

# The Outcomes of Treatment of Giant Cell Tumor of Bone around the Knee

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**Background:** Giant cell tumor of bone has been characterized as an aggressive benign bone tumor and commonly occurs at the distal femur and the proximal tibia. The recommended treatment has ranged from intralesional curettage to wide excision and the decision depends on severity of the tumor extent, rate of local recurrence, functional and morbidity outcomes.

**Objective:** To compare extended curettage and wide excision in Grade II-III giant cell tumor of bone around the knee with regard to their effectiveness in tumor control and complication.

**Material and Method:** There were 54 patients with a giant cell tumor which involved the distal femur or proximal tibia who had been managed consecutively at Siriraj Hospital between 1994-2009. The lesion of all patients were staged according to the system of Campanacci et al. There were 21 males and 33 females with mean age of 34 years. Thirty-five tumors located at distal femur and 19 located at proximal tibia. Fourteen patients had a Grade II lesion and 40 had a Grade III lesion. Thirty patients received extended curettage whereas other 24 patients had a wide excision. Fisher's exact analysis was used for statistical analysis for the outcome of tumor recurrence in each surgery.

**Results:** The mean follow-up time was 59 months. There were 7 (23.3 percent) local recurrences in the extended curettage group and 2 (8.3 percent) in the wide excision group. Most recurrences occurred within one year postoperatively. There was no statistical difference for the outcome of tumor recurrence in each group ( $p = 0.270$ ). All patients with tumor recurrence were successfully treated with re-curettage, except for 3 patients who was treated by above-knee amputation. The functional analysis was excellence in the extended curettage group (94 percent) and good in the wide excision group (77.6 percent) according to the Musculoskeletal Tumor Society functional classification.

**Conclusion:** The authors believe that using extended curettage was not significantly different in percentage of local recurrence when compared with wide excision for Campanacci's Grade II-III of giant cell tumor of bone. Even better function was found in extended curettage group, the choice of surgical treatment should be considered in individual patient which depends on the extent of bone destruction and risk of tumor recurrence.

**Keywords:** Giant cell tumor, Knee, Extended curettage, Wide excision, Local recurrence

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Giant cell tumor of bone has been characterized as a benign but often locally aggressive neoplasm that commonly occurs in proximity to a major weight bearing joint. This tumor is an uncommon disease but still comprises 20 percent of benign bone tumors<sup>(1)</sup>. The incidence peaks around the third decade and there is a slight predominance in women over men<sup>(1-3)</sup>. In most series, almost half of the lesions involve the distal end of the femur or proximal end of the tibia. Giant cell tumor often causes major destruction of the affected bone,

and it usually occurs in a subchondral area or in the epiphyseal part of the bone. It may occasionally invade and destroy the joint adjacent to the bone lesion.

According to Campanacci et al, 280 lesions of Giant cell Tumor were classisied in Grade II and III more than 95%<sup>(9)</sup>. The recommended treatment has ranged from intralesional curettage to wide excision of the tumor. The outcomes of each treatment have been reported. Intralesional curettage has been associated with a high rate of local recurrence that has ranged from 27 to 54 percent<sup>(4-9)</sup>. An extended curettage by using combination of curettage and high-speed burr was therefore introduced. With alternative adjuvant methods that have been used, such as phenol, liquid nitrogen, electrocautery and zinc chloride, the rate of local recurrence has been reduced 6 to 23 percent<sup>(10-16)</sup>. Wide excision, especially for a large lesion, has been

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reported to be more effective in prevention of tumor recurrence. The rate of local recurrence ranges from 0 to 16 percent<sup>(9,11,17,18)</sup>. However, wide excision usually requires sacrifice of affected bone and joint surface. Bony reconstruction is needed following the wide excision procedure<sup>(4,7-9,11,19-22)</sup>. In attempts to avoid the wide excision procedure for the treatment of some large lesions, many surgeons try to alternatively perform an intralesional curettage combined with adjunctive local application of chemical agent such as liquid nitrogen, phenol, or polymethylmetacrylate (PMMA). With this regimen, the joint and adjacent ligaments are preserved. Fewer complications can be expected and the function of the joint and extremity is retained. The purpose of the present study was to compare extended curettage and wide excision with regard to their effectiveness in the treatment of giant cell tumor of the bone Grade II-III located around the knee, with regard to their effectiveness in tumor control and reduction of complications.

#### **Method and Material**

The authors reviewed the results for 54 patients in a tumor registry database who had been treated consecutively for a giant cell tumor of bone which involved the distal femur and the proximal tibia, with a minimum 2-year follow-up, at Siriraj Hospital from 1994-2009. Patients with pathologic fractures were not included in the present study. Thirty patients had an extended curettage with adjunctive application of phenol and electrocautery and then PMMA was used to fill the defect after tumor removal. The patients had been managed with a wide excision with bone reconstruction.

All patients were evaluated preoperatively by plain radiography, computed tomography (CT), or magnetic resonance imaging (MRI). All medical records and pathological slides were all reviewed during this period. The system of Campanacci's classification for giant cell tumor was used with Grade I defining an intraosseous lesion, Grade II defined as an intraosseous lesion with cortical thinning; and Grade III defined as an aggressive lesion with extension outside the cortex and showing as well soft tissue extension<sup>(9)</sup>.

All patients were assessed postoperatively by complete physical examinations and radiographs at 6 weeks, every 3-4 months for 2 years and then every 6 months. In addition, plain radiographs of the affected knee and chest were obtained post-operatively in order to look for local recurrence, degenerative changes and lung metastasis at each visit time. Local recurrences were confirmed by re-curettage and histologic

examination by an experienced bone pathologist. The functional outcomes were analyzed by using the Musculoskeletal Tumor Society functional classification regarding the levels of pain, emotional acceptance, function of the lower extremity, use of mechanical supports, gait and walking ability<sup>(23)</sup>. Each category of classification had a maximum of five points for a total of 30 points. The local recurrence rates for patients with extended curettage and wide excision were ascertained. Fisher's exact analysis was used to compare these rates and the level of significance was considered at  $p < 0.05$ .

#### **Operative technique**

The extended curettage was performed in a precise stepwise manner. After the diagnostic confirmation was established histologically with an open biopsy, the tumor was exteriorized completely. A procedure included removal of all thinned cortical bone, so that all spaces occupied by the tumor could be visualized. Next the tumor was removed, first with large curette and then with smaller instruments and suction catheter until no tumor tissues remained when observed grossly. Next, the entire osseous surface of the tumor cavity was removed using a high-speed burr (Hall Cebotome, Zimmer Inc, Warsaw, IN). Then, the entire exposed surface of the cavity was treated with adjuvants to extend the tumor cell kill. These adjuvant modalities included hydrogen peroxide (5 percent solution) irrigation, phenol (90 percent) irrigation and electrocautery (Bovie cautery machine, Valleylab, Inc, Boulder, CO) set to its highest cauterization setting. Phenol cauterization was applied to exposed osseous surface by using a cotton-tipped applicator and then the solution was removed followed by pulse lavage. Finally the cavity was packed with PMMA for bone reconstruction. Internal fixation was applied if the lesion involved more than 50 percent of the involved bone circumferential.

Wide excision was performed in patients with unsalvageable bone in which tumor destroyed bone was too extensive for a biomechanically sound reconstruction. The procedure consisted of removal of the tumor with either wide or marginal margin, then bone reconstruction was individualized for patients according their age, tumor site, functional demands and patient preference. In the present study, either arthroplasty by osteochondral allograft or autogenous bone arthrodesis was performed in our patients. Patients underwent osteosynthesis by using plate and screw fixation.

## Results

Of the 54 patients, there were 21 males and 33 females. The mean age of patients was 34 years (range from 19 to 58 years). The anatomical site of the lesions included 35 distal femurs and 19 proximal tibias. Fourteen patients were classified as Campanacci's Grade II and 40 patients were Grade III. The mean follow-up time was 59 months (range from 24 to 165 months).

Thirty patients underwent an extended curettage. Nineteen tumors were located at the distal femur and 11 tumors were at the proximal tibia. Tumors were Campanacci's Grade II in 17 patients and Grade III in 13 patients. Seven patients in this group had a local recurrence (23.3 percent) (Fig. 1A-E). Five patients were successfully treated by re-curettage and 2 patient was performed an above-knee amputation (6.67 percent). Twenty-four patients underwent a wide excision with a mean tumor length of 12.2 cm (range from 4 to 17 cm). Eleven patients underwent an osteochondral allograft reconstruction, 9 had an autogenous bone arthrodesis and 4 had a distraction arthrodesis following tumor removal. The tumor location was at distal femurs in 16 and proximal tibia in 8. All 24 patients had been classified



**Fig. 1** A Grade 2 GCT of the distal femur in a 45-year-old woman (A) Anteroposterior and (B) lateral preoperative radiographs (C) Anteroposterior and (D) lateral radiographs of the lesion 3 months postoperatively after intralesional curettage, electrical cauterization, phenol cauterization and PMMA (E) Lateral radiograph 4 years postoperatively with progression of the recurrence (\*)

at Campanacci's Grade III. There were 2 local recurrences of the tumor in this group (8.3 percent). One patient underwent 2 re-curettages and no local recurrence was detected at her last follow-up. Another patient underwent an above-knee amputation (4.2 percent). Six out of 9 patients in the present study had a local recurrence within 1 year (66.7 percent). There was no statistically different outcome of tumor recurrence in each group ( $p = 0.270$ ). Only one patient in the present study revealed lung metastasis and died of disease 56 months postoperatively.

No postoperative complication was found other than local recurrence in the group with extended curettage. Eight (33.3 percent) patients in wide excision had complications postoperatively and needed at least one operation for treatment. Six out of 8 patients with complications had an osteochondral allograft reconstruction. Five graft fractures (20.8 percent) were found in patients reconstructed with osteochondral allograft. One patient was successfully treated by casting. Two patients were performed autogenous bone grafting and plate-screw revision. Another 2 patients were underwent a knee arthrodesis with a long Kuntscher nail (Fig. 2A-E). One patient had superficial wound infection and successfully treated by debridement. One patient had a deep wound infection. She was performed allograft removal, 2 systemic debridements and appropriate antibiotics and finally underwent a knee arthrodesis. All patients could walk independently without any gait support. All patients were assessed for functional outcomes except for 2 patients in the wide excision group. The average Musculoskeletal Tumor Society functional analysis was 94 percent (range from 88 to 100 percent) in the extended curettage group and 77.6 percent (range from 46.7 to 100 percent) in the other group.

## Discussion

Giant cell tumor of bone is a benign but locally aggressive neoplasm with a tendency for local recurrences. The incidence of this tumor is more common in the Asian population<sup>(6)</sup>. The age, gender and localization data of the present study was similar to that found in the standard literature. Surgical treatment is the standard care for giant cell tumor of bone and curettage is still being used in most patients with giant cell tumors of bone. The rate of local recurrence after simple intralesional curettage, from some previous literature, is 27-54 percent<sup>(4-9)</sup> and has been reduced by the technique of extended curettage with some adjunct agents (6-23 percent)<sup>(10-16,24,25)</sup>.



**Fig. 2** A Grade 3 GCT with huge extraosseous lesion of the distal femur in a 58-year-old man (A) Anteroposterior preoperative radiograph (B) Anteroposterior and (C) lateral radiographs of the lesion 4 months postoperatively after wide excision and osteochondral allograft reconstruction (D) Anteroposterior and (E) lateral radiograph 1 year postoperatively with displaced graft fracture

PMMA was first reported to be used as an adjunct treatment and to fill in the defect after curetting giant cell tumor of bone<sup>(26)</sup>. The cytotoxic effect and heat dispersion during polymerization has been reported to enhance the margin of the tumor cavity by 1.5 to 2 mm in cancellous bone and 0.5 mm in cortical bone<sup>(26,27)</sup>. The rate of local recurrence has been reduced dramatically from 55 percent to 14 percent when PMMA was used in the same institution<sup>(25,26)</sup>. However, Turcotte et al from the Canadian Sarcoma Group Study, reported that 148 patients with giant cell tumor of bone underwent an extended curettage by supplement high speed burring after curettage (135 patients), cementation (64 patients), various combinations of autograft or allograft bone (61 patients), phenol in 37 patients and liquid nitrogen in 10 patients. Structural allograft was used in 25 patients. The recurrence rate after curettage was 18 percent<sup>(11)</sup>. They concluded that the nature of the filling

material used or the type of adjuvant method used, or any combination of both, failed to show any statistical impact on the recurrence risk.

Complete removal of the tumor with wide margins and reconstruction following tumor resection might be necessary in patients with tumor recurrence, aggressive tumor cases with extraosseous extension or when there is a large tumor lesion with marked bone or joint destruction. Wide excision has the benefit of completely removing all tumor cells to avoid risk of tumor recurrence. The rate of local recurrence ranges from 0 to 16 percent<sup>(9,11,17,18)</sup>. Following tumor removal, bone reconstruction with structural autograft, allograft or tumor prosthesis needs to be considered on an individual basis for each patient. Many authors suggested that extraosseous extension of giant cell tumor (Campanacci's Grade III) could be treated successfully with intralesional surgery and adjuvant therapy with curettage and cementation<sup>(13,14,28)</sup>. The authors agree with previous authors that Campanacci's Grade III of giant cell tumor can be managed by extended curettage and PMMA cementation with good results. Saiz et al reported a series of 40 patients with Grade II and Grade III giant cell tumors treated with a protocol using intralesional curettage, high-speed burring, electrocauterization, phenol cauterization and PMMA. Their local recurrence rates of 11 percent for Grade II lesions and 25 percent for Grade III lesions were not found to be different statistically<sup>(13)</sup>. Lackman et al found no difference in the local recurrence rate of 26 Grade II and 37 Grade III giant cell tumors treated with intralesional curettage, burring, phenol cauterization and PMMA application<sup>(14)</sup>. The rate of local recurrence in the extended curettage group was 23.3 percent (7/30) and only 8.3 percent (2/24) in the wide excision group. There was no statistical difference for the outcome of tumor recurrence in each group ( $p = 0.270$ ). Most of the local recurrence occurred within the first year after index treatment of the tumors. Six out of 9 patients in the present study had a local recurrence within 1 year (66.7 percent). All patients with local recurrence were successfully treated with re-curettage except 2 patients in extended curettage group and 1 patient with wide excision group were performed an above-knee amputation.

In present series, the average Musculoskeletal Tumor Society functional analysis was higher in the extended curettage group (94 percent) than in the wide excision group (77.6 percent) which was comparable with previous reports<sup>(11,13,14)</sup>. The reasons for lower functional scores in patients with wide excision were

caused by a greater number of complications and more complicated rehabilitation following bone reconstruction<sup>(29)</sup>. All complications occurred in wide excision group (33.3 percent) and most complications (6/8) were found in patients with osteochondral allograft reconstruction. All 5 graft fractures (20.8 percent) in the present study were found in patients reconstructed with osteochondral allograft. One patient was treated conservatively, 2 patients were underwent autogenous bone grafting and plate-screw revision and another 2 patient were performed a knee arthrodesis with a long intramedullary nail. One patient had superficial wound infection and successfully treated by debridement. One patient had a deep wound infection. She was performed allograft removal, 2 systemic debridements and appropriate antibiotics and finally underwent a knee arthrodesis. Subsequently, both patients could walk independently without any gait support.

In conclusion, the authors believe that the extended curettage as described in the present report, leads to no difference in local recurrence from wide excision, for properly selected patients. A multicenter study or meta-analysis would be necessary to include more patients for valid evaluation to provide enough power to detect statistical significance for the rate of local recurrence between groups.

#### Potential conflicts of interest

None.

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## ผลการรักษาเนื้องอกกระดูกชนิด giant cell บริเวณหัวเข่า

อภิชาติ อัครมงคลกุล, พีระจิตร เอี่ยมโสภณา, สารเนตร์ ไวกกุล, ระพินทร์ พิมลสานดี

**วัตถุประสงค์ :** เพื่อศึกษาเปรียบเทียบผลการผ่าตัดชนิด extended curettage และ wide excision ในผู้ป่วยที่ได้รับการวินิจฉัยโรคเป็นเนื้องอกกระดูกชนิด giant cell รอบหัวเข่า ซึ่งมีภาพรังสีปกติที่ถูกจัดแบ่งตาม Campanacci's classification เป็น grade II และ III โดยวัดผลจากอัตราการเกิดเนื้องอกซ้ำใหม่ ปัญหาแทรกซ้อนหลังผ่าตัด และการใช้งานของขาข้างที่มีพยาธิสภาพภายหลังผ่าตัด

**วัสดุและวิธีการ:** เป็นการศึกษาย้อนหลังของผู้ป่วยจำนวน 54 ราย ที่ได้รับการวินิจฉัยเป็นเนื้องอกกระดูก giant cell ของกระดูก femur ส่วนปลาย และกระดูก tibia ส่วนต้น ซึ่งได้รับการผ่าตัดที่โรงพยาบาลศิริราช ระหว่างปีพ.ศ. 2537-2552 ผู้ป่วยมีอายุเฉลี่ย 34 ปี เป็นชาย 21 ราย หญิง 33 ราย ผู้ป่วย 35 ราย มีเนื้องอกบริเวณกระดูก femur ส่วนปลาย และ 19 ราย มีเนื้องอกบริเวณกระดูก proximal ส่วนต้น ผู้ป่วย 14 ราย มีภาพรังสีปกติชนิด grade II และผู้ป่วย 40 ราย เป็นชนิด grade III ผู้ป่วย 30 ราย ได้รับการผ่าตัดชนิด extended curettage ผู้ป่วย 24 ราย ได้รับการผ่าตัด wide excision ผู้ป่วยทุกรายได้รับการตรวจติดตามภายหลังผ่าตัดอย่างต่อเนื่องเพื่อเฝ้าระวังเนื้องอกที่อาจเกิดซ้ำใหม่ รวมถึงการแพร่กระจายไปที่ปอด รวมทั้งบันทึกปัญหาแทรกซ้อนภายหลังผ่าตัด และการใช้งานของรยางค์ส่วนขาตามแบบบันทึกของ the Musculoskeletal Tumor Society functional classification การเปรียบเทียบวิเคราะห์อัตราการเกิดเนื้องอกซ้ำใหม่ของแต่ละชนิดการผ่าตัดจะใช้วิธีวิเคราะห์ทางสถิติ fisher's exact analysis

**ผลการศึกษา:** ผู้ป่วยมีระยะเวลาติดตามเฉลี่ย 59 เดือน (24 ถึง 165 เดือน) พบเนื้องอกเกิดซ้ำใหม่ในผู้ป่วยที่ได้รับการผ่าตัด extended curettage 7 ราย (ร้อยละ 23.3) และพบในผู้ป่วยที่ได้รับการผ่าตัด wide excision 2 ราย (ร้อยละ 8.3) การเกิดเนื้องอกซ้ำใหม่ในผู้ป่วยส่วนใหญ่เกิดภายในระยะเวลา 1 ปีภายหลังผ่าตัด ไม่พบความแตกต่างอย่างมีนัยสำคัญทางสถิติของการเกิดเนื้องอกเกิดซ้ำใหม่ของผู้ป่วยทั้ง 2 กลุ่ม ( $p = 0.270$ ) ผู้ป่วยที่มีเนื้องอกเกิดซ้ำใหม่ทั้งหมดได้รับการผ่าตัดด้วยวิธี re-curettage จนหายเป็นปกติ ยกเว้นผู้ป่วย 3 ราย ได้รับการผ่าตัดขาออกระดับเหนือหัวเข่า (above-knee amputation) ผู้ป่วยที่ได้รับการผ่าตัด extended curettage มีค่าวัดการใช้งานของรยางค์ส่วนขาอยู่ในเกณฑ์ดีมาก (ร้อยละ 94) เมื่อเปรียบเทียบกับผู้ป่วยที่ได้รับการผ่าตัด wide excision ซึ่งอยู่ในเกณฑ์ดี (ร้อยละ 77.6)

**สรุป:** การศึกษานี้พบว่าผลการผ่าตัดชนิด extended curettage และ wide excision ในผู้ป่วยที่เป็นเนื้องอกกระดูกชนิด giant cell ที่มีลักษณะภาพรังสีปกติชนิด grade II และ III ตาม Campanacci's classification ไม่มีความแตกต่างอย่างมีนัยสำคัญทางสถิติของการเกิดเนื้องอกเกิดซ้ำใหม่ของผู้ป่วยทั้ง 2 กลุ่ม แม้ว่าผู้ป่วยที่ได้รับการผ่าตัดชนิด extended curettage มีผลการใช้งานของรยางค์ส่วนขาดีกว่าผู้ป่วยที่ได้รับการผ่าตัด wide excision การเลือกวิธีการผ่าตัดที่เหมาะสมในผู้ป่วยแต่ละรายขึ้นกับความรุนแรงของการทำลายกระดูก รวมถึงโอกาสการเกิดซ้ำใหม่ของเนื้องอก

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