cases, which is in accordance with the literature. Shemesh et al.[7] found in their systematic review a mean event rate of 0.108 for their intralesional subgroup. In our previous study on cryosurgical therapy, we had a much higher complication rate mainly due to 14% postoperative fractures.[10] Prophylactic plating was only used in 8.5% of the cases, whereas in this study, prophylactic plating was used in 31% of the cases. As a result, our postoperative fractures decreased till 5%. We recommend prophylactic plating after curettage and cryosurgery for tumors located in the (meta)diaphysis. However, the high rate of secondary operations due to plate removal ($n = 30$) needs to be mentioned.

This study is limited by its retrospective design, which is common in the sarcoma field due to the rarity of these tumors. Whereas other studies often cover long time periods (e.g., 37, 92 years)[23,24] and different case mixes to reach large study populations, we only included patients with cartilaginous tumors located in the long bones operated on between 2004 and 2017 to reduce inhomogeneity.

No control group was available to compare our results of curettage and cryosurgery with either other commonly used adjuvants or wide resection. We agree with Dierselhuis et al.[6] that a randomized control study comparing intralesional treatment with wide resection is unwarranted as local recurrence of ACT is rare and most importantly did not have a negative effect on patient survival.

Another limitation of our study is the use of radiographs in most cases during follow-up. MRI was only performed for adjacent pathology or when a residual tumor or local recurrence was suspected. As shown by Verdegaal et al.,[25] radiographs overestimate the disease-free survival. In this retrospective series, the residual tumor was detected on radiographs in 13 out of 20 cases and on MRI only in 7 out of 20 cases. The clinical relevance of performing MRI postoperatively to detect asymptomatic residual tumors seems to be low due to the benign behavior of these tumors. We would, therefore, only perform MRI postoperatively for patients with persistent pain complaints to rule out other pathology or local recurrence. As well for patients with conventional radiologic appearance of growth of remaining tumor tissue.

In conclusion, curettage and cryosurgery are recommended as surgical treatment of enchondroma and ACT. Excellent oncological results were achieved in our large cohort of enchondroma and ACT in the long bones, no transformation to higher grade chondrosarcoma was seen.

Although several complications occurred (11%) and the secondary operation rate was high (24%), this was in the majority of cases due to complaints of plates.

With the current knowledge of the behavior of ACT in the long bones, the negative side effects of operative treatment should be considered before opting for surgery.[13,26]

Further research should define criteria regarding which specific cartilaginous tumors require surgical intervention.

CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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