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Combined preoperative denosumab and adjuvant microwave ablation for high-risk giant cell tumor of bone: a retrospective study in a single center

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Abstract

Background Giant cell tumor of bone (GCTB) is a locally aggressive neoplasm with a high propensity for recurrence following intralesional curettage. The introduction of denosumab, a RANKL inhibitor, has shown potential in facilitating joint-sparing surgery. However, concerns exist regarding its impact on local recurrence rates. This study aimed to evaluate the efficacy and safety of combined preoperative denosumab with adjuvant microwave ablation (MWA) for the treatment of high-risk GCTB.

Methods We conducted a retrospective review of 19 patients with high-risk GCTB who underwent preoperative denosumab treatment followed by curettage and adjuvant MWA. The primary outcome measure was the local recurrence rate, with secondary outcomes including functional status assessed by the Musculoskeletal Tumor Society (MSTS) score and safety profile of the treatment.

Results In this retrospective analysis, we evaluated the outcomes of 19 patients with high-risk GCTB treated with preoperative denosumab and adjuvant MWA. The median follow-up duration was 33.1 months, 3 patients (15.8%) experienced local recurrence at a median of 21.6 months postoperatively and the local recurrence-free survival was 81.2% at two years. Notably, no patient developed lung metastasis, and all recurrences were successfully managed with repeat curettage and MWA, with a mean MSTS score of 27.3. No patient required joint replacement due to tumor recurrence, resulting in a 100% joint preservation rate.

Conclusion The combination of preoperative denosumab and adjuvant MWA is a feasible and effective strategy for the management of high-risk GCTB, providing effective local control with preserved joint function. This approach may offer a surgical alternative for young patients where joint preservation is paramount.

Keywords Denosumab, Giant cell tumor of bone, Joint preservation, Microwave ablation, Recurrence

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Introduction

Giant cell tumor of bone (GCTB) poses significant challenges in orthopedic oncology due to its aggressive nature and potential for recurrence and metastasis [1]. The primary treatment modality has historically been surgical intervention, with curettage and bone grafting being preferred to maintain joint function and reduce complications [2]. Nevertheless, this method is correlated to increased rates of local recurrence, whereas en-bloc resection provides a lower risk of recurrence but may compromise the native joint function [3, 4]. This conflict between preserving function and achieving optimal oncological outcomes presents a challenging clinical scenario for surgeons.

The introduction of denosumab, a monoclonal antibody that targets the nuclear factor kappa-B ligand (RANKL) pathway, has significantly transformed the treatment landscape for GCTB [5, 6]. Denosumab has demonstrated notable effectiveness in eliciting tumor response and facilitating surgical downstaging, allowing for joint-salvage procedures in cases previously considered unsuitable for preservation [7]. Acting as a monoclonal antibody, denosumab exerts therapeutic effects by specifically inhibiting the receptor activator of RANK. Within the context of GCTB, RANKL plays a central role in osteoclastogenesis, bone resorption and tumor progression [8]. The mechanism of action of denosumab involves the suppression of osteoclast activation, reduction in tumor size and formation of ossification in the lesions, thereby facilitating surgical intervention [9]. Denosumab is increasingly being recognized as a valuable neoadjuvant therapy for locally advanced GCTB, especially in cases where resection is not feasible or carries high risks of morbidity. While the benefits of denosumab in tumor response and downstaging are well-documented, debates persist regarding its role in GCTB, particularly concerning the impact on local recurrence rates following curettage.

The efficacy of denosumab relies on inducing osteosclerotic changes within the tumor matrix and facilitating less invasive surgical approaches like curettage. Preoperative denosumab has been shown to improve the feasibility of joint-salvage surgery by strengthening bone structural integrity, while osteosclerosis may present challenges during curettage procedures [10]. The consolidation of periarticular cortical subchondral bone could hinder the accurate delineation of tumor extent and complete removal, which potentially increased the risk of local recurrence [11]. Certain patients may necessitate arthroplasty as a result of multiple recurrences, and impede the success rate of joint salvage [12, 13]. Additionally, the implementation of various adjuvant therapies, such as high-speed burring, phenol application, and bone cement utilization, has not notably decreased rates of local recurrence [14]. Therefore, there is an urgent demand for treatment modalities that are both safer and effective to address the dual goals of local tumor control and preservation of joint function.

In recent years, microwave ablation (MWA) has been identified as a promising modality for the management of various tumors. The advantages of MWA include the ability to achieve larger ablation volumes in shorter procedural times through rapid induction of coagulation necrosis when compared to alternative techniques [15, 16]. Furthermore, MWA has been shown to elevate intertumoral temperatures, enhance tumor destruction and disrupt tumor vasculature and perfusion, resulting in increased therapeutic efficacy [15, 16]. As a result, MWA has garnered recognition as a safe and effective treatment for primary bone tumors and bone metastases [17, 18]. Therefore, the objective of this study is to investigate whether curettage following preoperative denosumab combined with adjuvant denosumab treatment could reduce the recurrence risk of periarticular GCTB and improve joint preservation rates and extremity function outcomes.

Patients and methods

Patients selection

Following institutional review board approval, we conducted a retrospective analysis of medical records pertaining to patients diagnosed with high-risk GCTB in the extremities. This study focused on cases treated at a single institution between 2019 and 2022. High-risk GCTB was defined as following: (1) the lesions with presence of extensive periarticular bone loss and minimal residual subchondral bone, (2) the lesions with a large soft tissue mass or pathological fracture. These factors were considered to render joint salvage impractical or uncertain, potentially leading to suboptimal functional outcomes and significant surgical morbidity. Preoperative assessment included radiographs, computed tomographic (CT) scans, and magnetic resonance imaging (MRI) to evaluate the bone destruction and lesion extent of involved sites. The inclusion criteria were defined as follows: patients with histologically confirmed GCTB, radiographically classified as Campanacci Grade II or III, and those who received preoperative denosumab therapy prior to definitive surgical intervention. Exclusion criteria included prior bisphosphonate or denosumab treatment for primary or recurrent GCTB, the presence of distant metastases from GCTB, or incomplete follow-up data precluding comprehensive outcome evaluation. All patients included in the study were skeletally mature and presented with either a primary diagnosis of GCTB or recurrent lesions. Following a thorough preoperative dental assessment, denosumab therapy was prescribed for patients with high-risk features that compromised

limb salvage and functional outcomes. The treatment regimen involved subcutaneous injections of 120 mg initially, followed by doses on days 8 and 15 of the first cycle, and subsequently at 4-week intervals until the scheduled surgical intervention. Concurrent administration of calcium (500 mg/day) and vitamin D (400 IU/day) supplements was provided to diminish potential adverse effects. Treatment response was assessed through serial plain radiographs and clinical evaluations conducted at 4 to 6-week intervals. Positive response indicators included the development of an ossified rim surrounding the soft-tissue component, thickening of subchondral bone, and progressive ossification within the lesion. Symptomatic improvements, such as reduced pain and swelling, along with enhanced mobility at the adjacent joint. Subsequently, the feasibility of extensive curettage with joint-preserving surgery was discussed by a multidisciplinary team. In cases where denosumab treatment rendered the periarticular bone and joint surface salvageable, intralesional extensive curettage was performed. However, if limb salvage was deemed unattainable, resection and reconstruction with a modular prosthesis were performed as an alternative strategy.

Surgical technique

After the completion of the preoperative denosumab regimen, all patients demonstrated residual tumors and subsequently underwent surgery, typically within one month following the final denosumab injection. Surgical management of high-risk GCTB in this study was conducted by the same group of orthopedic surgeons using standardized protocols. The surgical procedures adhered to established extensive curettage protocols, with meticulous exposure to facilitate tumor debulking. Before ablation, careful dissection was performed to separate tumor-involved bone and infiltrated soft tissues from adjacent normal tissues using gauze, particularly crucial in cases with pathological fractures. Ablation procedures were carried out utilizing a microwave ablation (MWA) system (2450 MHz, MTI-5 A, Great Wall, Nanjing, China), with the insertion of multiple MWA antennas into the lesion site. Simultaneously, a thermometer needle was strategically placed in normal tissue to monitor surrounding tissue temperature throughout the ablation process, minimizing the risk of inadvertent damage to neurovascular structures. To ensure optimal tumor cell inactivation, lesions were subjected to temperatures ranging from 60 to 80 °C, with power settings of 30 to 50 watts applied for durations of 3 to 5 min, adjusted according to lesion size and extent. During ablation, the microwave antennas were repositioned to ensure overlapping ablation zones and placed at lesion peripheries to achieve a broader ablation margin. Additionally, cryogenic saline was employed to cool adjacent normal tissue, thereby reducing the risk of thermal injury to critical neurovascular structures.

Once the lesion showed thoroughly coagulative necrosis, the ablation procedure was conducted. Subsequently, meticulous intralesional curettage was performed through a large cortical bone window using curets of various sizes to excise all visible regions of the tumor. Further curettage of the cavity was carried out with a high-speed burr to debride the sclerotic bone and tumor matrix, followed by irrigation with distilled water to remove any remaining tumor tissues. To ensure the complete eradication of residual tumors, electrosurgical inactivation was used with a spray coagulation mode, allowing for thermal penetration beyond the visible tumor margins. The residual cavity was then meticulously curetted again to remove any burnt tissue, paying close attention to the periphery of the lesion where tumor cells may be present. Following the placement of bone chip allografts in the subchondral area to shield the articular surface from cement-induced thermal effects and provide mechanical support to the articular surface, the cavity was subsequently filled with cement. The prophylactic stabilization with internal fixation was performed to reduce the risk of pathological fracture depending on the extent of lesions (Fig. 1).

Postoperative management

None of the patients included in this study received postoperative denosumab. Follow-up appointments were scheduled monthly in the outpatient clinic for the first 3 months, followed by evaluations every 3 months thereafter. At each follow-up visit, both clinical and radiological assessments were required to evaluate the functional outcomes and local disease control. Additionally, chest radiographs were performed semi-annually to screen for lung metastasis. Functional outcomes were assessed using the Musculoskeletal Tumor Society (MSTS) score, which comprehensively evaluates pain, upper or lower limb function, emotional acceptance, and ambulatory status. Recurrence-free survival was defined as the duration from the initial surgery to the detection of local recurrence on radiographic imaging during follow-up.

Statistical analysis

The statistical analysis for this study utilized STATA Statistical Software (version 16, College Station, TX, USA) and was conducted by the authors Chuanxi Zheng and Jin Qiu. Descriptive statistics, comprising mean and standard deviation or range for continuous variables and number and percentage for categorical variables, were computed. To assess the association between categorical variables, a chi-square test (or Fisher exact test) was employed, while continuous variables were compared using an unpaired Student t-test. Survival estimates were

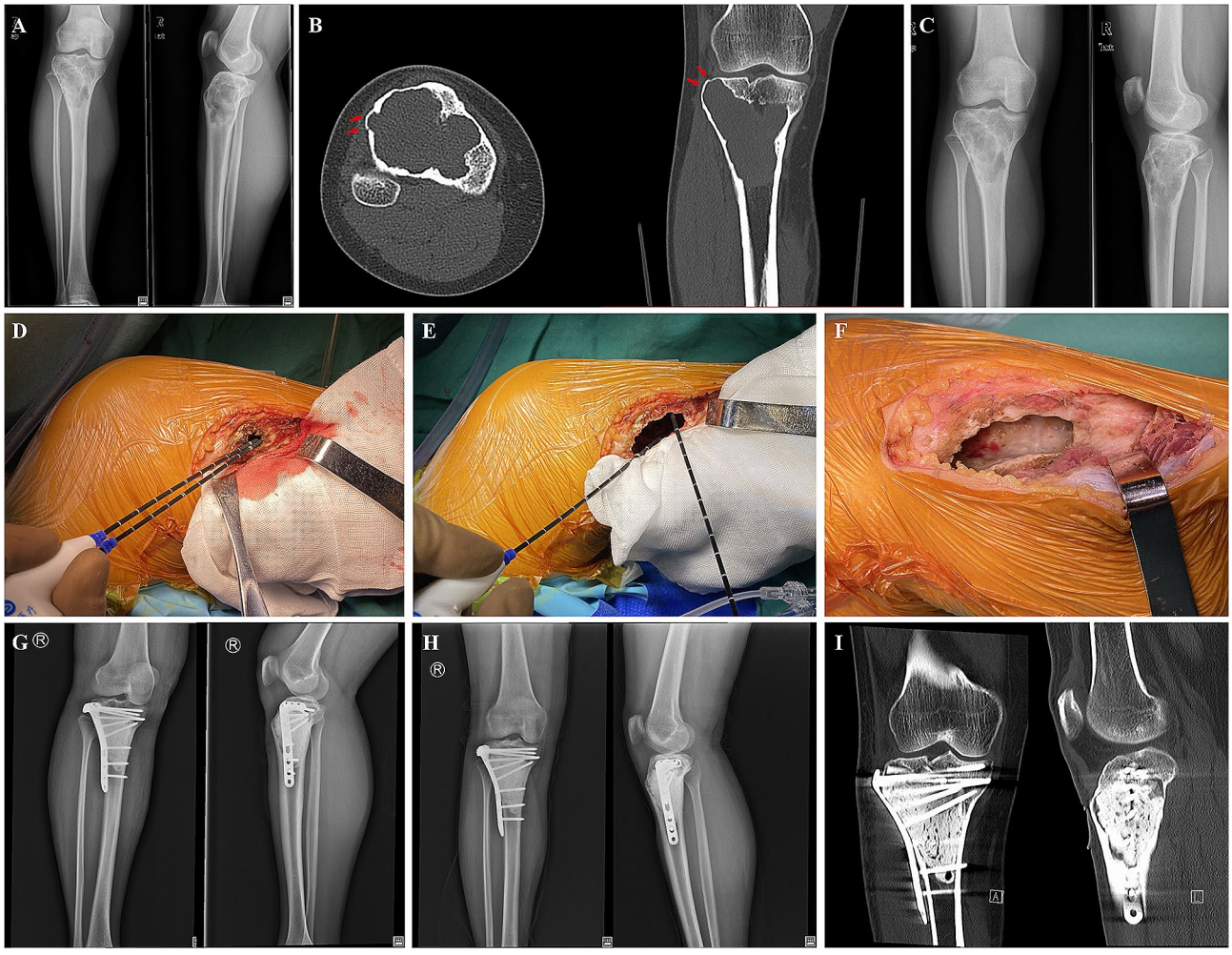

Fig. 1 A patient with a giant cell tumor of the proximal tibia was administered two doses of denosumab. An expansile osteolytic lesion with involvement of the cortical bone and articular cartilage as shown by the red arrow was seen on the anteroposterior plain radiograph (**A**) and CT image (**B**). After the patient responds to denosumab treatment, there is mineralization within the lesion (**C**). Two microwave ablation antennas were inserted into the lesion after fully exposing the lesions and protecting the adjacent normal tissues with gauze (**D**). The microwave antennas were repositioned to ensure overlapping ablation zones and strategically placed at lesion peripheries to achieve a broader ablation margin (**E**). The extensive curettage was performed through a large cortical bone window to excise all visible regions of the tumor. (**F**). The cavity was filled with allografts and bone cement with prophylactic internal fixation (**G**). There was no recurrence on the radiograph (**H**) and CT image (**I**) at 29.9 months of follow-up

generated using the Kaplan-Meier method, with statistical significance set at a two-tailed p-value of 0.05.

Results

Patients' characteristics

In this retrospective study spanning from February 2019 to September 2022, we identified 19 patients with high-risk GCTB in the extremities, based on initial radiological imaging and presentations. Table 1 presents the baseline demographics and clinical characteristics of the patients. The mean age of patients at the time of surgery was 31.5 years (range: 23–54 years), comprising 11 males and 8 females. None of the patients had respiratory or cardiovascular comorbidities. The knee region is the most frequently affected site, with 9 patients (47.4%) in the proximal tibia and 7 (36.8%) in the distal femur. Other anatomical sites include the proximal femur in 1 patient (5.3%) and the distal radius in 2 patients (10.5%). Among them, 4 patients (21.1%) presented with pathologic fractures identified by CT scans, and 11 patients (57.9%) experienced decreased range of motion upon presentation. Based on radiological appearance, lesions in 11 patients (57.9%) were classified as Campanacci grade II, and 8 (42.1%) as grade III. Of the 19 patients, 16 (84.2%) patients presented with primary lesions, while 3 (15.8%) patients had a history of curettage surgery, but none of patient previously received the denosumab treatment.

Table 1 Patient demographics and clinical baseline characteristics

Characteristics		Patients (%)
Age		
	Mean	31.5
	Range	23–54
Gender		
	Female	8 (42.1%)
	Male	11 (57.9%)
Anatomical site		
	Distal Femur	7 (36.8%)
	Proximal femur	1 (5.3%)
	Proximal Tibia	9 (47.4%)
	Distal Radius	2 (10.5%)
Campanacci classification		
	II	11 (57.9%)
	III	8 (42.1%)
Clinical Presentation		
	Pain and Swelling	4 (21.1%)
	Decreased range of Motion	11 (57.9%)
	Pathologic Fracture	4 (21.1%)
Previous Treatment		
	None	16 (84.2%)
	Curettage surgery	3 (15.8%)
Perioperative Denosumab dose		
	3	12 (63.2%)
	4	6 (31.6%)
	5	1 (5.2%)

Clinical and functional outcomes

During denosumab treatment, all patients tolerated the regimen well, and no severe drug-related adverse events occurred. Among the 19 patients, 12 patients received 3 doses, and 6 patients received 4 doses until mineralization occurred within the lesion. One patient with a pathological fracture in the proximal tibia received up to 5 doses, leading to the development of a complete sclerotic rim surrounding the lesion and enabling joint preservation surgery. At the time of surgery, preoperative radiographs and CT scans indicated thickened subchondral and cortical bone and complete or nearly complete development of a sclerotic rim surrounding the tumors. Patients with pathological fractures showing near disappearance of the fracture line were considered suitable for curettage instead of en-bloc resection. Eventually, no patient required resection and reconstruction with an endoprosthesis. All patients underwent extensive curettage to preserve the native joint followed by adjuvant MWA. Bone defects following tumor curettage were reconstructed with allograft and PMMA in 14 cases, with or without supplemental internal fixation. In 5 patients, PMMA alone was used when the subchondral bone was intact after tumor curettage. None required autogenous bone grafting in addition to the allograft. Functional outcomes significantly improved following denosumab treatment and surgical reconstruction, with substantial pain reduction and improved joint range of motion within the first month. The postoperative functional status of patients with high-risk GCTB around the joints was assessed using the MSTS score. The findings revealed a mean MSTS score of 27.3±0.26, with individual scores ranging from 26 to 29. Specifically, patients with GCTB in the lower extremities had a mean MSTS score of 27.4±0.28, while those with GCTB in the distal radius had a mean score of 26.5±0.50. Notably, all patients demonstrated satisfactory function (MSTS score≥24) in the affected limb, and none of the patients with GCTB in the lower extremity relied on walking aids or crutches during the final follow-up period (Table 2).

Local recurrence and complications

For the 19 patients who underwent curettage with preoperative denosumab and adjuvant MWA, the median follow-up time was 33.1 months (range 20.4 to 62.8 months). Regarding oncologic outcomes, local recurrence occurred in 3 patients following intralesional curettage, none of whom had a history of GCTB recurrence. Two patients with GCTB in the proximal tibia and one in the distal femur experienced local recurrence at postoperative 15.5, 21.6, and 29.3 months, respectively. The local recurrence rate was 15.8% (3/19), with a median interval of 21.6 months between the initial surgery and recurrence. Lung metastasis did not occur during the follow-up period. The local recurrence-free survival (LRFS) for all cases was 81.2% (95% CI: 51.5–93.7%) at two years (Fig. 2). Despite the 3 patients experiencing local recurrence, all patients were successfully treated with repeat curettage combined with MWA and remained disease-free during subsequent follow-up. None of the patients required wide resection, and all patients with high-risk GCTB retained their joints, achieving a joint preservation rate of 100%.

Regarding adverse events, only 3 patients experienced surgery-related complications. One patient developed a superficial wound infection 2 weeks postoperatively, which was resolved with antibiotic treatment. Another patient with proximal tibia GCTB experienced superficial skin necrosis and delayed wound healing due to thermal injury from electrosurgical inactivation using a spray coagulation mode. Although this patient did not develop wound infection, successful management was achieved following debridement and reconstruction with a local flap. Additionally, one patient with GCTB in the proximal femur presented with femoral head collapse and joint degeneration on radiographs 12 months after surgery, and this patient was successfully managed with non-steroidal anti-inflammatory drugs. A representative case

Table 2 Preoperative management, surgical characteristics and outcomes of patients with high-risk GCTB

Patients	Gender	Age	Anatomical location	Primary / Recurrent	Campanaci stage	Denosumab dose	Reconstruction Method	Postoperative Complications	Current status	LRFS (m)	Follow up (m)	MSTS
1	F	36	Proximal tibia	Primary	III	3	Allograft + PMMA	Delayed wound healing	NED	29.9	29.9	28
2	M	25	Proximal tibia	Primary	III	4	PMMA alone	None	NED	20.4	20.4	28
3	F	39	Distal femur	Primary	III	3	PMMA alone	None	NED	31.0	31.0	26
4	M	54	Distal femur	Primary	II	3	PMMA alone	None	NED	33.1	33.1	27
5	M	24	Proximal femur	Primary	II	3	Allograft + PMMA	Femoral head necrosis	NED	37.0	37.0	28
6	F	24	Distal femur	Primary	II	3	Allograft + PMMA	Local recurrence	NED	21.6	60.8	29
7	M	33	Proximal tibia	Recurrent	III	3	Allograft + PMMA	None	NED	53.0	53.0	27
8	M	29	Proximal tibia	Primary	III	4	Allograft + PMMA	Local recurrence	NED	29.3	62.8	26
9	M	23	Distal radius	Primary	III	4	PMMA alone	None	NED	21.3	21.3	27
10	F	31	Distal femur	Primary	II	4	Allograft + PMMA	None	NED	30.7	30.7	27
11	M	28	Proximal tibia	Primary	II	4	Allograft + PMMA	None	NED	23.8	23.8	26
12	M	39	Distal radius	Primary	II	3	PMMA alone	None	NED	25.9	25.9	26
13	M	32	Proximal tibia	Primary	II	3	Allograft + PMMA	Local recurrence	NED	15.5	24.7	28
14	M	31	Distal femur	Primary	II	4	Allograft + PMMA	Superficial infection	NED	25.4	25.4	29
15	F	23	Distal femur	Primary	II	3	Allograft + PMMA	None	NED	34.6	34.6	29
16	F	29	Proximal tibia	Recurrent	III	5	Allograft + PMMA	None	NED	38.0	38.0	26
17	F	36	Distal femur	Primary	II	3	Allograft + PMMA	None	NED	47.4	47.4	27
18	F	24	Proximal tibia	Recurrent	III	3	Allograft + PMMA	None	NED	42.8	42.8	29
19	M	38	Proximal tibia	Primary	II	3	Allograft + PMMA	None	NED	57.9	57.9	26

Abbreviations: LRFS, local recurrence-free survival; MSTS, Musculoskeletal Tumor Society score; NED, no evidence of disease

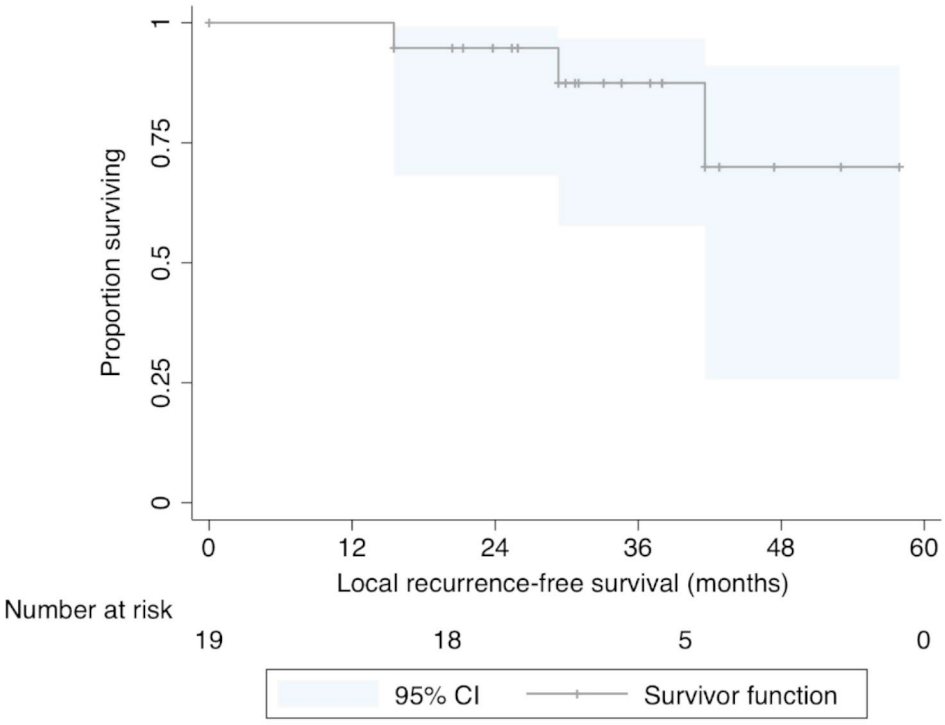

Fig. 2 Kaplan-Meier curve displays the local recurrence-free survival of patients with giant cell tumor of bone treated with preoperative denosumab and microwave ablation treatment

involved a 33-year-old female presenting with periarticular bone loss and minimal subchondral bone. Following 3 doses of preoperative denosumab treatment, radiographs revealed ossified rim formation that facilitates curettage and joint preservation surgery. (Fig. 3).

Discussion

The therapeutic landscape for GCTB has experienced notable advancements with the introduction of denosumab, which has demonstrated a significant impact on promoting osseous consolidation and inhibiting tumor activity [19, 20]. Despite these advancements, the treatment of locally advanced GCTB poses a considerable challenge and complicates joint salvage procedures. In this regard, preoperative denosumab treatment has demonstrated a definitive benefit in facilitating the surgical procedure and converting a lesion initially planned for resection into one that could potentially be managed with curettage and joint preservation [21–23]. Therefore, denosumab plays a pivotal role in surgical downgrading and joint-salvage operations for patients with high-risk GCTB.

Recent studies have indicated a potential association between denosumab treatment and increased risk of local recurrence in GCTB following curettage, suggesting a cautious approach to its use [23, 24]. A systematic review encompassing 7 studies and 619 patients found recurrence rates ranging from 20 to 100% in the curettage with preoperative denosumab group, compared to rates of 0–50% in the curettage-alone group [24]. It has been demonstrated that denosumab selectively targets osteoclastic cells and impedes osteoclastogenesis, while the inhibition effect on neoplastic stromal cells is relatively weak in vitro study [25]. Even though the neoplastic stromal cells remain quiescent during exposure to denosumab, they exhibit increased proliferation once the drug is no longer present in the microenvironment [25]. The formation of a new osseous matrix induced by denosumab around the tumor may potentially entrap neoplastic stromal cells, complicating the accurate determination of tumor extent during intralesional curettage procedures [26]. Nevertheless, the strengthening of periarticular and subchondral bone following denosumab treatment may make curettage a more attractive option compared to wide resection. This risk may be considered acceptable in young patients to maintain joint function. In such clinical scenarios, a higher risk of local recurrence may be consciously acknowledged in an attempt to preserve the joint and avoid complex osteoarticular reconstructions in young patients.

In this study, we analyzed 19 consecutive patients diagnosed with periarticular GCTB in the extremities, characterized by high-risk factors making joint preservation challenging. All patients received

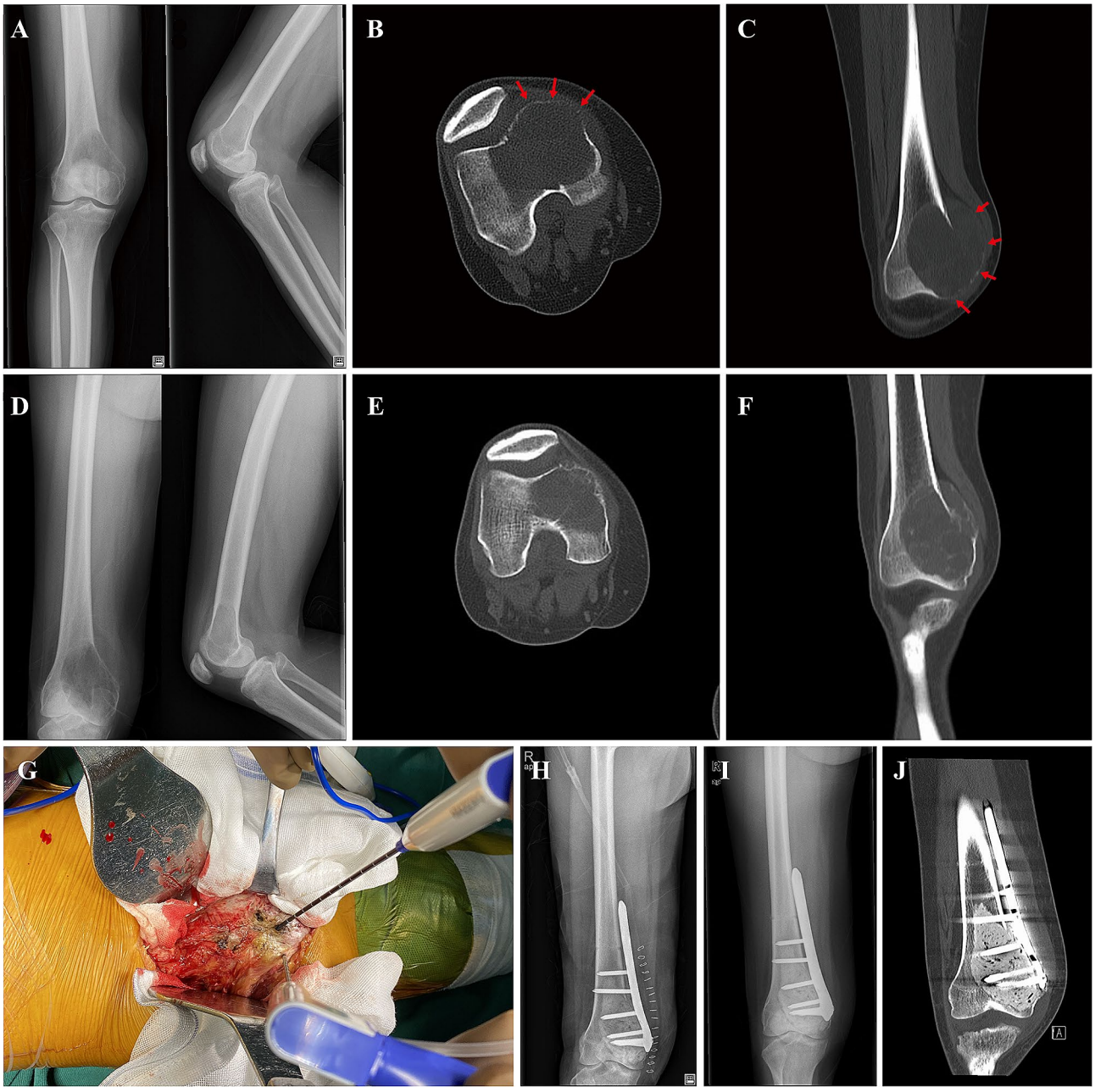

Fig. 3 A 33-year-old female patient with a giant cell tumor of the bone in the distal femur preoperatively received three doses of denosumab treatment. Anteroposterior plain radiograph (**A**) and CT image (**B, C**) showed an expansile osteolytic lesion with periarticular bone loss and minimal subchondral bone (as indicated by the red arrows). Anteroposterior plain radiograph (**D**) and CT image (**E, F**) six weeks after the third injection of denosumab showed the formation of a thickened sclerotic rim around the tumor and the margin became clear. The adjacent normal tissues were exposed and protected with gauze, then the microwave ablation was performed (**G**). The extensive curettage combined with internal fixation was performed following the microwave ablation procedure (**H**). Follow-up radiograph at 31 months after curettage and no local recurrence was observed (**I, J**)

preoperative denosumab treatment with the goal of restoring subchondral and periarticular cortical bone, thereby enabling joint-preserving surgery. The mean number of denosumab doses administered in our series was 3 injections, which constitutes a considerably shorter course (approximately one month of therapy) compared to other published series [26]. Previous studies involving GCTB treatment with preoperative denosumab and surgery have reported a median of eight cycles and a median duration of six months on denosumab before surgery [21, 26]. With escalating denosumab doses, there is a progressive thickening of the ossified rim. The typical friable giant cell tumor tissue is replaced by gritty and fibro-osseous tissue that further poses challenges to the

complete removal of lesions [26]. Hindiskere et al. documented that patient with GCTBs treated with more than 3 doses of preoperative denosumab experienced no benefits in clinical, radiological, or histological responses compared with patients who received 3 or fewer doses [27]. The shorter course of preoperative denosumab was suggested to reduce local recurrence rates while still permitting joint preservation surgery in select cases [27]. This approach could explain the absence of drug-related toxicity observed in our patients. Even with this shorter duration, denosumab treatment showed clear evidence of radiologic shrinkage and calcification of the lesion in all patients.

Over the past few decades, the investigation of various adjuvant modalities aimed at reducing recurrence has contributed to gradual improvements in outcomes following intralesional surgery [28]. The clinical efficacy of physical (mechanical/thermal) or chemical adjuvants in local tumor control remains a subject of debate, with ongoing discussions regarding the optimal combination of local adjuvants. The meticulous tumor curettage through wide exposure of the tumoral cavity and high-speed burring were recognized as essential elements to attain effective local tumor control [29]. However, despite these efforts, several studies have reported relapse rates ranging from 28 to 75% after extensive curettage without the use of local adjuvants [30, 31]. It is plausible that extensive curettage may not always ensure complete removal of residual tumor, particularly in regions like the subchondral bone or near the articular surface, where the utilization of a burr may be constrained by potential complications. Therefore, several authors have suggested that combined extensive curettage with multiple adjuvant agents may provide the most effective and comprehensive impact on residual tumor cells situated in high-risk zones [30, 32].

Microwave ablation is a thermal technique known for significant power efficiencies in comparison to other ablative modalities, which rapidly induces coagulative necrosis of tumor cells through the inserted needle tips within the lesions [33]. In a retrospective study conducted by Ke et al., the results revealed that out of 54 patients with GCTB, only 2 patients developed recurrence following curettage combined with MWA, with a mean MSTS score of 28.7 [34]. Similarly, Jiao et al. reported a 10% local recurrence rate among patients with GCTB of the distal radius who underwent curettage and MWA, with a mean follow-up of 34 months [35]. In a more recent analysis by Jiang et al., involving 30 GCTB patients who underwent MWA surgery, no instances of local recurrence or reoperations were observed over an average follow-up period of 63.79 months [36]. These results highlight the outcome of intralesional curettage followed by MWA, particularly in cases of GCTB with pathological fractures or those located in the distal radius. However, it should be noted that the efficacy of preoperative denosumab treatment combined with intraoperative MWA in the surgical management of GCTB patients has not been explicitly assessed.

In our study, all patients diagnosed with high-risk GCTB received preoperative denosumab treatment followed by a combination of MWA and curettage surgery. After an average follow-up period of 33.1 months, recurrence occurred in 3 patients, resulting in a local recurrence rate of 15.8% with a median interval of 21.6 months from the initial surgery. Noteworthy, the local recurrence-free survival rate at two years reached 81.2%, which is relatively higher than the rates reported in previous literature [37]. This improvement could be attributed to tumor scrape removal following adequate thermal treatment and coagulative necrosis, potentially reducing the risk of soft tissue contamination. The robustness of MWA in withstanding heat-sink and charring effects, and limited susceptibility to bone impedance, facilitates enhanced heat penetration into osteosclerotic lesions [38]. The rapid generation of thermal energy by MWA enables thorough penetration of the sclerotic lesions induced by denosumab treatment, which might eradicate the residual tumor cells trapped within the bone structure. Although local recurrence occurred in 3 patients, all were effectively addressed through repeated curettage in conjunction with MWA, resulting in no further recurrences during subsequent follow-ups. Eventually, all patients underwent successful joint salvage with a joint perseveration rate of 100% and a mean MSTS score of 27.3. Thus, even in cases of GCTB recurrence, repeated curettage and local adjuvant therapy may facilitate joint preservation and sustain optimal limb function. The prioritization of joint salvage is crucial for long-term functional improvement, especially considering the young adult demographic of most GCTB patients.

This study has several limitations that warrant consideration. Firstly, the retrospective design and lack of a comparison group may limit the generalizability of the findings. Although sufficient to capture most local recurrences of GCTB within the first two years, the relatively short follow-up duration may not fully elucidate long-term outcomes and metastasis. Furthermore, the optimal time and energy settings for microwave ablation to achieve effective tumor ablation while preserving normal articular cartilage remain uncertain, as no consensus has been reached in the literature. Given the integration of supplementary adjuvant treatments (such as high-speed burring, electrocauterization, and bone cement application) during curettage surgery following denosumab therapy, it is crucial to acknowledge the potential bias these interventions may introduce when evaluating the efficacy of microwave ablation. Therefore, further multicenter

research with larger sample sizes, longer-term follow-up periods, and randomized controlled trials is warranted to provide more robust evidence in this area.

Conclusion

Preoperative denosumab treatment plays a crucial role in the management of patients with high-risk GCT, while its impact on local recurrence rates following curettage is controversial. Our study suggests that the combination of preoperative denosumab and adjuvant microwave ablation is a safe and effective strategy for achieving good disease control and functional outcomes. This approach offers a promising surgical alternative for patients with high-risk GCTB, particularly for young patients where joint preservation is critical. However, future studies with larger cohorts and longer follow-up periods are needed to validate these preliminary findings.

Author contributions

Chuanxi Zheng and Gang Xu: collected and analyzed the data and wrote-original draft preparation. Xiayi Zhou, JinQiu, Gang Xu and Tao Lan: conceptualised the study, developed the methodology, and revised manuscript; Wei Li, Shiquan Zhang: Writing-review and supervision. All authors have read and contributed to the final text and also approved the submitted version.

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Data availability

No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate

The Ethics Committee of the First Affiliated Hospital of Shenzhen University reviewed and approved this study (2023-248-01PJ). The Ethics Committee of the First Affiliated Hospital of Shenzhen University has waived the informed consent for the study due to its retrospective nature. In addition, patient records were anonymized and de-identified before undergoing analysis.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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