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Giant cell tumour of bone around the knee: a systematic review of the functional and oncological outcomes

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- Giant cell tumour of bone (GCT) is a relatively rare, locally aggressive benign neoplasm observed in the long bone epiphyseal-metaphyseal regions of young adults.

- The optimal treatment strategy for these tumours remains controversial, and a huge amount of contradictory data regarding the functional and oncological outcomes can be found. Therefore, we performed a systematic review intended to investigate the functional and oncological outcomes after surgical treatment of GCTs arising around the knee, namely in the distal femur and proximal tibia.

- A trend towards better oncological control was found using wide resections, nonetheless, curettage-based techniques achieve a highly acceptable recurrence rate with overall better knee function. A slight advantage favouring proximal tibia GCTs regarding the Musculoskeletal Tumor Society (MSTS) score was also observed.

- Prospective studies comparing groups of more homogeneous patients, tumours, and treatment options should be developed to obtain more conclusive and definitive results regarding the optimal strategy for treating GCTs.

Introduction

Giant cell tumour (GCT) of bone is a relatively rare, locally aggressive benign neoplasm associated with a wide pathological spectrum, ranging from latent benign to highly recurrent and, occasionally, malignant meta-static potential.[1–4] This tumour is commonly observed in the long bone epiphyseal-metaphyseal regions of young adults, with the most common age of onset being between 20 and 40 years old. The clinical symptoms are non-specific and may include local pain, swelling, and a limited range of motion (ROM) in the adjacent joint. Radiographs and magnetic resonance imaging (MRI) are the imaging modalities of choice for the diagnosis of this tumour.[1–3] One of the most distinguishing clinical features of GCTs is the formation of extensive osteolytic lesions in the long bone epiphyseal-metaphyseal transitional areas.[3,5] Histologically, mononuclear cells are the primary feature, and they determine the biological behaviour of this tumour.[2,6,7] GCTs occur mainly around the knee joint, involving the distal femur or the proximal tibia. Nonetheless, this tumour can involve virtually any bone, with the distal radius, proximal humerus, or the proximal femur as other frequent locations.[5,8]

Wide resection and intralesional resection with curettage are two of the most common options for surgical treatment. When curettage is performed, local adjuvant therapies are often used to reduce the probability of a local recurrence, which is usually high.[5,8] Observational data indicate higher rates of local recurrence with intralesional curettage in comparison to more extensive surgery, even with the addition of an adjuvant.[8] As such, and despite the common use of local adjuvants after curettage, the role of these adjuvant therapies remains controversial. It is important to note that GCTs are not sensitive to radiotherapy or chemotherapy, often used against other primary bone tumours.[1,9]

Distant metastases and malignant lesions may also occur in GCTs, but they are rare.[1,2,4] Additionally, pulmonary metastases do not carry the same connotation as metastases associated with malignant tumours,

such as sarcoma. In most cases, the clinical behaviour is benign, and metastatic disease does not lead to patient's death.[10,11]

Methods

This study is a systematic review of published studies in the English-language literature concerning the outcomes obtained with surgical treatment of GCTs of bone located around the knee, namely those arising in the two most common anatomical sites: distal femur and proximal tibia.

To develop a systematic review, two electronic databases were used: Medline/PubMed and Scopus databases, using a search from 2000 to September 2020. We systematically searched for studies that included the keywords/MeSH words:(((("Osteoclastoma" OR "giant cell tumor" OR "giant cell tumour" OR "GCT") AND ("proximal humerus" OR "distal radius" OR "proximal femur" OR "distal femur" OR "proximal tibia")) AND ("outcomes" OR "surgical revision" OR "pain" OR "range of motion" OR "recurrence" OR "metastases" OR "infection"))). Our initial search included GCT of bone from all the most affected locations in the appendicular skeleton, from which we finally retrieved the studies that solely involved the distal femur, the proximal tibia, or both. The last search date was 24 September 2020.

For the inclusion criteria, we applied the Population, Intervention, Comparison, Outcome (PICO) strategy. We defined the following as:

1. Population: adult population (+18 years) with diagnosis of GCT of bone in the distal femur and/or proximal tibia.
2. Intervention: any given surgical technique with or without local adjuvants used to treat GCTs of bone.
3. Comparison: to compare the functional and oncological results obtained after surgical treatment of distal femur and/or proximal tibia GCTs.
4. Outcomes: local recurrence of the disease; ROM; infection; need for surgical revision; metastatic disease; functional status (using the Enneking/ Musculo Skeletal Tumor Society (MSTS) score).

We included all prospective and retrospective observational studies, randomized controlled trials, case-controlled studies, and cohort studies. We excluded review articles, case report studies, articles with full text in languages other than English; articles with only abstracts available, and articles where the full text was not accessible. To achieve more consistency in the information retrieved, papers that did not include at least 10 patients and 24 months mean follow-up were also excluded.

Whenever needed, the Enneking/MSTS score was converted to its percentage form to provide more homogeneous and comprehensive information for analysis.

Results

Article selection

A total of 851 articles (304 from PubMed/Medline and 547 from Scopus databases) were initially identified using the above-specified criteria. With the software available in rayyan.qcri.org we identified articles with more than 90% duplication, which were eliminated. After excluding the duplicated articles between both databases, 586 articles were pre-selected. The initial selection was followed by a title and abstract analysis for confirmation of the MESH keywords searched, the inclusion and exclusion criteria. The title and abstract analysis allowed us to further exclude 538 articles and, as such, 48 articles remained for full reading and analysis. After further reading we additionally excluded 34 papers due to conflicting information, lack of clarity of the information, extremely heterogeneous series, insufficient follow-up or series numbers, as these would have invalidated a proper analysis. For the final selection, we included 14 articles (Fig.1): two prospective and 12 retrospective studies.

Epidemiology

A careful analysis of the articles included in this systematic review allowed us to identify a total of 670 patients with GCT around the knee, with 356 of these located in the distal femur and 302 in the proximal tibia. The majority of these tumours (628) were primary GCTs, while the remaining 42 cases were recurrences. A male predominance was observed with 369 cases compared with 301 female patients. The majority of these GCTs were classified as Campanacci (or Enneking in fewer occasions) grade III lesions (316 among 566 tumours classified and reported).[12,13] We could also identify 57 pathologic fractures at presentation (8.7% of whole study group) – Table 1.

All tumours were surgically treated using one of two surgical techniques: intralesional curettage supplemented with different local adjuvants, bone graft or/and polymethyl methacrylate (PMMA); or wide tumour resection followed by reconstruction, which also could include a wide range of options (Table 2).

Outcomes

Almost all studies included in this systematic review reported on local recurrence, except the paper published by Zheng et al (Table 2).[14] In the 13 studies where local recurrences were reported, we found an overall recurrence rate of 7.1% (38 local recurrences out of 534
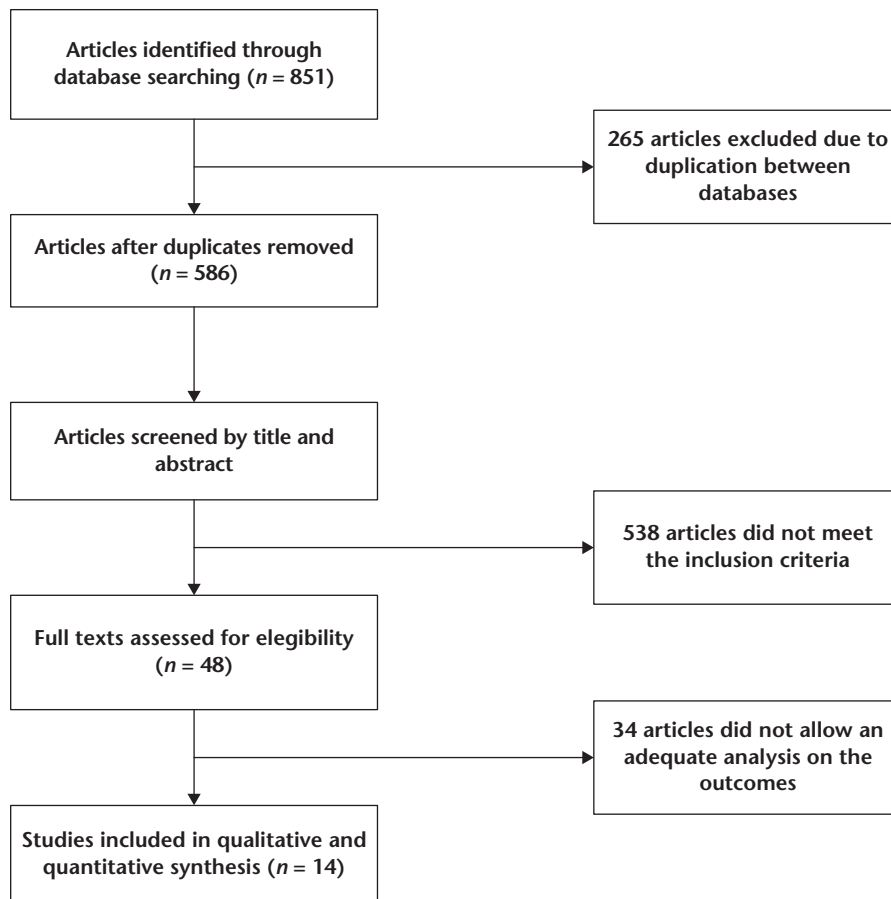
Fig. 1 Flowchart illustrating the search strategy and number of records screened and included.

patients). Among these 38 recurrences, it was only possible to identify the specific anatomical location in 20 cases, with 10 arising in the distal femur and the remaining 10 in the proximal tibia. Also, among the 38 local recurrences, the tumour grade was only mentioned in 14 cases, with Campanacci grade III tumours identified in 50% of this group (7 out of 14). Local recurrence occurred in 11% (35 out of 317) of all patients treated with curettage and local adjuvants. Meanwhile, local recurrences arose in three patients among the 217 treated with wide resection, corresponding to a 1.4% local recurrence rate.

Among the 38 recurrences reported, we could only find information regarding the revision surgical option in 21 occasions, and an equal distribution was seen between curettage-based techniques, and wide resection with endoprosthetic replacement (Table 2).

In this review, metastatic disease was reported in two studies: the one published by Chen et al and the one published by Teng et al.[15,16] In the first case, only one patient with metastasis was identified (2.6%), and in the second

report, two patients had metastases, which meant an overall metastatic rate of 1.9%. Since metastatic disease is not mentioned in seven of the papers herein included, we used the remaining seven where the authors report on this topic to estimate an 0.8% overall metastatic rate (3 out of 360 patients).[15–21]

Only a few studies reported on the knee's ROM after surgical treatment for GCT of bone (Table 3). Nonetheless, some authors in this review published on this topic.[18,19,22,23] Based on these four studies, the overall mean ROM was 107° (range, 30–140°). The reports promoted by Ayerza et al and Kundu et al,[22,23] where curettage was applied, presented a mean ROM of 114° (range, 96–136°), while a mean ROM of 95° (range, 30–140°) was documented in the studies published by Li et al and Yu et al,[18,19] where tumoral wide resections were used. Additionally, Kundu et al were the only authors presenting data regarding the ROM and GCT location for each of their 25 patients. The mean ROM found for the GCTs in the distal femur was 123° (range, 98–130°), while the proximal tibia achieved a ROM of 124° (range, 96–136°).[18,19,22,23]

Table 1. Epidemiological data on the studies included in this systematic review

Author	Year	Nature of the study	N	M/F ratio	Anatomical location (number of cases)	Primary/ Recurrent GCTs	Campanacci classification	Pathologic # at presentation	Mean follow-up (months)
Chen et al[15]	2005	Retrospective	38	19/19	Distal femur (17); proximal tibia (21)	All primary GCTs	Grade I – 3 pts; Grade II – 20 pts; Grade III – 15 pts	5	58
Suzuki et al[27]	2007	Retrospective	30	21/9	Distal femur (17); proximal tibia (13)	All primary GCTs	Grade I – 10 pts; Grade II – 10 pts; Grade III – 10 pts	∅	57
Natarajan et al[17]	2007	Retrospective	143	81/62	Distal femur (87); proximal tibia (56)	Primary (134) / Recurrent (9)	Grade II – 14 pts; Grade III – 129 pts (Enneking)	40	65
Li et al[18]	2008	Retrospective	13	8/5	Proximal tibia (13)	Primary (3) / Recurrent (9)	Grade I – 1 pts; Grade II – 5 pts; Grade III – 7 pts	∅	108
Abdelrahman et al[25]	2009	Prospective	28	10/18	Distal femur (14); proximal tibia (14)	All primary GCTs	Grade I – 10 pts; Grade II – 14 pts; Grade III – 4 pts	∅	34
Ayerza et al[22]	2009	Retrospective	22	16/6	Distal femur (12); proximal tibia (10)	Primary (19) / Recurrent (3)	Grade II – 18 pts; Grade III – 4 pts	∅	48
Yu et al[19]	2010	Retrospective	19	11/8	Distal femur (12); proximal tibia (7)	Primary (9) / Recurrent (10)	Grade III – 19 pts	4	129
Saikia et al[26]	2010	Retrospective	32	18/14	Distal femur (17); proximal tibia (15)	Primary (27) / Recurrent (5)	Grade II – 5 pts; Grade III – 27 pts	3	96
Yu et al[20]	2013	Retrospective	16	7/9	Distal femur (16)	Primary (12) / Recurrent (4)	Grade I – 2 pts; Grade II – 11 pts; Grade III – 3 pts	∅	28
Saibaba et al[28]	2014	Retrospective	36	22/14	Distal femur (13); proximal tibia (23)	Primary (34) / Recurrent (2)	Grade I – 2 pts; Grade II – 18 pts; Grade III – 16 pts	5	60
Kundu et al[23]	2015	Prospective	26	15/11	Distal femur (15); proximal tibia (11)	All primary GCTs	Grade II – 10 pts; Grade III – 16 pts	∅	41
Zheng et al[14]	2017	Retrospective	136	72/64	Distal femur (67); proximal tibia (69)	All primary GCTs	Grade I – 15 pts; Grade II – 63 pts; Grade III – 58 pts	∅	86.5
Wu et al[21]	2018	Retrospective	27	11/16	Distal femur (18); proximal tibia (9)	All primary GCTs	Grade I – 5 pts; Grade II – 14 pts; Grade III – 8 pts	∅	33
Teng et al[16]	2019	Retrospective	104	58/46	Distal femur (63); Proximal tibia (41)	All primary GCTs	NF	∅	33

Notes. NF, data not found; N, number; M/F, male/female; GCTs, giant cell tumours; #, fracture; PMMA, polymethyl methacrylate.

When reporting on functional data in the oncology setting, the MSTS score is the most commonly used metric. Of the 14 papers included in this systematic review, 12 presented data on this subject; however, we could only extract valid information from 11 reports.[24] The mean overall MSTS score was 88.9% (range, 75.6–95.0%), with a mean MSTS score of 90.1° (range, 85.7–94.3°) for the curettage group, and a mean MSTS score of 85.6% (range, 75.6–95.0%) for the wide resection group. When analysing the MSTS score for each anatomical location, we could only find enough data in seven of the 14 reports.[18,19,21–23,25,26] Based on these seven studies, an overall MSTS score of 87.2% was found in the distal femur group (which included 85 cases); while for the proximal tibia, the overall MSTS score was 90.6% (which included 77 cases). Regarding the treatment strategy, we found data concerning 57 distal femurs treated with curettage, with a mean MSTS score of 90%. Among the 28 distal femur cases where a wide resection was

performed, the mean MSTS score was 81.6%. In this setting, 43 proximal tibias underwent curettage, and the mean MSTS score was 92.7%. For the 34 cases where wide resection was applied, the mean MSTS score was 88%. The range values regarding the mean MSTS scores for these groups (distal femur and proximal tibia) were not possible to determine, since some authors only provided a mean MSTS score for a specific anatomical location.[18,22] Also, we could not correlate the anatomical location, function, and tumour classification grade due to the lack of data.

After a meticulous analysis of all articles included in this review, we found a very low global infection rate, since the overall infection rate was 4.5%. Additionally, among the curettage group, the mean infection recorded was 4.1%, while in the resection group, it was 5.3%. These data were extracted from 10 papers since four did not present information regarding infection.[16,20,27,28] Also, a correlation between infection and anatomical location was

Table 2. Oncological outcomes after surgical treatment and revision techniques after local recurrence

Author	Surgical technique	Local recurrence	Mets	Surgical revision due to LR or Mets
Chen et al[15]	Curettage plus bone graft (28 patients) vs. wide resection and reconstruction using hemijoint allograft (6 patients), custom-made endoprosthesis (3 patients) or an alloprosthetic composite (1 patient)	13.2% (5 patients)	2.6% (1 patient)	6 patients; NOS for the technique used
Suzuki et al[27]	Curettage plus high-speed burr plus electrocauterization plus saline/water plus autogenous bone graft (18 patients) vs. curettage plus high-speed burr plus electrocauterization plus saline/water plus autogenous bone graft and PMMA (9 patients) vs. curettage plus high-speed burr plus electrocauterization plus saline/water plus PMMA (3 patients)	33.3% (10 patients)	NF	10 patients (9 cases treated with new curettage plus PMMA without further recurrences; 1 case treated with endoprosthetic replacement)
Natarajan et al[17]	Wide resection (en bloc) and custom-made knee endoprothesis	0.7% (1 patient)	0%	1 patient (local wide resection)
Li et al[18]	Wide resection (en bloc) and reconstruction with bone graft (using a fibula graft as strut and iliac crest graft) plus screws	7.7% (1 patient)	0%	1 patient (wide resection and endoprosthesis replacement)
Abdelrahman et al[25]	Curettage plus cryotherapy and bone graft (optional) plus PMMA (10 patients) vs. curettage plus cryotherapy plus bone graft (optional) plus PMMA and internal fixation with intramedullary hardware (18 patients)	3.6% (1 patient)	0%	1 patient (wide resection and endoprosthesis replacement)
Ayerza et al[22]	Curettage plus phenol plus cancellous bone plus structural allograft plus internal fixation (LCP plate)	9.1% (3 patients) – 2 cases with bone recurrence and other with a soft tissue recurrence	NF	3 patients (2 cases treated with wide resection and allograft-prosthetic composite; the other case managed only with resection)
Yu et al[19]	Wide resection (en bloc) and tumoral endoprosthesis (15 hinge knee and 4 rotating-hinge knee)	0.0%	0%	∅
Saikia et al[26]	Wide resection (en bloc) and knee arthrodesis with dual fibulae plus cancellous bone graft plus 95° condylar blade plate	3.1% (1 patient)	NF	1 patient (treated with an above-knee amputation due to local recurrence with extensive soft tissue involvement and fungation)
Yu et al[20]	Curettage plus PMMA plus internal fixation and oral bisphosphonates	0.0%	0%	∅
Saibaba et al[28]	Curettage plus phenol plus subchondral bone graft plus gel foam layer plus PMMA	2.8% (1 patient)	NF	1 patient (treatment option not revealed)
Kundu et al[23]	Curettage plus high-speed burr plus electrocautery on spray plus autograft in the subarticular area plus gel foam layer and PMMA	11.5% (3 patients)	NF	3 patients (1 case treated with new curettage plus high-speed burr plus electrocautery on spray plus autograft in the subarticular area plus gel foam layer and PMMA; 2 cases treated with resection and knee arthrodesis)
Zheng et al[14]	Curettage plus PMMA (50 patients) vs. curettage plus bone graft (86 patients)	NF	NF	Yes but NOS
Wu et al[21]	Curettage plus subchondral bone grafting plus PMMA	3.7% (1 patient)	NF	1 patient (wide resection and endoprosthesis replacement)
Teng et al[16]	Curettage plus PMMA alone vs. curettage plus PMMA-combined bone grafting	10.6% (11 patients)	1.9%	NF

Notes. NF, data not found; NOS, no other specification; LR, local recurrence; Mets, distant metastasis; PMMA, polymethyl methacrylate; LCP, locking compression plate;

impossible to establish due to the low number of infections and the lack of information on this particular topic.

Among the 14 articles herein included, only three authors did not report on the specific need for another surgery after the initial treatment.[14,16,28] The remaining 11 studies highlighted the need for surgical revision, which took place mainly due to local recurrences, infections, and orthopaedic-implant-related problems (Table 2). Despite some difficulty in identifying throughout the papers the exact number of patients in need of surgical revision, and for what reasons, the available data allowed us to calculate that at least 18% (71 out of 394) of the patients needed additional surgical procedures. However, this number is underestimated (Tables 2 and 3). Among the curettage group, the calculated surgical revision rate was 15.8% (28 out of 177 patients), while among the wide resection group, this rate was higher at 20.1% (43 out of 207 patients).

Table 3. Functional outcomes after surgical treatment and surgical revisions for other causes than local recurrence

Author	Mean ROM	MSTS score	Infection rate	Osteoarthritis	Surgical revision for other causes than LR
Chen et al[15]	NF	88%	0%	5 patients had severe post-op osteoarthritis	Ⓘ
Suzuki et al[27]	NF	NF	NF	10 patients developed secondary osteoarthritis	3 patients (due to post-operative fractures)
Natarajan et al[17]	NF	Excellent in 90 patients (62%); good in 39 patients (27%); fair in 7 (5.5%); poor in 7 (5.5%)	6.3%	NA	29 patients (9 due to infection; 2 cases of flap necrosis; 12 peri-prosthetic fractures; 2 cases of prosthetic mechanical failure; and 4 cases of aseptic loosening)
Li et al[18]	132.5°	95%	0%	NA	1 patient (due to wound fat necrosis)
Abdelrahman et al[25]	NF	93.9%	3.6%	Ⓘ	Ⓘ
Ayerza et al[22]	119°	94.3%	0%	Ⓘ	∅
Yu et al[19]	74.4°	75.6%	5.3%	NA	8 patients (1 case due to infection; 1 case of aseptic loosening with fracture; 3 cases of aseptic loosening; 2 cases of septic loosening; and 1 case of peri-prosthetic fracture)
Saikia et al[26]	NA	87%	3.1%	NA	2 patients (1 for infection; 1 due to wound dehiscence)
Yu et al[20]	NF	89%	NF	Ⓘ	Yes (due to mechanical problems NOS)
Saibaba et al[28]	NF	92%	NF	Ⓘ	NF
Kundu et al[23]	118°	90%	3.8%	Ⓘ	1 patient (due to infection)
Zheng et al[14]	NF	85.7%	5.8%	Ⓘ	Yes (due to infection; post-operative fractures; rejection reaction NOS)
Wu et al[21]	NF	87.3%	3.7%	2 patients (7.4%) had progressed to KL grade 1 arthritic changes and 1 patient had progressed to KL grade 2 (3.7%).	Ⓘ
Teng et al[16]	NF	NF	NF	Ⓘ	Ⓘ

Notes. NF, data not found; NA, not applicable; NOS, no other specification; ROM, range of motion; MSTS score, Musculoskeletal Tumour Society score; PMMA, polymethylmethacrylate; LR, local recurrence; KL, Kellgren and Lawrence system for classification of osteoarthritis.

Discussion

Since GCTs arise most often in the long bone epiphyseal-metaphyseal regions, articulations are often involved, and even though GCTs of bone can arise in virtually any anatomical location, the distal femur and proximal tibia are by far the most common regions affected.[5,8,29,30] Our choice for the subject of this systematic review was based on the above-mentioned facts, fed by the need to summarize the functional and oncological outcomes provided by the current practice.

Depending on the involvement of the articular surfaces, the tumour can be removed either by wide resection (Fig. 2) or curettage with or without local adjuvants (Fig. 3).[1,9,31,32] As expected, and based on historic series, optimal outcomes arise when a tumour is removed with free margins, minimal morbidity and an acceptable functional outcome.[13,33] In this setting, several studies report higher rates of local recurrence with intralesional curettage, even with the introduction of extensive curettage and local adjuvants.[8,30,32,34–39] In a large retrospective study of 384 patients with a decade of follow-up,

recurrence rates were higher in patients treated with intralesional curettage versus those treated with wide excision (33% vs 2%). Nonetheless, among those patients treated with curettage, the addition of bone cement as an adjuvant decreased the local recurrence rate to 22%.[8] The use of a wide range of adjuvants after curettage, such as the local application of phenol, PMMA, liquid nitrogen or a combination of several options, is the consequence of a systematic attempt to minimize recurrence rates. The use of phenol and PMMA is probably the most established treatment to use following curettage, but without clear superiority compared to other options.[30,34–37]

Local recurrence is a devastating event, and, as such, all oncological series take this into account. Some papers in this systematic review documented low recurrence rates with curettage-based techniques. Abdelrahman et al are an example of this finding, reporting a 3.6% local recurrence rate in a prospective study including 28 patients.[25] Another example can be found in the paper by Yu et al, who operated on 16 patients performing curettage and tumoral cavity filling with PMMA, complemented with internal fixation and oral bisphosphonates, without local
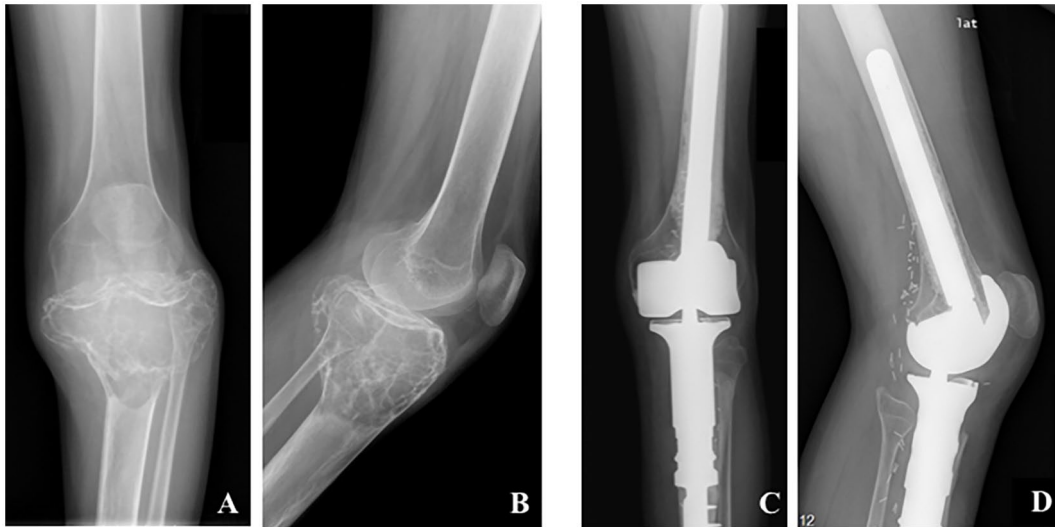
Fig. 2 Proximal tibia giant cell tumour (GCT) treated with wide excision and an allograft-prosthesis composite. (A) Pre-operative anteroposterior (AP) view; (B) pre-operative lateral view; (C) post-operative AP view; (D) post-operative lateral view.
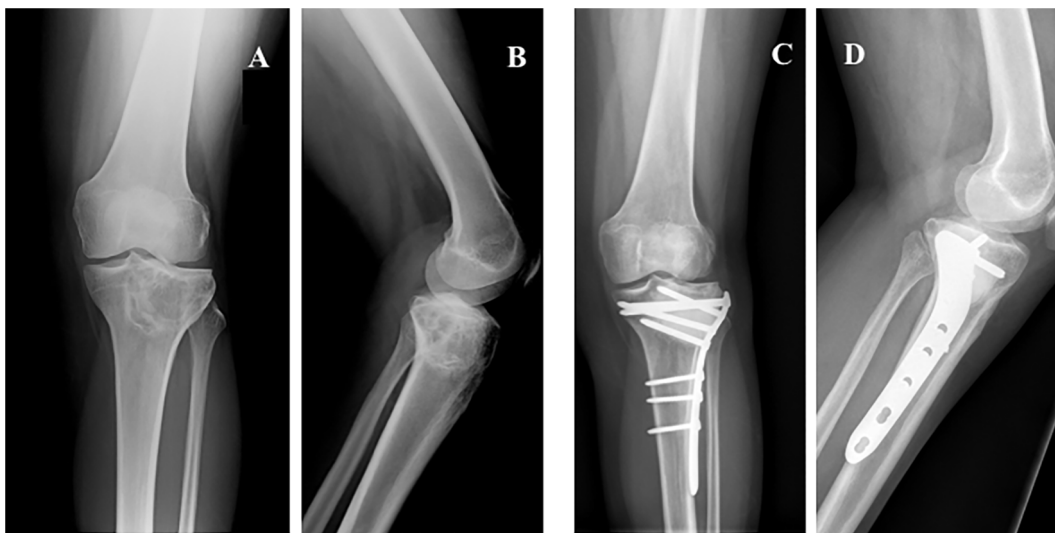

Fig. 3 Proximal tibia giant cell tumour (GCT) treated with intralesional curettage plus subchondral bone graft plus polymethyl methacrylate (PMMA) and internal fixation. (A) pre-operative anteroposterior (AP) view; (B) pre-operative lateral view; (C) post-operative AP view; (D) post-operative lateral view.

recurrences detected.[20] The scientific basis behind using oral bisphosphonates in this scenario would be the ability of this drug to stabilize local and even metastatic GCTs. However, the level of evidence for the efficacy of this practice is admittedly low and cannot be recommended as current practice.[40,41] Saibaba et al also reported a very low recurrence rate despite the 16 Campanacci grade III GCTs in their series.[28] Wu et al also found a similar result with a 3.7% local recurrence rate.[21] Taking into account all these findings, and excluding the report by Suzuki et al, the overall recurrence rate associated with intralesional

curettage supplemented by adjuvants was below 15%, which contradicted higher recurrence rates often reported in literature.[32,39,42] These results can be explained by the heterogeneity of patients included in the published series, since we often find different tumour grades, primary, and recurrent GCTs among them. The effort towards building a more homogeneous series in recent years can explain the progressively lower recurrence rates documented.

The results herein summarized for wide resections of GCTs regarding local recurrence support an extremely low local recurrence rate with this technique. The series

reported by Natarajan et al included 143 patients with 129 tumours classified as Enneking grade III. Nonetheless, and after wide resection and reconstruction using a custom-made knee endoprosthesis, the recurrence rate was 0.7%.[17] Similar findings were reported by Li et al, with no recurrences after performing wide resections.[18]

To manage local recurrences, an equal distribution between curettage-based techniques and wide resection could be observed. Regarding this topic, Balke et al reported acceptable re-recurrence rates after new curettage, burring and additional PMMA, and also Raskin et al, in their revision, considered additional intralesional curettage after recurrence, an appropriate procedure.[32,43] Van der Heijden et al also support the possibility for curettage after recurrence at the expenses of a reasonable re-recurrence rate.[31]

This review confirms GCT metastatic disease as a rare phenomenon. Only two studies reported on lung metastasis associated with GCTs, and in both cases, the metastatic rate was below 3%, with an overall metastatic rate estimation of 0.8%. In none of the cases, deaths were reported as being related to the metastatic disease.

For the majority of orthopaedic oncologists, the decision between curettage and wide resection in GCTs is based on the Campanacci classification, since there is a historical tendency to perform more aggressive surgery for grade III tumours.[1,9,13,31,32] However, a grade III tumour does not preclude the curettage technique, and even though Campanacci grade III tumours seem to recur more often after curettage, the recurrence rates herein presented are often low. In this setting, it is important to highlight a trend toward pathologic fractures at presentation with Campanacci grade III tumours, as published by Saibaba et al, who reported five pathologic fractures in 36 patients.[28] Chen et al also found five pathologic fractures at presentation, all associated with Campanacci grade III tumours.[15]

One of the most difficult balances when operating on patients with GCTs is the surgical morbidity and future function of the joint. Herein, the best functional results were obtained when curettage-based techniques were used.[22,23] Also, the limited analysis on the ROM achieved within distal femur and proximal tibia GCTs showed a mean ROM of 123° (range, 98–130°) for the distal femur and 124° (range, 96–136°) in the proximal tibia, which meant a similar outcome.

The MSTS scores published in the different series very often reflected good or excellent functional outcomes.[24,25] Nonetheless, the worst MSTS scores were seen after wide resections.[19] In the end, the overall MSTS score found for the curettage group was 90.1%, while the wide resection group had a mean MSTS score of 85.6%. Additionally, a slightly better MSTS score was found for the proximal tibia when compared with the distal femur (90.6% vs. 87.2%).

This systematic review highlights a low overall infection rate with a 4.1% infection rate recorded for the curettage group and 5.3% in the wide resection group. These data were extracted based in only 10 papers, since four did not present information regarding infection. Among them, Zheng et al published the largest series on intralesional curettage procedures included in this systematic review, reporting a 5.8% infection rate.[14] Similarly, Natarajan et al reported the largest series of wide resections included in this review and observed a 6.3% infection rate.[17] Overall, and based on the findings gathered in this review, it is not possible to attribute a higher infection rate proportion towards wide resections, when compared with intralesional curettage. Additionally, a correlation between infection and anatomical location was also impossible to establish due to the low number of infections and the lack of information on this particular topic.

The need for surgical revision was common (Table 2 and 3). Most often, the underlying causes were local recurrence, infection, or implant-related complications. In the study published by Yu et al, almost 50% of patients presented aseptic loosening and infections related to the endoprosthesis.[19] Natarajan et al also highlighted an important number of patients with similar complications (Table 3).[17] For Suzuki et al, the need for surgical re-interventions reached more than 40% of the series (13 patients), particularly due to local recurrence and fractures.[27] In their large series, Teng et al found a considerable number of mechanical failures associated with reconstructions after curettage and local adjuvants.[16] These authors also found that reconstructions in the distal femur are three times more at risk for mechanical failure, when compared with the proximal tibia. The explanation could lie in the rotational force that is applied to the femoral condyles during the last 20° of knee flexion and extension.[16]

Based on the available data, we estimated a minimum of 18% for new surgical procedures, which is an underestimation. This revision rate was higher among patients treated with wide resections (22.7%).

This systematic review represents a sum of the functional and oncological outcomes published regarding GCTs in the distal femur and proximal tibia. Overall, among 14 papers included, only two were prospective case series, with the remaining 12 being retrospective studies. Despite the limitations, this review allows us to gain important insights. First, there is a trend towards fewer local recurrences when wide resections are performed to treat GCTs. Nonetheless, the recurrence rates after curettage-based techniques seem to be lower than previously reported in the literature, and, as such, could be an acceptable approach even for Campanacci or Enneking grade III tumours and in the presence of pathologic fractures. Second, there is also a trend towards better function in the knee when curettage and local adjuvants are used. However, the results obtained

with wide resection are also good, reporting acceptable ROMs and MSTS scores. In this particular setting, slightly better MSTS scores were achieved for GCTs that arose in the proximal tibia. Third, this systematic review did not find any evidence of higher infection rates associated with aggressive resections and reconstructions. Additionally, intralesional curettage and local adjuvants presented significant failures due to subchondral fractures and articular collapse, while reconstructions with tumoral endoprosthesis were prone to aseptic loosening or periprosthetic fractures. In the end, each surgical option has its pros and cons, but based on this review, we should promote, whenever possible, techniques that allow maximal preservation of the knee articulation.

Conclusions

The optimal treatment for GCTs arising around the knee remains controversial. Despite the trend towards better oncological control of this tumour after wide resections, the recurrence rates achieved through a more conservative procedure such as the curettage-based interventions seem to be acceptable. Additionally, curettage and local adjuvants allow for overall better function of the knee, in particular with proximal tibia GCTs.

There is a clear lack of high-quality studies regarding GCTs of bone to support a gold-standard option. As such, prospective studies comparing groups of more homogeneous patients, tumours, and treatment options, should be designed, to achieve more conclusive results regarding the optimal strategy to follow.

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ICMJE CONFLICT OF INTEREST STATEMENT
The author declares no conflict of interest relevant to this work.

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