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Research Article

Intralesional curettage and cementation of low-grade chondrosarcomas of the appendicular skeleton: Long-term results from a single center

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ABSTRACT

Objective: The purpose of this study was to investigate the results and complications in patients who had low-grade chondrosarcomas in the appendicular skeleton and were treated by intralesional curettage and cementation within the scope of 25 years of experience in a single center.

Methods: Ninety-one patients (72 female and 19 male) were retrospectively analyzed. The median at the time of surgery was 43 (17-78) years, and the median follow-up was 102 (26-288) months. All patients were treated by intralesional curettage followed by cementation with high-viscosity bone cement (polymethylmethacrylate). Complications and local recurrence rates, as well as clinical outcome scores were recorded.

Results: Five patients (5.49%) developed local recurrence at an average of 6.6 (6-9) months postoperatively. Four were treated with local-wide excision and reconstruction with tumor prosthesis. One patient received recurettage and cementation. Two recurred patients were dedifferentiated into grade II chondrosarcomas in the last intervention. No major postoperative complication was identified in the series. Patients achieved an average Musculoskeletal Tumor Society scoring system of 92.4% (standard deviation 5.2; range 80-100) in the sixth postoperative month. Musculoskeletal Tumor Society scores in the recurrent patients decreased from an average of 90% to 75.3% after the final intervention.

Conclusion: Intralesional curettage and cementation seem safe and reliable techniques with low recurrence and complication rates in treating low-grade chondrosarcomas of the appendicular skeleton. Clinical, radiological, and pathological evaluations are mandatory before surgical intervention, and a multidisciplinary approach is crucial. A strict follow-up regimen in the early postoperative period is needed and strongly recommended to detect local recurrence.

Level of Evidence: Level IV, Therapeutic Study

Introduction

Chondrosarcomas are the most common primary malignant bone neoplasms after osteosarcoma, constituting approximately 25% of all primary bone tumors.[1,2] Clinical course and prognosis of chondrosarcomas are directly related to histological grade. Tumors with higher grades tend to metastasize more frequently and have a poor survival rate; while low-grade chondrosarcomas (LGC) behave in a local aggressive manner that rarely metastasizes, thus having a higher survival rate and a better outcome.[1-3]

The treatment of chondrosarcomas is primarily based on surgical means because they rarely respond to chemotherapy and irradiation.[4-7] There are different surgical alternatives in the literature regarding the treatment of chondrosarcomas including wide resection, marginal excision, and intralesional curettage with or without additional thermal or chemical adjuvant applied locally.[8-11] Recently, there has been an increasing trend toward the intralesional treatment of LGC, in terms of "less extensive," "limited," or "conservative" surgical treatment.[12-15]

In this study, our aim is to investigate the results and complications of our patients who underwent intralesional curettage and cementation for LGC in the appendicular skeleton.

Materials and Methods

We retrospectively evaluated 91 patients who were treated for low-grade cartilaginous tumor in the appendicular skeleton and underwent intralesional curettage and cementation surgery, between the years 1993 and 2020 at our orthopedic oncology department. Upon approval of our Institutional Review Board, we reviewed the clinical, radiological, and pathological records of the patients. We excluded patients who had LGC in the axial skeleton, who had a history of previous biopsy or surgery for the tumor and local recurrence or distant metastasis before the initial surgery at our institution. Written informed consent was obtained from all participants who participated in this study.

All patients were referred to our orthopedic oncology department with persistent pain as the presenting

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symptom. After obtaining a detailed history and physical examination, all patients had plain anteroposterior and lateral radiographs, computed tomography (CT) scans of both the lesion and the chest, Tc99-technetium-labeled whole body bone scintigraphy, and gadolinium-enhanced magnetic resonance imaging (MRI). Our clinicorad iopathological council suspected malignancy radiologically in case one or more of the following criteria exist: (i) endosteal scalloping of more than two-thirds of the thickness on CT, (ii) intramedullary cartilaginous tumor with a dimension above 5 cm, (iii) peritumoral edema or periosteal reaction on MRI, (iv) greater radionuclide uptake of the lesion compared to the anterior iliac crest in bone scan, and (v) cortical expansion in any of the radiological modalities.

Surgical intervention was planned with the council's decision, according to the clinical and radiological malignancy features of the patients. 27 of 91 patients underwent a 2-stage procedure, former biopsy and definitive intervention, while the rest had an intraoperative frozen-section biopsy. An experienced bone tumor pathologist reevaluated and approved all intraoperative frozen sections and final biopsy specimens in the study. All surgeries were performed by the same senior orthopedic surgeon who had been experienced in musculoskeletal oncology for many years.

The surgical technique involved an incision immediately above the preoperatively localized and identified cortical window on MRI, making drill holes and combining the holes with an osteotome for the cortical window, meticulous curettage of the tumor, followed by debridement of the microscopic residual tumor tissues—located both intramedullary and on the cortical window itself— which was supplemented with the use of a high-speed burr, lavaging with saline and finally applying high-viscosity (polymethylmethacryl ate, PMMA) bone cement (Versabond®, Smith & Nephew, UK) as a local adjuvant (Figure 1). Macroscopic removal of all the tumoral tissue was confirmed in fluoroscopic view among suspected patients. Fifteen of the patients had 1 or 2 titanium screws embedded into the bone cement to provide the fixation and stability of the cortical window postoperatively; the rest had no internal fixation or osteosynthesis.

Active physiotherapy regarding the range of motion exercises began on the second postoperative day. Patients who were operated for their upper extremities used a sling, while those operated for their lower extremities used crutches for 3 weeks. All patients were allowed full weight-bearing after approximately 3 weeks postoperatively. In the first postoperative year, all patients had plain radiographs every month and MRIs every 3 months. Plain radiographs and MRIs were obtained every 6 months during the second postoperative year. In the local recurrent group, chest CT scans were also evaluated every 6 months for 2 years. After the second year, the patients were examined at regular annual intervals. The assessment of clinical outcome was performed during every follow-up, using the Musculoskeletal Tumor Society (MSTS) scoring system, which consists of measurement for pain, functional capacity, and emotional acceptance of the situation.[16] Disease progression, complications, duration to local recurrence, or distant metastasis were also retrieved from medical records.

HIGHLIGHTS

- Intralesional curettage and cementation of low-grade chondrosarcomas is a safe and reliable surgical technique with low recurrence and complication rates in the management of low-grade chondrosarcomas.
- Patients should carefully be followed especially in the early postoperative period for local recurrence.
- A multidisciplinary approach consisting of is strongly recommended for the management of low-grade chondrosarcomas.

Statistical and data analysis were performed using Statistical Package for the Social Sciences (version 25.0 for Mac; Armonk, NY, USA). Kolmogorov–Smirnov test was used for the distribution of the data. Categorical variables were analyzed with chi-square test. Non-parametrical variables were given as median and minimum-maximum (min-max) values. Mann–Whitney *U*-test was used for the comparison of numerical variables in 2 independent groups since non-parametrical distribution condition was provided. Statistical significance level was accepted as a *P*-value of <.05.

Results

The study consisted of 72 female (79.12%) and 19 male (20.88%) patients with a median age of 43 ± 13.1 (17-78) years. The median follow-up was 102.30 ± 34.7 months (26-288). Anatomical localizations of the tumor were as follows: 34 proximal humerus, 30 distal femur, 20 proximal femur, 4 proximal tibia, 1 tibial diaphysis, 1 iliac bone, and 1 distal radius (Figure 2). The median of the longest dimension of lesions was 6.20 cm (4.2-8.6). All patients had grade IA tumors (low grade, intracompartmental) according to the MSTS staging system.[17] In 2 patients who had intraoperative frozen biopsies, permanent histopathological evaluation of the excised specimens turned out to be cellular-rich enchondromas.

Five patients out of 91 (5.49%; 95% confidence interval 0.8% to 10.2%) developed local recurrence (2 proximal humerus, 2 distal femur, and 1 proximal femur) at a median time of 6 (6-9) months postoperatively. There was no statistically significant difference between recurrent and non-recurrent patients regarding tumor size (median: 7 cm, min: 5.40, max: 7.90 vs. median: 6.20 cm, min: 4.20, max: 8.60 cm, $P=.644$; respectively) (Figure 3), and age (median: 36, min: 30, max: 78 vs. median: 43, min: 17, max: 65 years old, $P=.425$; respectively). Features of the recurrent patients are described in Table 1. Four of them were treated with local wide excision and reconstruction with tumor prosthesis (Figure 4). One recurrent patient received recurettage and cementation for the proximal femoral lesion. A second local relapse developed in one of the patients in the distal femur 18 months later following wide excision and reconstruction with tumor prosthesis and she was amputated. This patient had also lung metastasis and received pulmonary metastasectomy in addition to ifosphamide-MESNA treatment and died of disease 6 months later. Two of the recurred patients—one of whom was the aforementioned metastasized patient—turned out to be grade II chondrosarcomas during the examination of newly resected specimens. All other patients had no local recurrence or metastasis and had been in good clinical condition until the final follow-up. No major postoperative infection, delayed wound healing, or pathological fracture occurred in the series. In one case, a superficial wound infection developed one month after the surgery and was resolved with oral antibiotics. All patients regained full joint motion at the end of 3 months postoperatively and returned to their daily activities and occupations with achievement of an average 27.7 ± 1.56 (min: 24, max: 30) (92.4%; SD: 5.2; min: 80, max: 100) of MSTS score in the postoperative sixth month. MSTS scores in the recurrent patients decreased from a median of 27 points (90%) to a median of 22.6 (75.3%) after the second surgical intervention. There was no statistically significant difference in terms of MSTS scores between patients who received osteosynthesis and those who did not.

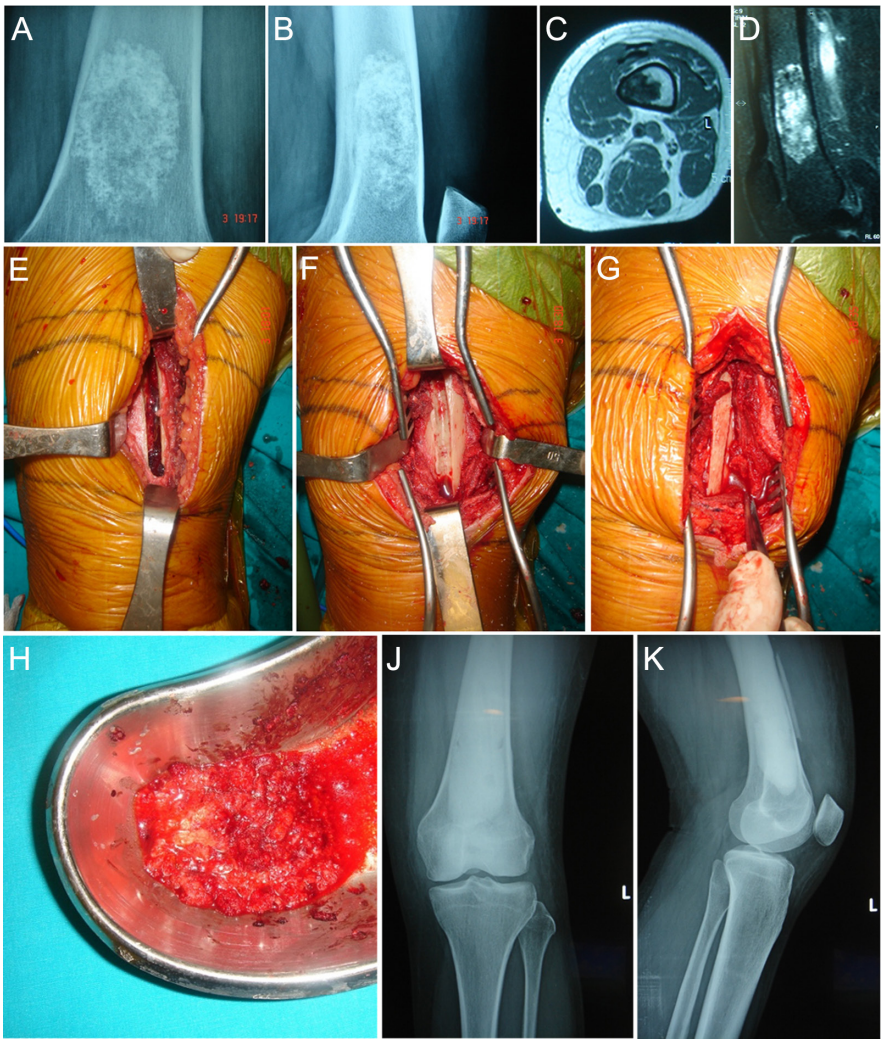

Figure 1. A-K. (A) Preoperative anteroposterior (AP) radiograph of a patient with low-grade chondrosarcoma on the distal femur. (B) Preoperative lateral radiograph. (C) Preoperative magnetic resonance imaging (MRI) axial view. (D) Preoperative MRI sagittal view. (E) Preoperative view of the cortical window with an anterior skin incision and anterior transquadriceps approach. The patient had a former biopsy from a previous anterior incision. The biopsy tract was removed during the intralesional surgery. (F) Preoperative view of the cement. (G) Preoperative closure of the cortical window. (H) Macroscopic appearance of the curetted material. (J) Early postoperative AP radiograph. (K) Early postoperative lateral radiograph.

All of the preoperative biopsies were concluded as LGC and frozen-section materials as low-grade cartilaginous tumors. In the final curettage specimens, only 2 patients revealed cellular-rich enchondromas (2.2%).

Discussion

Our study showed that intralesional curettage and cementation seems to be a feasible procedure to reduce morbidity by achieving excellent MSTS scores (92.4%) with low complication and recurrence rates (5.49%) in the management of LGC. To the best of our knowledge, this is the study with one of the largest number of patients and the longest follow-up in the management of LGC. We believe the key success of this treatment modality is a multidisciplinary approach of combining the perspectives of orthopedic oncology, radiology, and histopathology together, as well as the surgical technique.

Low-grade chondrosarcomas are slow-growing malignancies of mesenchymal tissue with cartilaginous origin. Unlike high-grade chondrosarcomas, they are less aggressive with a lower rate of local recurrence and metastasis. Nevertheless, it is literally accepted that these tumors do not respond to chemotherapy or irradiation in most circumstances, leaving surgical intervention as the only curative treatment option. These characteristics of LGC have forced surgeons who deal with musculoskeletal oncology to search for a more "conservative" surgical technique. This may be an approach that should not only remove the tumoral load in an effective manner but also provide the highest possible functional outcome for an individual at the same time. Although there is no gold standard surgical procedure currently in the literature, intralesional treatment either alone or in combination with local adjuvant therapy seems a feasible treatment modality and it has been considered as a safe and effective method with good clinical outcomes and low rates of recurrence in the treatment of LGC.[3,6,8,9,12,14,18-21]

There is no consensus in the literature about which local adjuvant therapy may be used in combination with intralesional curettage. Phenol application, cryotherapy, and cauterization, followed by applying different types of bone grafts or PMMA may be preferred. We used PMMA in our patients as a local adjuvant with the known effects of methylmethacrylate monomer as a direct cytotoxic agent and necrotizing effect as a result of tissue hyperthermia from the

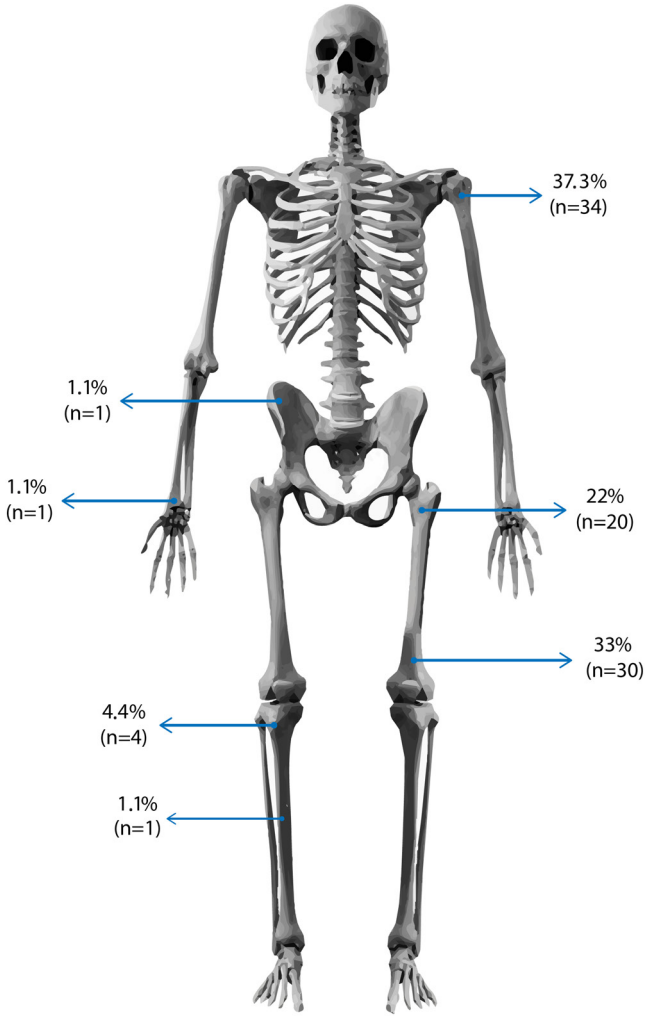

Figure 2. Anatomical distribution of the tumor.

exothermic polymerization process of the cement.[14,20,22] It is worth noting that most of the authors agree that the use of a local adjuvant (regardless of type) is necessary after intralesional curettage in order to achieve tumor control. In the study of Streitbürger et al.[21] 9 patients with LGC in the extremities were treated with intralesional curettage. Three patients out of 9 were treated without additional use of PMMA, while the remaining 6 were treated with PMMA as cementation in addition to intralesional curettage. After a mean follow-up of 26 months, they found that all of the 3 patients who were treated without PMMA developed a local recurrence.

The concept of osteosynthesis after intralesional treatment was questioned in various studies. Omlor et al[23] found no significant difference in terms of clinical and functional outcomes between intralesional curettage and bone cement of proximal humeral enchondromas and LGC with or without osteosynthesis. Besides, they had longer surgery times, more blood loss, and longer hospitalization in the osteosynthesis group. In another study by Omlor et al.[12] it was found that complications were almost twice as high in cases with additional osteosynthesis.[12] In our study, we applied a simple method of internal fixation with 1 or 2 titanium screws embedded in the cortical window and bone cement in 15 of our patients. We did not observe any complications related to the fixation of the cortical window. There were not any other postoperative complications in our series, such as infection, delayed wound healing, pseudoarthrosis, or nerve palsy, and the overall MSTS score in our series was 92.4%, consistent with the literature as intralesional treatment has favorable results with low complication rates compared to more aggressive surgical techniques.[9,10,13,14,18,19]

Local recurrence following intralesional treatment is between 0 and 17.9% in the literature.[3,6,15] In a meta-analysis of Shemesh et al.[6] the recurrence rate was not found to be significantly different between patients treated with intralesional curettage or wide local excision. We agree with the authors suggesting that the poorer outcome and higher local recurrence rates may be due to having all grades

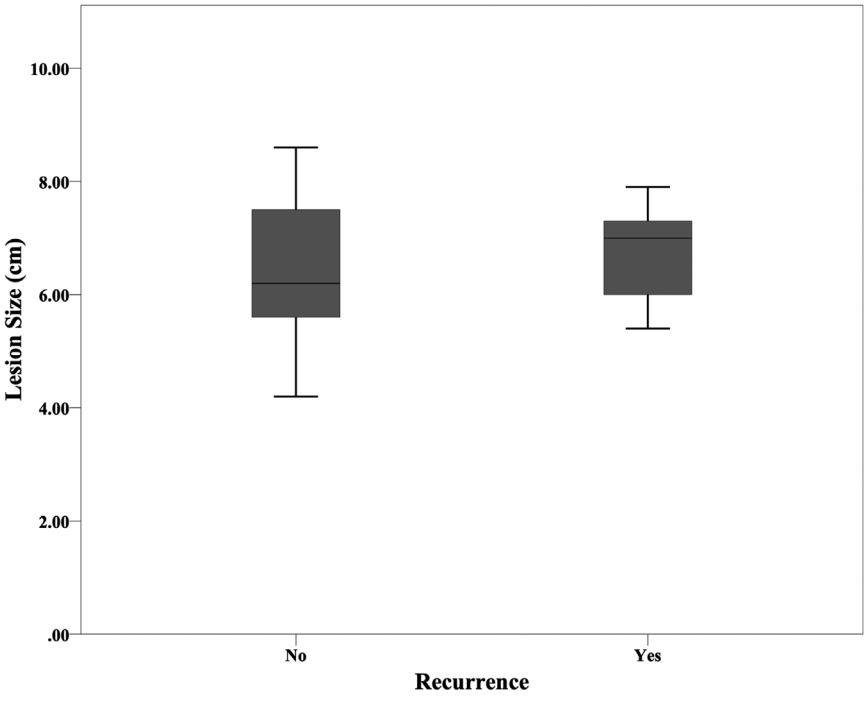

Figure 3. Lesion sizes of the patients with recurrence and nonrecurrence.

Table 1. Characteristics of the patients who had recurrence

Patient no	Sex	Age	Localization	Lesion size (cm)	First recurrence time (month)	Second surgical intervention	Pathologic diagnosis of the second intervention	Second recurrence time (month)	Third surgical intervention	Metastasis	Chemotherapy/ radiotherapy	Complication	Death	Postoperative MSTS	Postoperative MSTS of second surgery
1	M	78	Distal femur	5.8	6	Local wide excision, reconstruction with tumor prosthesis	Grade II chondrosarcoma	None	None	None	None	None	None	28	22
2	F	30	Proximal femur	5.4	6	Recurettage and cementation	Grade I chondrosarcoma	None	None	None	None	None	None	27	25
3	M	36	Proximal humerus	7.9	6	Local wide excision, reconstruction with tumor prosthesis	Grade I chondrosarcoma	None	None	None	None	None	None	27	24
4	F	34	Distal femur	6.7	6	Local wide excision, reconstruction with tumor prosthesis	Grade II chondrosarcoma	18	Amputation	Chest	Ifosphamide+MESNA	None	Died 6 months later	28	20
5	F	46	Proximal humerus	6.3	9	Local wide excision, reconstruction with tumor prosthesis	Grade I chondrosarcoma	None	None	None	None	None	None	25	22

MSTS, Musculoskeletal Tumor Society Scoring System.

Figure 4. A-D. (A) Surgical intervention with tumor prosthesis for a recurrent patient. (B) Macroscopic view of the resected specimen. (C) Postoperative anteroposterior radiograph of the recurrent patient. (D) Postoperative lateral radiograph of the recurrent patient.

of chondrosarcomas or axial chondrosarcomas included in study designs.[4,8,19,24] In our study, the local recurrence rate was 5.5%, in consistence with the literature. The duration of local recurrence after surgical intervention is between 2 months and 9 years in the literature.[25] The mean duration of local recurrence after surgery was 6.6 months in our study; therefore, we believe that a close and careful follow-up is mandatory, especially shortly after the surgical intervention. The literature also lacks data about how long the LGC patients need to be followed for after surgical intervention. While some authors suggest that 2 years of follow-up is adequate, others recommend 5 years of minimum follow-up.[5] Regardless of the maximum duration, the first 2 years postoperatively seem to be the most important period in terms of recurrence.[14,25]

The role of a preoperative biopsy in the evaluation of LGC is also controversial. Recent studies have demonstrated the safety of surgical intervention for LGC without preoperative biopsy as there could be disadvantages of preoperative biopsy such as sampling errors, delay in treatment, seeding, morbidity, and cost.[15] We performed preoperative biopsies for our 27 patients, the last of which were during the late 90s and early 2000s with less experience as a clinicoradiopathological tumor council. Recently, intraoperative biopsies have been suggested by our council for patients with low-grade cartilaginous lesions demonstrating malignancy features on radiological and clinical evaluation. In the recent study, our misclassification of benign enchondroma as LGC rate is low, as the final pathological evaluation of the resected specimens revealed 2 cellular-rich enchondromas (2.2%). We attribute this accurate rate to the critical role of a multidisciplinary approach in the evaluation of LGC.

There are several limitations to this study. First of all, this is a retrospective study that includes patients with a minimum of a 26-month follow-up period. The local recurrence rate could be higher if we had been able to follow those patients for a longer period. Nevertheless, we think that a follow-up period with an average of 102 months is sufficient to observe the clinical course and outcome of LGC patients as most of the recurrences occur during the first 2-5 years. We also excluded patients with tumors located in the axial skeleton, which would have a worse prognosis compared to the appendicular skeleton. On the contrary, it was found that almost all of our recurrent patients were operated a long time ago, in which the surgical technique would have naturally been below today's standards. A possible bias would be the learning curve of the surgical team. Local recurrence rates could be lower if we had excluded patients who were operated before the last decade.

Secondly, despite all attempts of looking through clinical, radiological, and histopathological perspectives together, there has still been no gold standard for the management of these lesions in the literature; we share the same difficulties as other orthopedic oncologists. Unfortunately, chondroid lesions may still be over- or underestimated. Histopathologically, they may include both low- and high-grade cellular properties in different parts of the tumor. Therefore, the accuracy of permanent histopathologic specimens may be low. In our study, 2 of the recurred patients were found to have grade II chondrosarcomas and we were not able to solve the controversy of whether those recurred patients preceded dedifferentiation of LGC or those local recurrences were the results of an underestimated high-grade tumor. These lesions may also be over- or underestimated by their radiologic and clinical features alone. We tried to overcome this issue by combining them with histopathology and switching to wide resection instead of intralesional treatment during the surgery for the patients who turned out to carry higher-graded tumor properties in the intraoperative frozen biopsies. However, larger and multicenter randomized prospective studies have been still needed in order to establish standard guidelines in the management of these lesions.

In conclusion, "low-grade (grade I) chondrosarcoma" is a complicated subject in terms of diagnosis, treatment, complication and recurrence rates, follow-up regimens and survival ratios. The main principles of treatment should cover both avoidance of recurrence and preservation of functional capacity. Intralesional curettage and cementation can be a safe, reliable, and successful technique with low recurrence and complication rates in the treatment of LGC. Clinical, radiological and pathological evaluations are mandatory before any surgical intervention as these may lower any any over- or undertreatment. This multidisciplinary approach would also decrease the potential disadvantages of former biopsies. A strict follow-up regimen, especially in the early postoperative period, is needed and strongly recommended in order to detect any complication or local recurrence. Any local recurrence following intralesional curettage and cementation should be treated with a more aggressive approach such as local wide excision due to the probability of progression and risk of metastasis.

Ethics committee approval: Ethical committee approval was received from the Ethics Committee of Haliç University (Approval No: 250522/108).

Informed consent: Written informed consent was obtained from all participants who participated in this study.

Author contributions: Concept - M.H.; Design - B.G., M.H.; Supervision - M.K.O., M.H.; Materials - C.D.D.; Data Collection and/or Processing - O.T.; Analysis and/or Interpretation - O.T., B.K., C.D.D.; Literature Review - M.K.O., B.K.; Writing - B.G.; Critical Review - M.H.

Declaration of Interests: The authors have no conflicts of interest to declare.

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