Original Article

How to Fill the Cavity after Curettage of Giant Cell Tumors around the Knee? A Multicenter Analysis

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Abstract

Background: Intralesional excision with curettage is the standard method of giant cell tumor (GCT) treatment, but the ideal filling material after curettage remains controversial. The purpose of this study was to compare the oncological and functional outcomes which underwent cementation or bone grafting after GCT curettage around the knee.
Methods: We reported 136 cases with GCTs in distal femur or proximal tibia who accepted curettage from five clinical centers during the last 15 years. All patients were divided into two groups according to filling materials. Recurrence-free survival proportions were used to evaluate oncological outcomes while the Musculoskeletal Tumor Society (MSTS) 93 functional score was used to evaluate functional outcomes. Other parameters including surgical complication, general condition, and radiological classification had been analyzed. The valid statisitical data was analyzed using SPSS 13.0 software.
Results: After GCT curettage, 86 patients (63.2%) accepted bone grafting while 50 patients (36.8%) accepted cementation. There was no statistical difference in age, gender, tumor location, radiological classification, fixation, follow-up time, and MSTS 93 functional score between cementation group and bone grafting group. The recurrence-free survival proportions showed that the recurrence rate in bone grafting group was higher than it in cementation group ($P = 0.034$). Surgical complication was lower in cementation group than that in bone grafting group but without statistically significant difference ($P = 0.141$).
Conclusions: Parameters including patients' age, gender, tumor location, and radiological classification did not affect surgeons' treatments in cavity filling after GCT curettage. Cementation should be recommended because of easy usage, the similar postoperative knee function with bone grafting, and the better local tumor control than bone grafting.

Key words: Bone Grafting; Cementation; Giant Cell Tumor; Knee

Introduction

Giant cell tumor (GCT) is a well-known primary bone tumor. It accounts for 20% of all benign tumors and 3–8% of all primary bone tumors.[1-3] However, the reported incidence in some Asian counties may account for 20% of all musculoskeletal tumors.[4] GCTs commonly have a lytic appearance on radiographs located in the epiphysis of long bones in young adults, mostly around the knee.[5] They may involve the subchondral bone but rarely the joint cartilage. GCT treatments are more difficult in the knee than in other locations because of the characteristic of weight bearing and many activities. It is valuable to focus the knee GCT treatments.

Due to the characteristic of aggressive and high recurrence rate, the ideal treatment should ensure local control of disease and maintain limb function. Although local control can be achieved well with *en bloc* resection, loss of limb function and risk of subsequent revision of the reconstruction are common.[6] Intralesional curettage has been the standard

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method of treatment, but is associated with a relatively high risk of local recurrence.[4,6] Some adjuvant agents, such as hydrogen peroxide, phenol, and alcohol, have been used to decrease the recurrence rates.[7] However, a recent meta-analysis demonstrates that local control was not improved with the use of adjuvants.[8]

How to fill the cavity after GCT curettage is an important question. For benign bone tumors, bone grafting is recommended after tumor curettage. Bone cement is used widely in cavity filling and structural reconstruction in aggressive bone tumors and some low-grade malignant bone tumors.[9] Acrylic cementation treatment after curettage immediately stabilizes the affected limb and releases heat during polymerization that may kill the remaining tumor cells.[10] A recent meta-analysis demonstrates that local recurrence is minimal in acrylic cementation patients.[11] Some authors worry that the usage of acrylic cement may damage the articular cartilage and increase stiffness of the subchondral bone leading to degenerative changes in the adjacent joint.[12,13] No literature confirms that there has been an increased risk of osteoarthritis with cementation following the treatment of GCTs.

Given the multicenter study of filling cavity after GCT curettage around the knee is rarely been reported in any literatures, in this study, we reviewed 136 cases treated by five bone tumor experts from five institutions, which hopefully provides information of great value to orthopedic surgeons and assist them to select the optimal treatment protocol in the process of cavity filling.

Methods

Ethical approval

We had prior ethics committee approval from the Institutional Ethical Committee of Jinan Military General Hospital (NO. 200811), and patient consent was obtained for this study. The research was carried out according to the principles set out in the *Declaration of Helsinki* 1964 and all subsequent revisions. Informed consent was obtained, and the relevant institutional review board had approved the study.

Patients

Five hundred and fifty-two patients with histologically benign GCTs of the bone around the knee were treated at these five institutions from 2001 to 2014, of which 136 patients who accepted curettage following by cementation or bone grafting were retrospectively reviewed. In this study, we included patients with the following criteria: (1) Pathological diagnosis of GCT was definite; (2) GCT involved the distal femur or proximal tibia; (3) no prior treatments of the tumor; and (4) complete clinical, radiographic, and pathologic records. Data extracted from the charts included gender, age, anatomic location of the lesion, Campanacci's bone destruction radiographic classification, fixation, tumor control, surgical complications, follow-up in months, and the Musculoskeletal Tumor Society (MSTS) 93 functional score at the end of follow-up.

The diagnosis of GCT was established based on the clinical data and imaging studies and confirmed by needle biopsy or open biopsy before surgery as well as pathology examination after surgery. Radiographical classification system of Campanacci[14] categorizes the lesion into three grades that Grade I indicates an intraosseous lesion, Grade II denotes an intraosseous lesion with cortical thinning and expansile borders, and Grade III refers to a lesion extending extraosseously and forming a soft-tissue mass. There were 15 patients with Grade I lesions, 63 patients with Grade II lesions, and 58 with Grade III lesions in this series. The MSTS 93 score[15] had been used for functional evaluation at the last follow-up in our study. The MSTS 93 score measures patient activity, including pain, function, emotional acceptance, and supports walking ability and gait. Each of these six variables was assessed on a 5-point scale, giving a maximum score of 30 points. To some extent, higher MSTS score signifies better functional results.

All the patients in this study accepted GCT curettage, after that, some patients accepted bone grafting filling defined to bone grafting group while other patients accepted cementation with polymethylmethacrylate bone cement defined to group cementation [Figure 1]. In these five institutions, GCT curettage was carried out through a large cortical window, which had same length to GCTs. The GCT curettage was done with a similar process including normal-appearing bone was seen after curettage, a high-speed burr was used to enlarge the cavity in 2 mm, and electrocauterization was used for the wall of cavity [Figure 2].

Postoperative reexamination had been carried out for all these patients in this study. As a normal follow-up request, once a

Figure 1: Bone grafting was used after GCT curettage in the distal femur (a). Bone grafting was used after GCT curettage in the proximal tibia (b). Cementation was used after GCT curettage in the distal femur (c). Cementation was used after GCT curettage in the proximal tibia (d). GCT: Giant cell tumors.

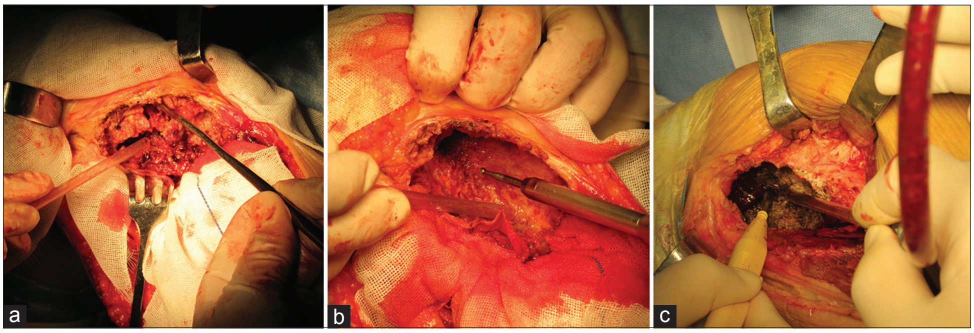

Figure 2: Curettage of the GCTs in the distal femur or proximal tibia. (a) GCT curettage was carried through a large cortical window, which had same length that of GCTs. (b) A high-speed burr was used to enlarge the cavity in 2 mm. (c) Electrocauterization was used for the wall of cavity. GCTs: Giant cell tumors.

month was done in the first half year, after that every 3 months in 0.5–2.0 years and annually after 2 years. The surgical complications consisting of incision infection, postoperative fracture, rejection reaction, and joint fluid leakage were recorded and treated as soon as possible. Local disease control was another important observed target. In the follow-up, for local recurrence suspected by radiographs or computerized tomography (CT), a biopsy was performed to confirm the suspicion. For the patients with GCT recurrence, some accepted repeated curettage and filling while others accepted wide resection followed by prosthesis reconstruction.

Statistical analysis

In this study, SPSS 13.0 (Chicago, IL, USA) statistical software was used for data analysis. All survival data were analyzed using the Kaplan-Meier method. Multiple comparisons of specific values between different groups of result-oriented indicators were performed. The method of analysis of variance (ANOVA) and Chi-square test were used for comparisons and the differences were considered statistically significant when $P < 0.05$.

Results

There were 86 patients (63.2%) in the bone grafting group while 50 patients (36.8%) in the cementation group. In the bone grafting group, the mean age of 86 patients was 33.4 ± 12.0 years while it was 34.4 ± 12.4 years in the cementation group. No statistically significant difference was found between these two groups ($F = 0.099$, $P = 0.754$). Gender difference was not obvious, and no statistically significant difference was found in these two groups ($\chi^2 = 0.036$, $P = 0.861$). In the 136 patients, 67 GCTs were located in the distal femur and 69 in the proximal tibia. There was no statistically significant difference in the tumor location between the two groups ($\chi^2 = 0.877$, $P = 0.378$). GCTs with Campanacci's Grade II and III were common in this series. Between these two groups, no statistically significant difference was found in the Campanacci's bone destruction radiographic classification ($\chi^2 = 3.932$, $P = 0.140$). After cavity filling, some patients accepted fixation with plate (52.9%), some with no fixation (41.2%), and individual patients accepted screw fixation only (5.9%). No statistically significant difference was found in fixation method between the two groups ($\chi^2 = 4.227$, $P = 0.121$). The mean follow-up time was 86.5 ± 33.3 months. There was no statistically significant difference between the two groups ($F = 2.014$, $P = 0.158$). The detailed demographical data are summarized in Table 1.

The Kaplan-Meier survival analysis was used to compare the GCT recurrence and surgical complications between the two groups. The result confirmed that cementation was significantly associated with a lower recurrence rate than bone grafting ($\chi^2 = 4.490$, $P = 0.034$) [Figure 3]. Two of the fifty patients accepted cementation that had delayed infection at 2 and 12 months after operation. Ten of the 86 patients accepted bone grafting that had surgical complications including six patients with infection, two patients with postoperative fracture, one patient with allograft rejection reaction, and one patient with joint fluid leakage. The surgical complication rate was lower in cementation group than in bone grafting group, but this difference had no statistical significance ($\chi^2 = 2.160$, $P = 0.141$) [Figure 4].

A radiolucent zone between the cement and cortical bone could be found in most patients who accepted cementation. It was usually obvious at the 6 months after operation and without width increase or disappearance [Figure 5]. There was no relationship between a radiolucent zone and clinical symptom in these clinical observations.

The mean MSTS 93 functional score at the last follow-up was 25.7 ± 3.8, with a mean score of 33.4 ± 12.0 years for 86 patients in bone grafting group and 25.6 ± 3.6 for 50 patients in cementation group. Statistically significant difference could not be found in MSTS 93 functional score ($F = 2.288$, $P = 0.133$).

Some patients in this study accepted CT and magnetic resonance imaging (MRI) evaluation in the follow-up. The subchondral bone could be observed in CT while the cartilage could be observed in MRI. Although the distance was close between the cement and cartilage, the cartilage damage was not obvious and knee function was normal [Figure 6]. Statistical analysis was not carried out because not all patients accepted CT and MRI evaluation in the follow-up.

Table 1: Statistical analysis results between bone grafting group and cementation group

Categories	Bone grafting	Cement	Total	Statistics	*P*
Number, *n* (%)	86 (63.2)	50 (36.8)	136 (100)	–	–
Age (year), mean ± SD	33.4 ± 12.0	34.4 ± 12.4	33.8 ± 12.1	$F = 0.099$	0.754
Sex, *n* (%)					
Male	45 (52.3)	27 (54.0)	72 (52.9)	$\chi^2 = 0.036$	0.861
Female	41 (47.7)	23 (46.0)	64 (47.1)		
Tumor location, *n* (%)					
Distal femur	45 (52.3)	22 (44.0)	67 (49.3)	$\chi^2 = 0.877$	0.378
Proximal tibia	41 (47.7)	28 (56.0)	69 (50.7)		
Campanacci, *n* (%)					
I	6 (7.0)	9 (18.0)	15 (11.0)	$\chi^2 = 3.932$	0.140
II	42 (48.8)	21 (42.0)	63 (46.4)		
III	38 (44.2)	20 (40.0)	58 (42.6)		
Fixation, *n* (%)					
No	41 (47.7)	15 (30.0)	56 (41.2)	$\chi^2 = 4.227$	0.121
Screw	4 (4.6)	4 (8.0)	8 (5.9)		
Plate + screw	41 (47.7)	31 (62.0)	72 (52.9)		
Follow-up (months), mean ± SD	91.0 ± 35.3	78.8 ± 28.4	86.5 ± 33.3	$F = 2.014$	0.158
MSTS, mean ± SD	25.8 ± 3.9	25.6 ± 3.6	25.7 ± 3.8	$F = 2.288$	0.133

SD: Standard deviation; MSTS: Musculoskeletal Tumor Society.

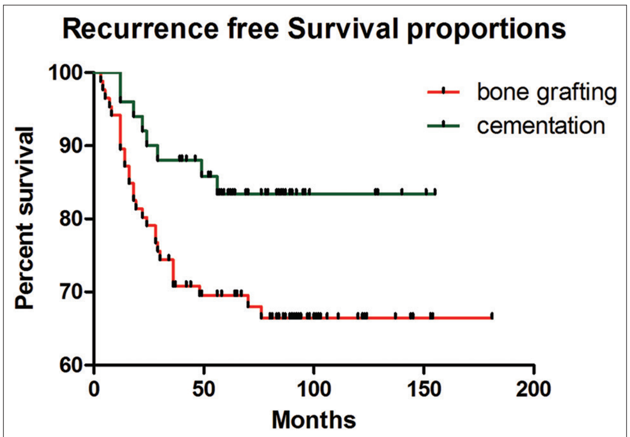

Figure 3: Recurrence-free survival after curettage in 136 GCTs of the knee. The result confirmed that cementation was significantly associated with a lower recurrence rate than bone grafting ($\chi^2 = 4.490$, $P = 0.034$). GCTs: Giant cell tumors.

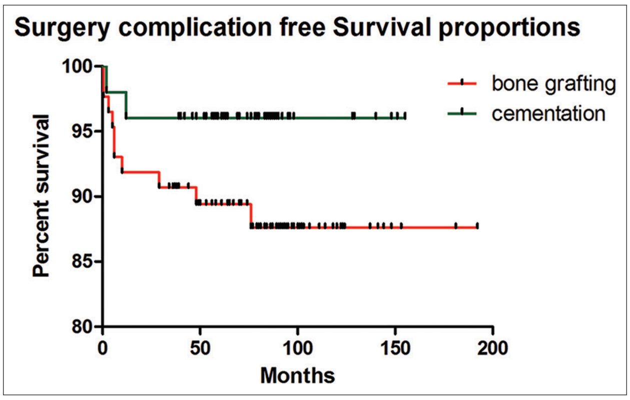

Figure 4: Surgical complication-free survival after curettage in 136 GCTs of the knee. The surgical complication rate was low in cementation group than in bone grafting group, but this difference had no statistical significance ($\chi^2 = 2.160$, $P = 0.141$). GCTs: Giant cell tumors.

Discussion

Treatment options for GCT include denosumab, serial embolization, interferon, radiation therapy, and surgical treatment. Denosumab was a fully humanized monoclonal antibody against the receptor activator of nuclear factor-κ B (RANK) ligand which had demonstrated significant activity in patients with unresectable or recurrent GCTs in bone.[16] Denosumab was approved by the Pure Food and Drug Administration (FDA) for the treatment of adults and skeletally mature adolescents with GCT of bone that was unresectable or where surgical resection was likely to result in severe morbidity in 2013. However, patients did not accept the denosumab treatment in China because the denosumab was not approved by China FDA and the patients' agreement was hard to get. Although serial embolization[17] and interferon[18] had been accepted in the GCT treatment, it was still necessary to perform surgical treatment thereafter. For GCTs of the extremity, surgical treatment was the first option.

Intralesional curettage was the main surgical treatment option for GCTs,[19,20] although simple curettage of GCT was associated with a high rate of local recurrence. In the recent years, with the application of aggressive curettage technology, which was characterized by the use of a high-speed burr and other auxiliary methods, the GCT recurrence rate had been well controlled.[21,22] For recurrent GCTs, some authors had suggested resection with a margin or wide margin followed by reconstruction with a prosthesis or allograft.[23,24] Others had recommended repeated curettage since it resulted in cure in 80% to 90% of cases.[25] Balke *et al*. reported a re-recurrence rate of 21.7%, with the need for further curettage, with 20.9% of the patients requiring

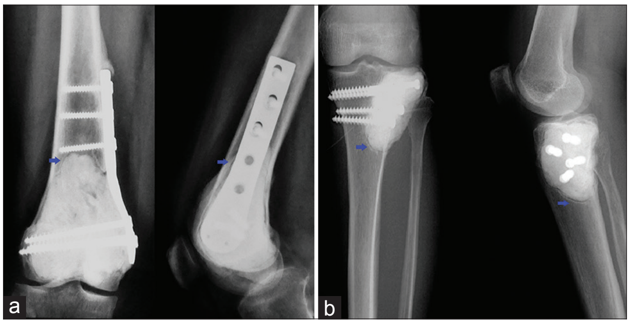

Figure 5: Development of the radiolucent zone (blue arrow) in the distal femur after cementation (a). Radiolucent zone (blue arrow) in the proximal tibia after cementation (b).

prosthetic replacement.[26] Although wide margin was well known to produce the lowest recurrence rate, it should not be done always because of the benign nature of GCTs and the poor functional results. Many articles indicated that the functional outcomes of curettage were significantly superior to wide resection.[25,27,28] Since extensive curettage resulted in satisfactory control of local recurrence and favorable functional outcomes, extensive curettage should be recommended for GCT treatment. Whatever, intralesional curettage helped to preserve joint integrity and maximize function without resorting endoprosthetic replacements.

Consensus was not obtained about how to reconstruct the cavity after curettage. The cavity can be reconstructed with bone grafting, bone cement, or calcium phosphate. Whatever material used, filling was commonly performed to provide structural support and prevent collapse. The advantage of bone grafting was that, if it was successfully incorporated, the reconstruction was permanent, but its disadvantages include difficulty in detecting recurrence, allograft rejection reaction, and the requirement of a bone bank. The advantages of cementation include cytotoxic and thermal effects to tumor cell in operation, immediate full weightbearing after operation and early recurrence detection in the follow-up. However, some surgeons worried the degeneration of articular cartilage in the subchondral region of the weightbearing area.[29] It had been suggested that bone grafting under the cartilage may prevent the thermal damage caused by cementation. However, there were no statistically significant difference in functional outcome when either cementation or bone grafting was used adjacent to the cartilage after curettage.[30] The similar result was found in this study, fifty patients accepted cementation that had same postoperative limb function as 86 patients accepted bone grafting in the mean follow-up with 86.5 months.

Another concern about the use of cementation was a radiolucent zone at the bone–cement interface. In this series, radiolucent zones between the cement and bone could be found in most patients. Mjöberg *et al*. reported that the radiolucent zone surrounding bone cement may be caused by thermal injury.[31] We agreed with the theory and considered that the special mechanical properties of cement may be another reason. In general, higher elasticity modulus was

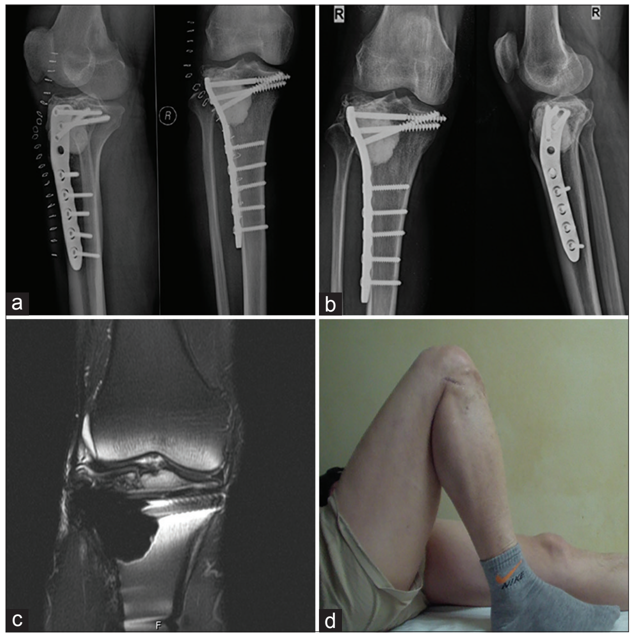

Figure 6: Cementation was used after GCT curettage in the proximal tibia (a). Mild collapse of the lateral tibia platform could be found in the follow-up at 4 years after operation (b). Cartilage damage was not obvious (c). Normal knee function without pain could be found in the last follow-up (d). GCTs: Giant cell tumors.

confirmed in cement than the bone. Concentrating pressure on the bone-facing cement made the bone to be a sclerotic rim. Nevertheless, a sclerotic rim was nonprogressive and did not affect fixation. However, some authors believed that a radiolucent zone might allow micromotion between the bone and cement which might cause fractures.[32,33] For this present series, no patient in cementation group got postoperative bone fracture while one patient in bone grafting group had postoperative bone fracture. The options of fixation should be decided by the tumor location, tumor volume, Campanacci's grade, and other factors. This study did not focus on it.

It is necessary to alert readers to be aware of the limitations of this study. First, the research interest was on cavity filling but not on the resection methods of GCTs. The authors wanted to alert readers how to choose filling material after GCT curettage. Second, this was a multicentric retrospective study and the patients' treatments were decided by five experienced bone tumor surgeons; consequently, the differences among surgical technologies cannot be avoided. Nevertheless, consensuses of treatments had been made by these surgeons, and postoperative situations of different treatment methods may provide valuable information for surgeons in the decision-making process. Third, the time span of follow-up was large. The minimum follow-up time was 24 months while the maximum follow-up time was 192 months. Nevertheless, most of the local recurrences occurred within 2 years in this study.

The results of this study indicated that the use of cementation after curettage shows promise in limiting early postoperative complications. Compared to bone grafting, the cementation had lower recurrence and easier usage in general. In the follow-up with long time, the patients who accepted cementation had same postoperative limb function with the patients who accepted bone grafting. No additional harm of cementation was found in this study. In light of these results, we recommend cementation after GCT curettage.

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Conflicts of interest

There are no conflicts of interest.

References

1. Karpik M. Giant cell tumor (tumor gigantocellularis, osteoclastoma) - Epidemiology, diagnosis, treatment. Ortop Traumatol Rehabil 2010;12:207-15.
2. Unni KK, Inwards CY. Dahlin's Bone Tumors: General Aspects and Data on 10,165 Cases. Philadelphia: Lippincott Williams & Wilkins; 2010.
3. Boons HW, Keijser LC, Schreuder HW, Pruszczynski M, Lemmens JA, Veth RP, *et al*. Oncologic and functional results after treatment of giant cell tumors of bone. Arch Orthop Trauma Surg 2002;122:17-23.
4. Sung HW, Kuo DP, Shu WP, Chai YB, Liu CC, Li SM, *et al*. Giant-cell tumor of bone: Analysis of two hundred and eight cases in Chinese patients. J Bone Joint Surg Am 1982;64:755-61.
5. Enneking WF. Lesions of uncertain origin originating in bone: Giant-cell tumor. In: Ennecking WF, editor. Musculoskeletal Tumor Surgery. Vol. 2. New York: Churchill Livingstone; 1983. p. 1435-76.
6. McDonald DJ, Sim FH, McLeod RA, Dahlin DC. Giant-cell tumor of bone. J Bone Joint Surg Am 1986;68:235-42.
7. Zhen W, Yaotian H, Songjian L, Ge L, Qingliang W. Giant-cell tumour of bone. The long-term results of treatment by curettage and bone graft. J Bone Joint Surg Br 2004;86:212-6.
8. Algawahmed H, Turcotte R, Farrokhyar F, Ghert M. High-speed burring with and without the use of surgical adjuvants in the intralesional management of giant cell tumor of bone: A systematic review and meta-analysis. Sarcoma 2010;2010:1-5. doi: 10.1155/2010/586090.
9. Fang L, Chen YJ, Wu GY, Zou QY, Wang ZG, Zhu G, *et al.* Ribs formed by prolene mesh, bone cement, and muscle flaps successfully repair chest abdominal wall defects after tumor resection: A Long-term study. Chin Med J 2017;130:1510-1. doi: 10.4103/0366-6999.207473.
10. Nelson DA, Barker ME, Hamlin BH. Thermal effects of acrylic cementation at bone tumour sites. Int J Hyperthermia 1997;13:287-306.
11. Zuo D, Zheng L, Sun W, Fu D, Hua Y, Cai Z, *et al.* Contemporary adjuvant polymethyl methacrylate cementation optimally limits recurrence in primary giant cell tumor of bone patients compared to bone grafting: A systematic review and meta-analysis. World J Surg Oncol 2013;11:156. doi: 10.1186/1477-7819-11-156.
12. Radev BR, Kase JA, Askew MJ, Weiner SD. Potential for thermal damage to articular cartilage by PMMA reconstruction of a bone cavity following tumor excision: A finite element study. J Biomech 2009;42:1120-6. doi: 10.1016/j.jbiomech.2009.02.005.
13. Szalay K, Antal I, Kiss J, Szendroi M. Comparison of the degenerative changes in weight-bearing joints following cementing or grafting techniques in giant cell tumour patients: Medium-term results. Int Orthop 2006;30:505-9. doi: 10.1007/s00264-006-0190-z.
14. Campanacci M. Giant cell tumor. In: Campanacci M, Enneking WF, editors. Bone and Soft Tissue Tumors: Clinical Features, Imaging, Pathology and Treatment. New York: Springer-Verlag; 1999. p. 99-136.
15. Enneking WF, Dunham W, Gebhardt MC, Malawar M, Pritchard DJ. A system for the functional evaluation of reconstructive procedures after surgical treatment of tumors of the musculoskeletal system. Clin Orthop Relat Res 1993;286:241-6.
16. Chawla S, Henshaw R, Seeger L, Choy E, Blay JY, Ferrari S, *et al.* Safety and efficacy of denosumab for adults and skeletally mature adolescents with giant cell tumour of bone: Interim analysis of an open-label, parallel-group, phase 2 study. Lancet Oncol 2013;14:901-8. doi: 10.1016/S1470-2045(13)70277-8.
17. Onishi H, Kaya M, Wada T, Nagoya S, Sasaki M, Yamashita T, *et al.* Giant cell tumor of the sacrum treated with selective arterial embolization. Int J Clin Oncol 2010;15:416-9. doi: 10.1007/s10147-010-0048-7.
18. Wei F, Liu X, Liu Z, Jiang L, Dang G, Ma Q, *et al.* Interferon alfa-2b for recurrent and metastatic giant cell tumor of the spine: Report of two cases. Spine (Phila Pa 1976) 2010;35:E1418-22. doi: 10.1097/BRS.0b013e3181e7bf5a.
19. Mendenhall WM, Zlotecki RA, Scarborough MT, Gibbs CP, Mendenhall NP. Giant cell tumor of bone. Am J Clin Oncol 2006;29:96-9. doi: 10.1097/01.coc.0000195089.11620.b7.
20. Raskin KA, Schwab JH, Mankin HJ, Springfield DS, Hornicek FJ. Giant cell tumor of bone. J Am Acad Orthop Surg 2013;21:118-26. doi: 10.5435/JAAOS-21-02-118.
21. Blackley HR, Wunder JS, Davis AM, White LM, Kandel R, Bell RS, *et al*. Treatment of giant-cell tumors of long bones with curettage and bone-grafting. J Bone Joint Surg Am 1999;81:811-20.
22. Niu X, Zhang Q, Hao L, Ding Y, Li Y, Xu H, *et al.* Giant cell tumor of the extremity: Retrospective analysis of 621 Chinese patients from one institution. J Bone Joint Surg Am 2012;94:461-7. doi: 10.2106/JBJS.J.01922.
23. Waldram MA, Sneath RS. Is bone grafting necessary? Analysis of twenty cases of giant cell tumour of bone treated by curettage without graft. Int Orthop 1990;14:129-33.
24. Prosser GH, Baloch KG, Tillman RM, Carter SR, Grimer RJ. Does curettage without adjuvant therapy provide low recurrence rates in giant-cell tumors of bone? Clin Orthop Relat Res 2005;435:211-8.
25. Turcotte RE. Giant cell tumor of bone. Orthop Clin North Am 2006;37:35-51. doi: 10.1016/j.ocl.2005.08.005.
26. Balke M, Ahrens H, Streitbuerger A, Koehler G, Winkelmann W, Gosheger G, *et al.* Treatment options for recurrent giant cell tumors of bone. J Cancer Res Clin Oncol 2009;135:149-58. doi: 10.1007/s00432-008-0427-x.
27. Deheshi BM, Jaffer SN, Griffin AM, Ferguson PC, Bell RS, Wunder JS, *et al.* Joint salvage for pathologic fracture of giant cell tumor of the lower extremity. Clin Orthop Relat Res 2007;459:96-104. doi: 10.1097/BLO.0b013e31805d85e4.
28. Saiz P, Virkus W, Piasecki P, Templeton A, Shott S, Gitelis S, *et al.* Results of giant cell tumor of bone treated with intralesional excision. Clin Orthop Relat Res 2004; 424:221-6.
29. Turcotte RE, Wunder JS, Isler MH, Bell RS, Schachar N, Masri BA, *et al*. Giant cell tumor of long bone: A Canadian Sarcoma Group study. Clin Orthop Relat Res 2002;397:248-58.
30. von Steyern FV, Kristiansson I, Jonsson K, Mannfolk P, Heinegård D, Rydholm A, *et al.* Giant-cell tumour of the knee: The condition of the cartilage after treatment by curettage and cementing. J Bone Joint Surg Br 2007;89:361-5. doi: 10.1302/0301-620X.89B3.18604.
31. Mjöberg B, Pettersson H, Rosenqvist R, Rydholm A. Bone cement, thermal injury and the radiolucent zone. Acta Orthop Scand 1984;55:597-600.
32. Wada T, Kaya M, Nagoya S, Kawaguchi S, Isu K, Yamashita T, *et al.* Complications associated with bone cementing for the treatment of giant cell tumors of bone. J Orthop Sci 2002;7:194-8. doi: 10.1007/s007760200033.
33. Benevenia J, Rivero SM, Moore J, Ippolito JA, Siegerman DA, Beebe KS, *et al.* Supplemental bone grafting in giant cell tumor of the extremity reduces nononcologic complications. Clin Orthop Relat Res 2017;475:776-83. doi: 10.1007/s11999-016-4755-x.