ORIGINAL ARTICLE

# SURGICAL TREATMENT RESULTS IN GIANT-CELL TUMOR OF THE BONE

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## Abstract

*Giant-cell tumor of the bone is a benign tumor with high local aggressiveness and risk of recurrences. The aim of our study is to emphasize the importance of the tumor's size, location and activity in choosing the proper surgical method for treating GCTB, in order to maintain a balance between minimal chance of recurrence and an optimal quality of life. We conducted a retrospective study of a series of 53 patients (age range 21-47 years old) with GCTB confirmed by anatomopathological examination. We used the Enneking grading system and we included 9 patients (16.98%) with first stage tumors, 36 patients (67.92%) with second stage tumors and 8 patients (15.09%) with third stage tumors. The tumors were located in: distal femur – 21 patients (39.62%), proximal tibia – 18 patients (33.96%), proximal femur – 9 patients (16.98%) and distal radius – 5 patients (9.43%). All patients underwent surgery (curettage, en bloc resection and reconstruction with structural autograft, modular tumoral prostheses). 4 recurrences (7.54%) were recorded: in 3 patients who underwent curettage and cancellous bone autograft and one patient with resection and reconstruction with structural autograft technique. According to local functional grading systems, all functional results were good and very good. Osteoarthritis was recorded in 5 patients, all of them being treated by curettage and bone cement technique. In order to obtain optimal surgical results, a rigorous assessment of both investigations' results and a correct classification of GCTB is needed.*

**Keywords***: giant cell tumor of bone, curettage, modular tumoral prostheses, recurrences*

## Introduction

Giant-cell tumor of the bone (GCTB), also known as osteoclastoma, is a benign bone tumor which from an epidemiological point of view accounts for 4-5% of primary bone tumors and 15% of benign bone tumors [1]. GCTB usually affects 20-45 years old adults, being slightly more common among females. GCTB affects the epiphysis of long bones, 50% of cases being localized near the knee (distal femur and proximal tibia), followed by distal radius, proximal femur, proximal humerus, distal tibia and proximal fibula, whereas 0.5% of GCTB are multicentric [2].

Although it is considered a benign tumor, GCTB has high local aggressiveness and high probability of recurrence. In less than 1% of cases, subsequent malignization was reported, especially in patients undergoing radiotherapy [3]. Also, in approximately 3% of GCTB lung metastasis were described [1].

Our article aims to emphasize the importance of the tumor's size, location and activity in choosing the proper surgical method for treating GCTB, in order to maintain a balance between minimal chance of recurrence and an optimal quality of life. For this purpose, we used the Enneking classification [4], which, based on the characteristics of the tumoral radiological margins and histological aspects assesses GCTB's activity stage:

Stage I: Latent tumor – confined totally by bone, asymptomatic, inactive on bone scan, histologically benign;

Stage II: Active tumor – expanded cortex without breakthrough, symptomatic, pathological fracture possible, active on bone scan, histologically benign;

Stage III: Aggressive tumor – cortical perforation with soft tissue mass, may metastasize, intense activity on bone scan, histologically benign;

Stage IV: Sarcomatous lesions.

We also discuss the importance of modern tumoral therapy, like denosumab, that can successfully reduce the tumor size, with subsequent decrease of surgery's complexity and the possible complications of using bone cement.

## Materials and methods

Between 2010 and 2017 we conducted a retrospective study from the records of the Orthopaedic and Traumatology Department of the Emergency University Hospital of Bucharest and we included a series of 53 patients with GCTB, confirmed by anatomopathological analysis. The patients had a mean age of 32 years old (age range 21-47), with no significant men/women ratio.

We used the Enneking grading system and thus included 9 patients (16.98%) in the first stage, 36 patients (67.92%) with stage II lesions and 8 patients (15.09%) that presented stage III lesions. The tumors were located in: distal femur – 21 patients (39.62%), proximal tibia – 18 patients (33.96%), proximal femur – 9 patients (16.98%) and distal radius – 5 patients (9.43%).

All patients underwent surgery. Curettage (Figure 1) was performed on 36 patients (67.92%) representing all stage I patients and 27 patients with stage II tumor, the resultant cavity being filled with morselized cancellous autograft in 14 cases (38.89%) and with bone cement in 22 cases (61.11%). En bloc resection and reconstruction (plate and screws) with structural autograft was performed on 12 patients (22.64%), while the remaining 5 patients (9.43%) underwent modular tumoral prostheses (Figure 2).

The mean follow-up period was 34 months (range 6-72 months).

## Results

Most patients were diagnosed in stage II of disease, the patients in stage I being diagnosed usually at routine tests.

4 recurrences (7.54%) were recorded in patients from our study: 3 of them that underwent curettage and cancellous bone autograft and one patient with resection and reconstruction with structural autograft technique. We mention that we haven't noticed any recurrences in patients treated by curettage and bone cement.

According to local functional grading systems, all functional results were good and very good.

Osteoarthritis (OA) was recorded in 5 patients, all of them being treated by curettage and bone cement technique.

## Discussions

GCTB is characterized by the presence of multiple osteoclast-like giant cells, which are being unevenly distributed among the mononuclear cells, macrophage-like cells and mesenchymal stromal cells [3]. Both macrophage-like cells, as well as osteoclast-like cells display a receptor activator of nuclear factor kappa B (RANK), whereas the mesenchymal stromal cells display a RANK ligand (RANKL) [5, 6]. RANK's presence is very important because modern drug therapies for GCTB, like denosumab, a human monoclonal antibody, downregulates RANK activation [7] and consequently inhibits

osteoclastogenesis and therefore bone destruction.

Given the fact that most patients with GCTB are young active adults, it is necessary for the treatment to have a double purpose: to be curative and to obtain a good functional result.
Martin-Broto et al. proved that denosumab is efficient in reducing pain intensity and also in performing a surgical procedure less invasive than initially planned [8-10]. After 3-4 months of denosumab treatment a reduction of tumor size was observed and also a better tumor delimitation by displaying a calcified border [11-13].


**Figure 1 - (A) Preoperative AP and LL view X-rays of a giant-cell tumor located on the external femoral condyle of the left knee, (B) Postoperative AP and LL view X-rays: external femoral condyle treated by curettage and bone cement**

Even in severe cases where amputation was taken in consideration, the radical surgical intervention after denosumab treatment was converted into an arthroplasty with modular tumor prosthesis and subsequently led to limb salvage [14,15].

Despite the favorable outcome for the majority of the patients treated with denosumab prior surgical intervention, there are some safety concerns that must be addressed. Some studies found that treatment with denosumab for more than 3-4 months, which is the limit for the lesion to surround itself with a calcified rim and facilitate surgery, led to alterations in tissue structure and made the curettage and complete tumor removal more difficult [16,17], thus leading to a higher recurrence rate [18].

Regarding curettage and filling with autograft or allograft bone, studies show a recurrence risk of 25-40% [19]. Usage of bone cement to fill the cavities has proved to bring many benefits: it reduces recurrence rates by half [19], helps detecting recurrences earlier [20] and improves the patients' rehabilitation by stabilizing the area [21]. However, bone cement usage also has some downfalls, such as intense heat from the cement exothermal polymerisation reaction [22], which can harm the cartilage and also an increased risk of intra-articular fractures if the cement is in close proximity of the joint [23]. In this regard, Suzuki et al. [24] showed in 2007 that the risk of developing OA following surgery is correlated to the thickness of the remaining subchondral bone and also the extension of the tumor. Hai-Rong et al. found that the risk of OA is significant if the tumor is less than 10 mm away from the joint surface [25], while in their study, Heijden et al. found a 4.2 increase in risk of developing OA when the tumor was less than 3 mm from the cartilage and a 9 fold increase when the tumor invaded more than 70% of the subchondral bone [26]. It

is of notice Hai-Rong et al. found that the interposition of cancellous bone graft between the cement and the cartilage, in tumors located less than 10 mm from the joint surface, reduced the risk of OA by nearly half [25].

In cases where a more conservative approach cannot be performed, including large tumors with a significant amount of bone loss or important cortical effraction, surgeons have to resort to modular endoprosthetic systems in order to save the limb. Some studies found that endoprostheses are preferred by patients, as opposed to limb loss, in terms of pain, strength and emotional acceptance [27]. The initial trend was to use cemented endoprosthetics, which had some disadvantages, such as aseptic loosening, mechanical breaking and infection, thus having quite high failure rates [28,29]. As a result, cementless stems have gained more and more popularity, having favorable outcomes [30,31]. However, all endoprosthethics show limitations in the range of motion, mainly due to loss of muscle mass, which increases the need for medical assistance.

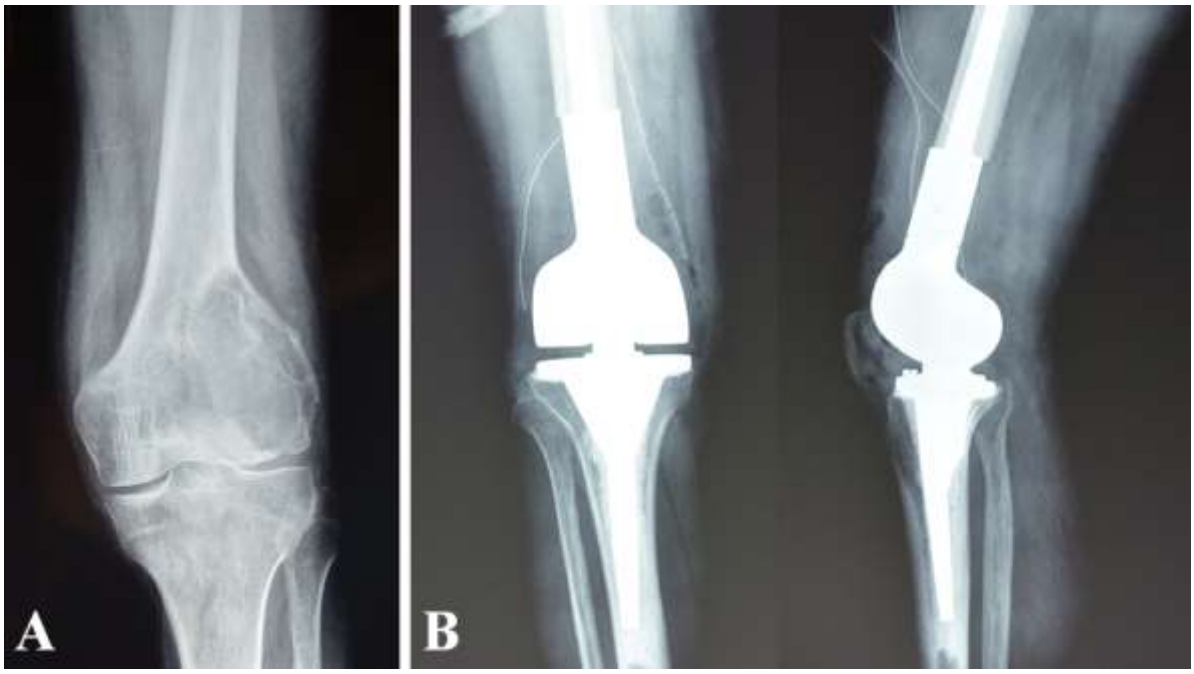


**Figure 2 – (A) Preoperative AP view X-ray of a giant-cell tumor of the right knee; (B) Postoperative AP and LL view X-rays: arthroplasty with modular tumoral prosthesis.**

## Conclusions

In order to obtain optimal surgical results, a rigorous assessment of both investigations' results and a correct classification of GCTB is needed. In stages I and II tumors the optimal surgical treatment is represented by curettage and filling with autograft or allograft bone or bone cement which is a less aggressive technique but with very good results. In stage III tumors, in case en bloc resection and reconstruction is not a viable option, arthroplasty with modular prosthesis should be taken in consideration as the functionality of the limb is well preserved.

In our study most of the patients were diagnosed in stage II of disease. Due to lack of clinical manifestations those in first stage of disease were accidentally diagnosed, while those in stage III neglected their symptoms for a long period of time.

Most recurrences appeared in patients where curettage and cancellous bone autograft was performed. Osteoarthritis was observed in patients treated by curettage and bone cement.

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