Oncology and functional prognosis are both vital in the surgical treatment of RGCTs around the knee joint

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Abstract

Aims

To explore and provide reasonable surgical options for recurrent giant cell tumors of bone (RGCTs) around the knee joint and compare the pros and cons of extended curettage (EC) and segmental resection (SR).

Materials and Methods

A retrospective analysis was performed of 22 patients (11 male, 11 female; mean age, 34.1 years) with RGCT around the knee joint treated in our hospital between June 2007 and June 2017. Average recurrence time was 14.2 ± 4.7 months. Basic clinical data, including Campanacci grade, lesion location, filler materials, pathological fracture, were recorded. Based on different reoperation methods, patients were divided into the EC and SR groups. Patients were regularly followed up; and recurrence, metastasis, local complications such as osteoarthritis, infection, prosthesis loosening, were recorded. Patient function and surgical efficacy were evaluated using the musculoskeletal tumor society (MSTS) score and Mankin score, respectively.

Results

Postoperative recurrence occurred in one patient in both groups, and no difference in the prognosis of oncology was observed between the groups. In the EC group, seven patients developed postoperative complications, but required no surgical treatment, whereas in the SR group, five patients developed postoperative complications and surgical treatment was performed on two patients. There were significant differences in the functional prognosis and surgical efficacy between the two groups; however, the EC group showed more satisfactory results.

Conclusion

The oncological and functional prognosis of patients with RGCT around the knee joint is vital. EC should be considered as the first-line treatment, unless the tumors severely invade the surrounding soft tissues or are accompanied by complex fractures with significant displacement leading to no surgical curettage boundary.

Introduction

Giant cell tumor of bone(GCTB) is a benign but invasive primary bone tumor, accounting for 5% of primary bone tumors that often occur at the ends of long bones of extremities [1]. GCTB has unpredictable biological behavior with locally aggressive growth, frequent local recurrences, multifaceted histological appearance, and potential pulmonary metastases [2]. In most cases, GCTB occurs around the knee joint, especially in the distal femur and proximal tibia, with a peak morbidity between the third and fourth decades and a slight predominance in females [3,4]. Surgical intervention is the most effective treatment, and the common surgical methods are extended curettage (EC)[5,6] and segmental resection (SR) [7-9]. EC has a higher unsatisfactory recurrence rate, but it preserves adjacent joint function [5]. On the other hand, SR has a lower recurrence rate, but joint function is greatly damaged, and bone reconstruction and joint intractability as well as long-term complications are more frequent [10,11]. Regardless of the type of surgery, postoperative recurrence of GCTB remains a major predicament in clinical diagnosis and treatment, especially around the knee joint.

As the treatment of recurrent GCTB (RGCTs) of bone around the knee is complicated, the likelihood of recurrence and secondary malignant transformation is further increased [12,13]. Hence, choosing an effective treatment method to balance the oncological and functional prognosis is the key and difficult point of reoperation. Unfortunately, no widely held consensus or clinical guidelines regarding the optimal treatment options exist. Therefore, we conducted this study to retrospectively analyze the clinical data of patients with RGCT around the knee between June 2007 and June 2017. We compared the clinical efficacy of EC and SR in the treatment of RGCT around the knee, focusing on the analytical difference between the two surgical methods in the oncological prognosis, functional prognosis, and postoperative complications, to provide clinical experience and a theoretical basis for treatment.

Materials And Methods

General conditions of the patients and selection criteria

Between June 2007 and June 2017, 275 patients with GCT were treated at our hospital. GCT was located around the knee joint in 128 patients, of whom 27 suffered relapse and the lesions were located in the distal femur or proximal tibia. Preoperative pathological diagnosis was confirmed by needle puncture and Campanacci grading II ~ III. X-ray, computed tomography (CT), and magnetic resonance imaging (MRI) of the lesions were routinely performed in all patients before surgery to determine the tumor size and soft tissue invasion. Pulmonary CT was performed to determine the presence of pulmonary metastasis. The inclusion criteria were: 1) patient with RGCT; 2) lesion located around the knee joint; 3) single-site lesion; 4) surgical treatment was performed; 5) complete follow-up data with a follow-up time > 24 months. The study was based on the Declaration of Helsinki 1964 and subsequent amendments and written informed consents were obtained from the patients or their legal guardians.

Surgical technique

Based on the classification methods of Enneking's [14] principle of resection of bone tumors and after considering the biological characteristics of local invasiveness of GCT, we adopted EC and SR for treatment.

EC was performed on Campanacci grade II and some grade III patients who had mild invasion of soft tissue, integrity of articular surface, and no obvious displacement of pathological fracture. The scar was excised from the original incision site, and the soft tissue around the lesion was strictly protected. The original filler and internal fixation materials were removed. The cavity of the tumors was treated with different sizes of curette, high-speed drilling, and argon air knife successively, followed by repeated flushing with a pulse gun. Iodine tincture was then smeared on the wall of the cavity, which was rinsed repeatedly every 2 minutes. The bone defect of the tumor cavity was repaired with allogeneic bone and bone cement (Fig. 1). The allogeneic bone was transplanted to the subchondral bone with a thickness of at least 1 cm. Finally, a locking plate was used to prevent 'ball effect' [15] (Fig. 2).

SR was performed for patients whose lesions broke through the bone cortex with extensive involvement of the surrounding soft tissue, complicated type C fracture or fracture involving the articular surface with obvious displacement (Fig. 3). The incision was made along the original biopsy puncture tract, and then the blood vessels and nerves of the lower limbs were properly freed. Osteotomy was performed at the diaphysis > 3 cm above the lesion and frozen margin examination was performed. Combined artificial prosthesis was used to reconstruct the bone defect and restore joint function (Fig. 4), and the sartorius or gastrocnemius muscle flap was transferred to properly cover the prosthesis.

Postoperative management and follow-up

Postoperative prophylactic anti-infection was administered for 72 h. Patients who underwent EC were able to perform partial half-weight-bearing activities after removal of the drainage tube, while those who underwent SR were fixed with plaster for 4 weeks, and functional exercises were performed after wound healing. The follow-up protocol consisted of radiography every 3 months to 2 years, followed by postoperative bi-annual radiographs for 4 years, and annual radiographs in the following years to evaluate oncological prognosis, functional prognosis, and complications. Additionally, pulmonary CT was reexamined bi-annually to prevent metastasis. The function was evaluated by the MSTS scoring system [16]. Furthermore, complications such as osteoarthritis, intra-articular fracture, infection, periprosthesis fracture, prosthesis loosening, etc. were recorded. The severity of osteoarthritis was assessed using Kellgren–Lawrence grades (K-L grades) [17].

Statistical Analysis

SPSS software version 20.0 (IBM Corp., Armonk, NY) was used for data analysis. Quantitative data were expressed as mean ± standard deviation, while qualitative data were expressed as frequency. Independent sample t-test was used to compare the mean among the two groups, and Chi square test or Fisher's exact test was used to compare the rates. $P < 0.05$ was statistically significant.

Results

There were 13 patients with pathological fractures before operation, 4 of who were complicated type C fractures with obvious displacement. Preoperative Campanacci grading included 2 cases of grade II and 20 cases of grade III. Twelve patients underwent EC and 10 underwent SR (Table 1).

Oncology prognosis

In the EC group, the follow-up time was 72.7 ± 40.2 months. Recurrence occurred in one case (8.3%) with no distant metastasis. Recurrence occurred 8 months after the initial curettage and cement filling treatment in our hospital. The RGCT was confirmed by puncture biopsy, followed by EC, subchondral bone grafting, and cement filling, and a follow-up of 54 months post-operation showed no signs of recurrence or metastasis (Figure 5). In the SR group, the follow-up time was 75.0 ± 25.7 months. Only 1 case (10%) recurred. Recurrence occurred 11 months after intracapsular curettage and bone grafting in the left distal femur. Subsequently, SR and artificial prosthesis reconstruction were performed. Unfortunately, the recurrence occurred again in the proximal part of the left tibia 15 months post-operation. On a repeat resection of the proximal tibial segment and reconstruction prosthesis after a definite diagnosis, no recurrence or metastasis was found after 52 months of follow-up. There was no significant difference in recurrence rate between the two groups (Table 2).

Complications

In the EC group, two patients had superficial wound infection and three patients had rejection reaction. The symptoms were controlled after debridement and anti-allergic treatment. Three patients had secondary osteoarthritis, including one case of K-L grade 1 and two cases of K-L grade 2. Nonneoplastic reoperation did not occur in this group. In the SR group, one patient had periprosthetic infection 4 months post-operation, and the infection was controlled after thorough debridement and lavage treatment. Aseptic loosening of prosthesis occurred in one patient, which was followed up with good limb function after prosthetic renovation. Three cases experienced joint stiffness in the early post-operative period; however, joint activity was satisfactory after rehabilitation. No periprosthesis fracture or fracture of the prosthetic stalk were observed. Cumulatively, nonneoplastic reoperation was performed twice in this group (Table 2).

Function and treatment evaluation

Postoperative function evaluation was based on the MSTS scoring system, and the best function before recurrence was considered as the evaluation index. A significant difference was observed between the EC group and SR group, which was 28.0 ± 1.6 and 24.9 ± 2.5, respectively. The Mankin criterion was used to evaluate the effect of operation. In the EC group, 10 cases were excellent, 1 good, and 1 poor. The overall excellent and good rate was 91.6%. In the SR group, 8 cases were excellent and 2 were poor. The overall excellent and good rate was 80%. A slight difference was observed between the two groups (Table 2).

Discussion

The focus of treatment options for GCT around the knee has gradually shifted from reducing the recurrence rate to focusing on the patient's joint function [18−20]. There is no standard optimal clinical treatment of recurrent GCT around the knee joint. Therefore, we conducted this study to evaluate the oncological and functional prognosis of EC and SR for recurrent GCT around the knee. Here we found no difference in the recurrence rate between the two surgical methods, but the incidence of joint function loss and post-operative complications in SR was higher than that in EC. Although most previous studies have shown that SR can achieve better oncological prognosis [21−24], the results of this study indicate otherwise, possibly due to the more aggressive treatment for patients with a high risk of recurrence. For Campanacci grade II and a few grade III patients, such as those with mild invasion of soft tissue, integrity of articular surface, and no obvious displacement of pathological fracture, prefer EC. Although this procedure has a certain risk of recurrence, it can retain the primitive joint structure as long as the tumor does not recur, and the patient's joint function can be guaranteed. However, for patients whose lesions break through the bone cortex and extensively involve the surrounding soft tissues, complicated type C fracture or fracture involving the articular surface with obvious displacement are at a higher risk of recurrence. Therefore, SR is preferred as a more aggressive treatment to reduce the risk of recurrence and achieve better prognosis of oncology; however, it is accompanied with considerable functional impairment and a higher risk of long-term complications. Simultaneously, there are several distinct limitations to this retrospective study. The number of cases is relatively small, resulting in weak convincing of statistical results; therefore, the correlation between local recurrence and surgical types cannot be effectively demonstrated. The follow-up time needs to be extended to evaluate the long-term complications and functional prognosis of different surgical methods. Hence, it is necessary to carry out long-term follow-up studies with large samples and multi-centers.

The core treatment concept of RGCT is early detection and treatment, effective postoperative rehabilitation, and follow-up [25−27]. Diagnosing recurrence on time is crucial for improving clinical efficacy and preserving joint function. Patients with early relapse often lack clinical symptoms, and symptomatic patients are more likely to have pathologic fractures [28]. The imaging manifestations of RGCT were obvious density reduction area around the cement filler [29] and irregular density reduction around the bone graft area [13].

In some cases, plaque-like or needle-like bone changes reappeared at the edge of the lesion, small pieces of osteolytic changes, and soft tissue masses appeared at the edge of the bone graft after healing [29]. CT and MRI can better reflect local lesions and soft tissue involvement [25]. All suspected recurrences should be confirmed by pathological examination to prevent sarcomatosis. Multiple studies have shown that patients with cement fillers can detect recurrence at an early stage as irregular low-density areas around the cement can be detected [29]. However, early recurrence of allograft-filled patients is often confused with allograft resorption, delaying diagnosis and affecting recovery [30, 31]. In this study, 10 patients were found to have recurrence after bone cement filling at an average of 10.5 ± 2.3 months, and 12 patients were found to have recurrence after allograft filling at an average of 18.6 ± 5.9 months ($P < 0.05$), indicating that cement filling was beneficial for identifying early recurrence, which was similar to previous studies [32, 33]. Therefore, we believe that patients should be regularly followed up. Upon occurrence of abnormal osteolysis, CT and MRI should be performed to prevent recurrence.

The therapeutic regimen for RGCT mainly depends on the extent of the lesion and surrounding bone condition [26, 27]. The purpose of the treatment is to prevent recurrence and maximize limb function preservation. RGCT clinical evaluation should be considered comprehensively, including initial treatment (bone grafting or cement filling, or artificial prosthesis reconstruction), nature and extent of invasion, and tumor comorbidity after recurrence, to make a judgment in accordance with clinical reality and provide basis for further treatment. Preoperative pathological examination of RGCT is particularly important to determine occurrence of sarcomatosis [12, 34]. Most cases of early recurrence are Campanacci grade I or II. The choice of treatment and therapeutic regimen can be appropriately conservative. EC combined with adjuvant therapy can effectively reduce the risk of local recurrence [2, 32]. Long-term complications are rare, and limb function can almost be completely preserved [19]. Even if the tumor recurs, it can still be treated with SR. For recurrent patients whose lesions break through the bone cortex and extensively involve the surrounding soft tissues, complicated type C fracture or fracture involving the articular surface with obvious displacement, the therapeutic regimen should be more aggressive [22, 23]. SR and artificial prosthesis reconstruction are conducive to a safer surgical margin and prevent recurrence to a greater extent; however, prosthesis-related complications (infection, aseptic loosening, periprosthetic fracture) and considerable functional impairment remain unavoidable.

Although rigorous preoperative design, sophisticated surgical techniques, and standardized post-operative follow-up can maximize the benefit of patients, the risk of recurrence of RGCT remains [35, 36]. The therapeutic regimen for recurrence post-operation can be referred to the initial recurrence, which is determined based on the specific conditions of the initial treatment, pathological characteristics, invasive extent, and tumor comorbidity after recurrence. In general, GCT is a locally invasive benign bone tumor, which mostly occurs in the third and fourth decade of life [37]. However, the knee joint, as an important weight-bearing joint of the lower extremity, has a high functional requirement, which is different from other bones, such as proximal fibula [37], distal radius [9], and distal ulna [31]. Therefore, despite a high risk of recurrence of RGCT, EC should be considered as the first-line treatment and SR should be avoided.

For RGCT around the knee joint, the patient's oncological and functional prognosis are vital. Unless the tumors break through the bone cortex and extensively involve the surrounding soft tissues, complicated type C fracture or fracture involving the articular surface with obvious displacement leading to patients without surgical curettage boundaries, EC should be considered as the preferred treatment.

Abbreviations

GCTB, giant cell tumor of bone; RGCT, recurrent giant cell tumors of bone; CT, computed tomography; MRI, magnetic resonance imaging; EC, extended curettage; SR, segmental resection; MSTS, Musculoskeletal tumor Society; K-L, Kellgren-Lawrence

Declarations

Conflicts of Interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Consent for publication

Figures in manuscript have been published with individuals' consent.

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Tables

Table- 1 Demographic and clinical follow-up data of patients

Patients number/ gender	Age and location	Filler materials**	Disease course (month)	Therapeutic Modalities	Follow-up (month)	Campanacci Grade	Pathological fracture	Post-op MSTS* score	Post-op recurrence	Complications
1/M	24/femur	BC+AB*	8	EC*	34	II	N	30	N	/
2/M	55/tibia	BC*	10	EC	145	III	N	25	N	osteoarthritis
3/F	42/tibia	AB*	14	EC	108	III	Y	27	N	/
4/M	50/tibia	AB	16	EC	102	II	N	29	Y	/
5/F	50/tibia	BC+AB	12	SR*	108	III	Y	24	N	joint stiffness
6/F	27/femur	AB	13	EC	26	III	N	26	N	osteoarthritis
7/M	37/tibia	AB	18	EC	83	II	Y	29	N	/
8/F	17/tibia	BC	8	SR	104	III	Y	23	N	joint stiffness
9/M	31/femur	AB	17	SR	94	III	N	29	N	/
10/M	27/femur	BC	9	EC	60	II	Y	30	N	/
11/M	43/femur	BC+AB	10	EC	69	II	N	26	N	osteoarthritis
12/M	36/tibia	AB	18	EC	142	III	N	28	N	/
13/F	28/tibia	AB	15	SR	67	III	Y	28	Y	/
14/M	30/tibia	AB	15	SR	64	III	Y	22	N	infection
15/F	29/femur	BC	10	SR	85	III	Y	24	N	/
16/F	32/tibia	BC	14	SR	105	III	Y	26	N	joint stiffness
17/M	28/tibia	BC+AB	8	EC	35	II	N	30	N	/
18/M	41/tibia	AB	22	EC	44	III	Y	28	N	/
19/F	31/femur	AB	31	SR	41	III	N	21	N	prosthesis loosening
20/F	26/tibia	AB	10	SR	29	III	Y	26	N	/
21/F	21/femur	AB	14	EC	27	II	Y	29	N	/
22/F	45/femur	BC	15	SR	68	III	Y	27	N	/

⦾ BC+AB, bone cement and allogeneic bone; BC, bone cement; AB, allogeneic bone; EC, extended curettage; SR, segmental resection; MSTS, musculoskeletal tumor society

⦾⦾ Materials for intracavity filling before recurrence

Table- 2 Data statistics and analysis of patients

Variable	EC* group(n=12)	SR* group(n=10)	P-value
Mean age, (sd)	37.0 ± 9.6	31.4 ± 8.5	
Gender, n (%)			
M	9	2	
F	3	8	
Campanacci Grade, n (%)			
II	2		
III	10	10	
Pathological fracture, n (%)	5	8	<0.05
Disease course(month)	14.2 ± 4.8	14.2 ± 6.2	
Duration of follow-up (mo)	72.7 ± 40.2	75.0 ± 25.7	
Local recurrence, n (%)	1(8.3%)	1(10%)	
Post-op MSTS* score	28.0 ± 1.6	24.9 ± 2.5	<0.05
Complication, n (%)			
osteoarthritis	3(25%)	0	
infection	1(8.3%)	1(10%)	
rejection reaction	3(25%)	0	
joint stiffness	0	3(30%)	
prosthesis loosening	0	1(10%)	
Reoperation, n (%)	1(8.3%)	2(20%)	<0.05
Excellent and good rate	11(91.6%)	8(80%)	<0.05

* EC, extended curettage; SR, segmental resection; MSTS, musculoskeletal tumor society

Figures

Figure 1

Characteristics of recurrence after curettage and bone grafting. (a,b,c) GCTB of the distal right femur recurred 9 months after curettage and bone grafting. Radiographs showed obvious eccentric expansion osteolytic lesions, CT and MRI can see the general boundary and the scattered high-density area in the focus is the original filling material. (d,e) Radiographs of 6 months after the treatment with expanded curettage, subchondral bone grafting and cement filling.
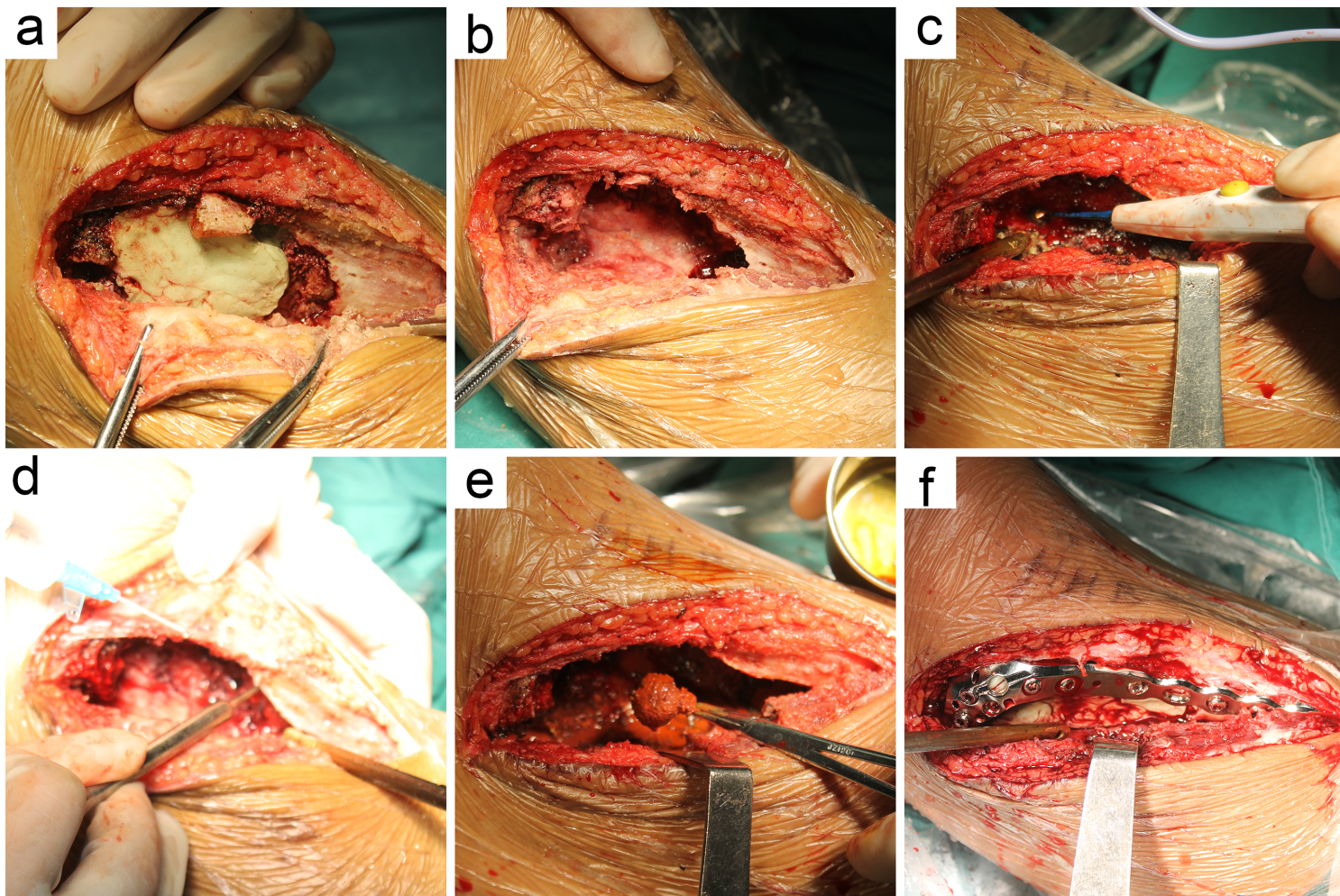
Figure 2

The procedure of expanded curettage and cement filling. (a) Thoroughly expose the lesion to ensure the operation under direct vision. (b) Remove the tumor tissue and flush the cavity to ensure that the visible lesions are removed. (c) Burn the cavity with argon knife to kill the remaining micro tumor lesions. (d) High speed drilling to remove the cauterization bone and residual bone ridge. (e) Cotton balls with iodine tincture were used to smear the cavity wall for 3 min. (f) Bone grafting, cement filling and steel plate fixation were performed successively.
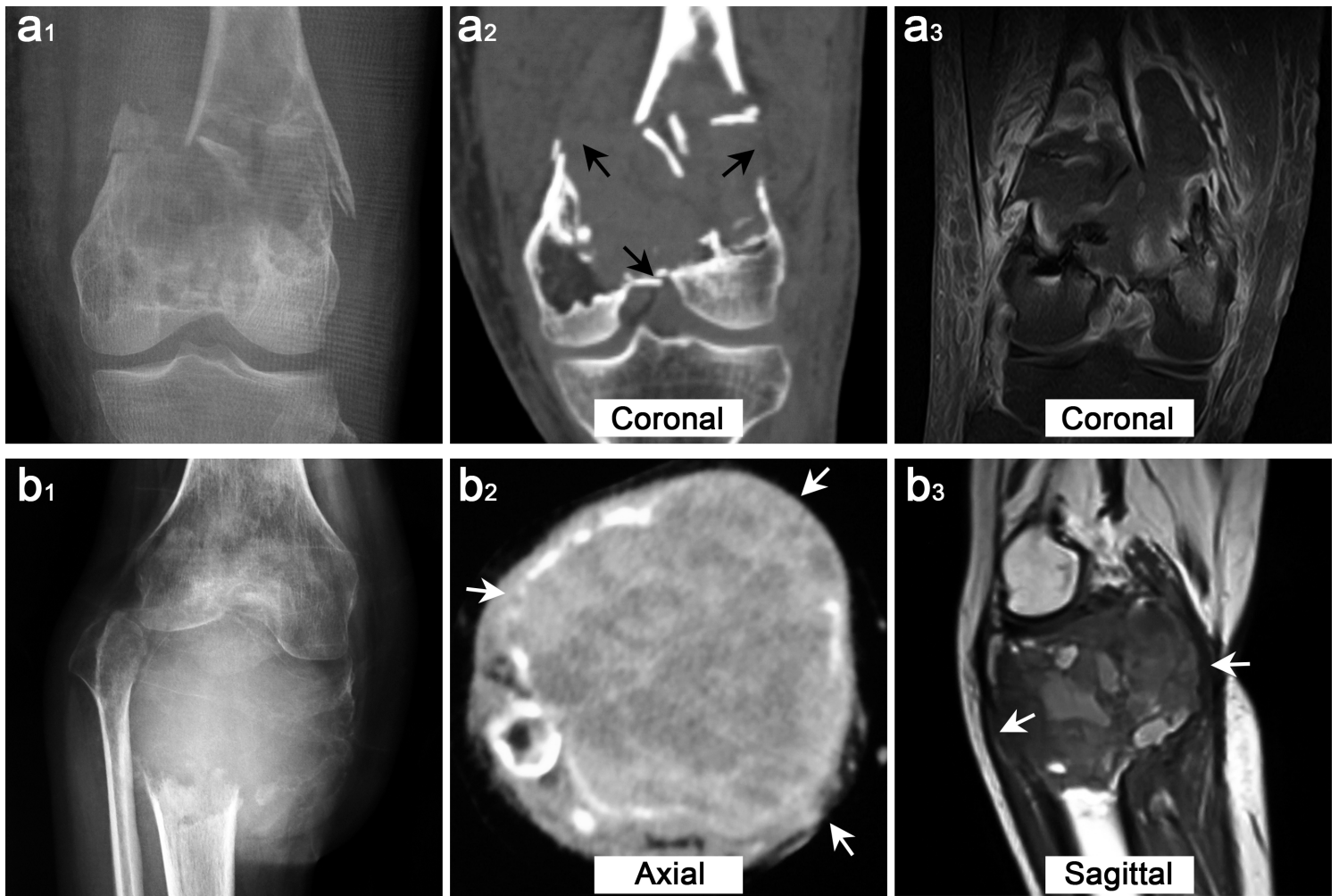
Figure 3

Indications for segmental resection (a1-a3) Pathological fractures occur in patients with GCTB. Complex type C fracture involving the articular surface (black arrow, fracture). Tumor tissue shows extensive contamination of the surrounding soft tissues in coronal magnetic resonance imaging. (b1-b3) GCTB of the proximal tibia breaks through the bone cortex, extensively affecting the surrounding soft tissues and invading the articular surface (white arrow, invading area).
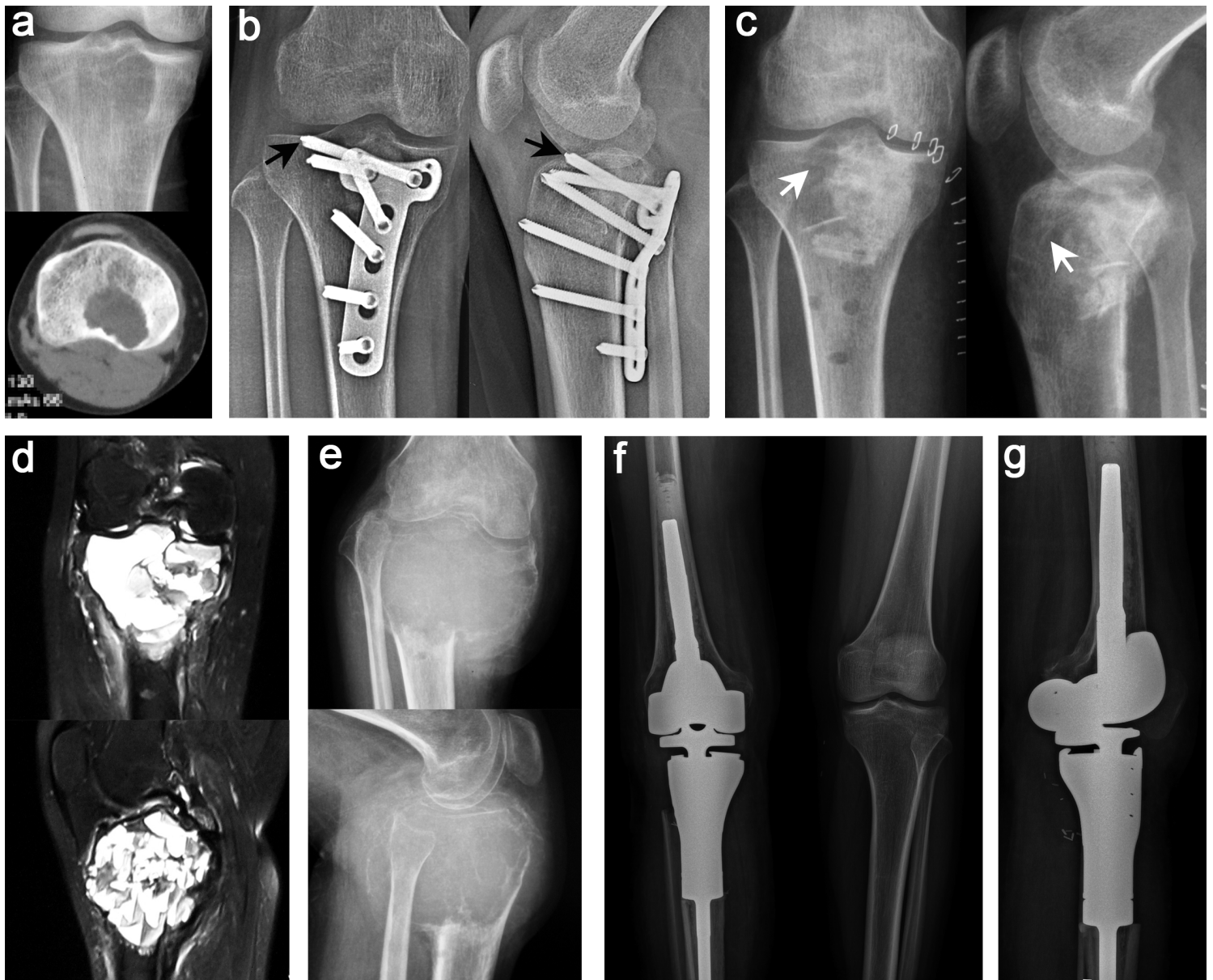
Figure 4

Typical imaging manifestations of recurrent giant cell tumor (RGCT) treated with segmental resection (SR) and artificial prosthesis reconstruction (a) Eccentric osteolytic lesions of the proximal tibia pathologically diagnosed with GCTB. (b) Intracapsular curettage and bone grafting performed in other hospitals. Screws penetrated the articular surface at 1 month post-operative follow-up (black arrow, articular surface penetration). (c) Recurrence in low density area after removal of the internal fixation (white arrows, low density areas). (d) MRI shows multilocular cystic changes 3 months after the removal of internal fixation, and the pathological diagnosis was GCTB with aneurysmal bone cyst. (e) Radiograph at 6 months after RGCT diagnosis (treatment delayed due to pregnancy). (f,g) Radiograph at 3 months after SR and artificial prosthesis reconstruction.

Figure 5

Typical imaging manifestations of recurrent giant cell tumor (RGCT) of the proximal tibia treated with extended curettage (EC) (a,b) GCTB of the proximal and lateral tibia treated with intracapsular curettage and cement filling. (c) A clear translucent area around the cement that extended to the diaphysis at 8 months post-operation. (d,e) CT shows low density changes around the bone cement and slight soft tissue invasion at the upper tibiofibular joint (black arrow, invading area). Pathological diagnosis revealed RGCT. (f) Radiograph at 3 months after EC, combined with subchondral bone graft and cement filling.