



## Original research

## Reconstruction using massive allografts after resection of extremity osteosarcomas the study design: A retrospective cohort study



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## HIGHLIGHTS

- We reviewed the clinical data of 15 patients.
- Neoadjuvant and postoperative chemotherapy was used in all patients.
- All patients were followed up for a mean of 61 months (range, 14–99 months).
- Bone union was evaluated using X-ray every 3 months.

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## ABSTRACT

**Purpose:** Allografts have been shown useful in the reconstruction of bone defects after tumor resection. This study aimed to investigate the feasibility of using massive allografts to reconstruct bone defects after resection of extremity osteosarcomas.

**Methods:** The clinical data of 15 patients treated with massive allograft reconstruction after resection of extremity osteosarcomas from January 2005 to January 2008 were retrospectively reviewed. Neoadjuvant and postoperative chemotherapy was used in all patients. The postoperative functions of the salvaged limbs were evaluated using the scoring system proposed by the Musculoskeletal Tumor Society (MSTS).

**Results:** All patients were followed up for a mean of 61 months (range, 14–99 months). No nonunion occurred during follow-up. The mean time to union was 9 months (range, 3–21 months). No immune rejection, allograft infection, allograft fracture, and limb length disparity occurred. However, 2 patients had broken implants. The mean MSTS score at the last follow-up was 26 points. Four patients died and 2 patients had tumor recurrence. The 5-year disease free survival rate was 73.3%.

**Conclusion:** Massive allograft reconstruction is safe and effective for bone defects caused by resection of extremity osteosarcomas.

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## 1. Introduction

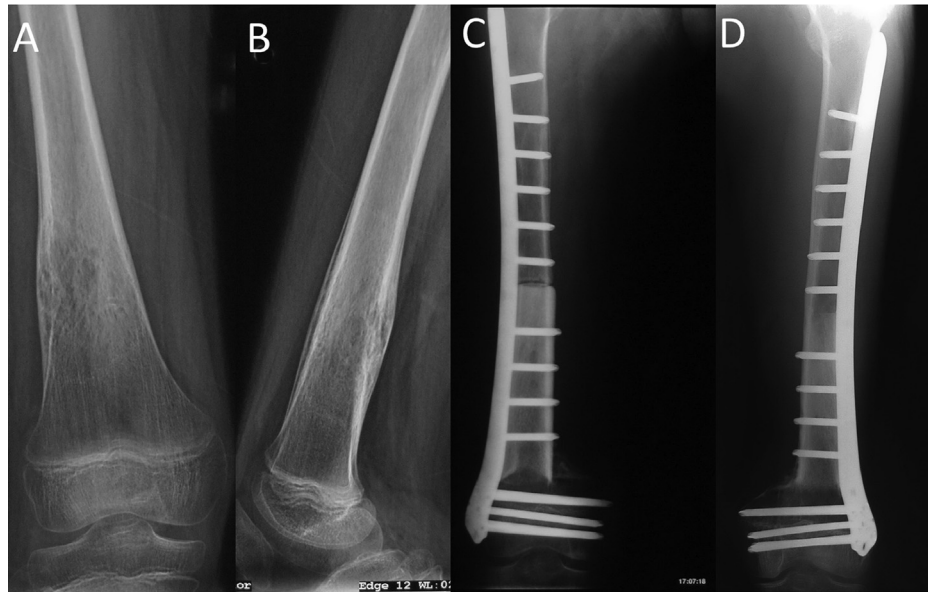
Osteosarcoma is the most common malignant bone tumors in adolescents. Previously, the prognosis of osteosarcoma is very poor with five-year survival rate less than 20% even after aggressive amputation [1–3]. In recent years, the use of neoadjuvant chemotherapy has increased the five-year survival rate of osteosarcoma patients to 60–80%, and advances in surgical

techniques have enabled limb salvage in over 80% of the patients [4–7]. Epiphysis and metaphysis of the long bones are the most frequent site of osteosarcoma, which often require resection of the joints. Accordingly, osteosarcomas in the metaphysis or diaphysis may enable salvage of adjacent joints [5,8]. Allografts have long been used to reconstruct the bone defect after bone resections of tumors with long-term success rates and good functional outcome [9,10]. In comparison with autografts, allografts have comparable mechanical stability and biological compatibility, and also advantages of rich sources and avoidance of donor site morbidity.

We have used massive allografts to reconstruct bone defects

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**Fig. 1.** Case 15. An 11-year-old boy with stage IIB osteosarcoma at the distal third of the femur. Preoperative X-ray showed the tumor on the anteroposterior view (A) and the lateral view (B). (C) At postoperative 6 months, bone union was observed at the distal allograft-host junction, and partial weight bearing was allowed. (D) At postoperative 1 year, bone union was observed at both allograft-host junctions, and full weight bearing was allowed.

after resection of extremity osteosarcomas in 15 patients. The clinical data and surgical outcomes are summarized in this report.

## 2. Materials and methods

The clinical data of 15 patients treated with massive allograft reconstruction after resection of extremity osteosarcomas were retrospectively reviewed. Our patients included 14 males and 1 female with a mean age of 19.5 years (range, 11–29 years). The Enneking stages included 1 case of IB, 12 cases of IIB (Fig. 1), and 2 cases of IIIB. The tumor locations were metaphysis in 6 cases and diaphysis in 9 cases (Table 1). This work is fully compliant with the STROBE criteria. This study was approved by the Institutional Review Board of our hospital.

All the lesions were diagnosed pathologically using preoperative biopsies under guidance of fluoroscopy or computed tomography. Neoadjuvant chemotherapy was used for 3 cycles and postoperative chemotherapy for 6 cycles. The chemotherapy regimen included ifosfamide 2 g/m<sup>2</sup> (days 1–5), methotrexate 8–12 g/m<sup>2</sup> (day 3) or cisplatin 100–120 mg/m<sup>2</sup> (day 6), and adriamycin 40 mg/m<sup>2</sup> (day 5). Vindesine sulfate 3 mg/m<sup>2</sup> was additionally used in patients with lung metastases on days 1 and 8.

Allografts were harvested from donated bodies under sterile conditions and were stored at –80 °C at the bone bank of our hospital. Preoperatively, the ipsilateral allografts with 2–4 cm extra length were selected for the planned bone defects. The allografts were thawed in normal saline and gentamicin in the operation room during tumor resection. The intramedullary fat tissue was thoroughly flushed. The tumor and its pseudocapsule were resected with 2–3 cm extra length then the preoperative magnetic resonance imaging. The mean length of the allografts was 13.7 cm (range, 6–24 cm). The allografts included joints in 3 cases and diaphysis in 12 cases (Table 1). No cancellous bone grafting or osteosynthesis materials were used at the allograft-host junctions.

Patients were encouraged to have muscle and joint exercises on bed within 6 weeks postoperatively. From 6 to 8 weeks, non-weight-bearing ambulation was allowed. Bone union was evaluated using X-ray every 3 months. Full weight bearing was allowed

when good bone union was achieved. The functions of the salvaged limbs were evaluated using the scoring system proposed by the Musculoskeletal Tumor Society (MSTS) [11].

## 3. Results

### 3.1. Bone union

All the patients were followed-up for a mean of 61 months (range, 14–99 months). Bone union was regarded as calluses or trabecular bone at the allograft-host junctions. The mean time to bone union was 9 months (range, 3–21 months).

### 3.2. Patient survival

Four patients died within 14–26 months, including both the two stage IIIB patients. One of the stage IIIB patient had metastases to multiple bones and organs. Another two stage IIB patients died from lung metastases. The other 11 patients survived without recurrence until the last follow-up. The five-year disease-free survival rate was 73.3%.

Tumor recurrence occurred in 2 stage IIB patients with osteosarcoma at the distal third of the femur within 1 year postoperatively. One patient was refractory to high-dose chemotherapy and had recurrence near the popliteal vessels. Despite amputation, the patient eventually died from lung metastasis. Another patient had recurrence at the popliteal fossa, which was treated with high-dose chemotherapy and radical resection. The allograft and plate were removed and total knee arthroplasty was performed. The patient showed no signs of recurrence or metastasis during follow-up of 5 years.

### 3.3. Complications

Two stage IIB patients had broken implants. In one patient with 24-cm bone defects, the allograft was fixed with intramedullary nails. The implants broke at 14 months postoperatively and the allograft was fixed with a plate. This patient was doing well within

**Table 1**  
Clinical data of the patients.

Patients	Sex	Age (years)	Tumor location	Enneking stages	Surgery	Follow-up time (month)	Allograft length (cm)	MSTS scores	Outcomes
1	Male	17	Distal femur	2B	1/2 joint + plate fixation	25	12	0	Died
2	Male	15	Distal third of femur	2B	Diaphysis + plate fixation	14	14	0	Recurrence and died
3	Male	22	Distal third of tibia	3	Diaphysis + nail fixation	26	10	0	Died
4	Male	15	Distal third of tibia	3	Diaphysis + nail fixation	16	15	0	Died
5	Male	14	Distal third of femur	1B	Diaphysis + plate fixation	62	13	23	Follow-up
6	Male	19	Distal third of femur	2B	Diaphysis + plate fixation	76	16	25	Recurrence
7	Female	23	Distal third of tibia	2B	Diaphysis + nail fixation	63	20	25	Follow-up
8	Male	20	Distal femur	2B	1/2 joint + plate fixation	97	9	26	Follow-up
9	Male	29	Distal third of femur	2B	Diaphysis + plate fixation	61	17	26	Follow-up
10	Male	25	Proximal third of tibia	2B	Diaphysis + plate fixation	75	10	26	Follow-up
11	Male	16	Proximal third of femur	2B	Diaphysis + nail and plate fixation	63	15	26	Follow-up
12	Male	29	Proximal tibia	2B	1/3 joint + plate fixation	98	6	27	Follow-up
13	Male	24	Distal third of femur	2B	Diaphysis + nail fixation	86	24	27	Broken implants
14	Male	13	Distal third of tibia	2B	Diaphysis + nail fixation	99	12	27	Broken implants
15	Male	11	Distal third of femur	2B	Diaphysis + plate fixation	88	12	28	Follow-up

5-year follow-up and showed no signs of recurrence and metastasis. Another patient had broken implants at 8 years post-operatively. The implants of the index surgery were impossible to be removed, and the allograft was fixed with a locking compression plate. No other complications were recorded during the follow-up, such as immune rejection, allograft infection, allograft fracture, and limb length disparity. The mean MSTS score at the last follow-up was 26 points.

#### 4. Discussion

Although osteosarcoma is a rare disease with an overall incidence of 0.2–3/100,000 per year (0.8–11/100 000 per year in the age group 15–19 years) [12], this disease is the third most common malignancy in adolescence [13]. The specific etiology of osteosarcoma is unknown, but it has been postulated to be associated with the rapid bone growth, given the tumor's typical metaphyseal location and its peak incidence during adolescence and early adulthood [14]. Osteosarcoma is best treated with complete surgical resection. Advances in imaging techniques and adjuvant chemotherapy have enabled limb salvage in around 80% of osteosarcoma patients [4,6]. Limb salvage surgery has slightly higher local recurrence rates (5–7%) than amputation (2–3%), but there is no significant difference in survival between the two treatment modalities [15,16]. Surgical margin is the most critical factor related with postoperative local recurrence, and a wide margin is considered safe [15,17]. Various surgical strategies have been developed to optimize the resection scope and preserve uninvolved tissues. However, the tumor resection unavoidably results in bone defects. Many biological and non-biological materials have been used for the reconstruction in limb salvage surgeries of extremity osteosarcomas.

When performing limb salvage after resection of extremity osteosarcomas, there are several factors that should be considered. The tumor must be completely resected. The salvaged limb is supposed to have better functions than prosthesis, and has lower risk for recurrence and better survival than amputation [18]. There are several treatment and reconstruction modalities for extremity osteosarcomas. Most of the osteosarcomas are in the epiphysis or metaphysis of the long bones, which can be treated with arthroplasty for the purpose of limb salvage. Microwave ablation is also an option. Osteosarcoma in the diaphysis is very rare and can be treated with replantation of inactivated tumor-bearing bone, bone

transportation, and massive allograft transplantation. Arthroplasty is an effective treatment method but the prosthesis may need several revisions. Children receiving arthroplasty may develop limb length disparity. Replantation of inactivated bone has high risks for tumor recurrence and fracture. Bone transportation is extremely time-consuming, and the patient cannot walk during the treatment. Poor local blood circulation and chemotherapy can increase the risk of failure of bone transportation. Massive allografts have high biological compatibility and good mechanical stability, and allow early ambulation of the patients. For patients with spared adjacent joints, massive allografts provide the best outcome for the reconstruction of bone defects after resection of extremity osteosarcomas, especially for those with an epiphyseal plate.

Gao et al. [19] reported the repair with massive allograft bones to preserve the epiphysis of the distal femur and knee function in 10 children with osteosarcoma. In this study, five cases were rated excellent, four cases good and one case fair, according to the functional evaluation criteria of the International Society of Limb Salvage (ISOLS) after operation. In another study of 15 patients with malignant tumors of the lower limb, massive allograft bones were used for the purpose of the epiphysis preservation after tumor resection [20]. In this study, normal knee joint flexion-extension was achieved in 14 patients, and all patients were able to walk unaided 24 months after surgery, suggesting a good function of the allografts. Jager et al. [21] combined massive bone allograft with free vascularized fibular flap for lower limb reconstruction after bone tumor resection in 7 children. These patients achieved partial weight-bearing about postoperative 2 months and full weight-bearing at about 5.5 months. Abed et al. [22] performed reconstruction using a combination of a free vascularized fibular graft and a massive allograft bone shell in 25 patients who had undergone resection of a primary bone sarcoma which extended to within 5 cm of the knee. In this study, full weight-bearing was achieved at a mean of 21.4 months (14–36), and the mean MSTS score at final follow-up was 27.4 (18–30).

#### 5. Conclusions

Our study showed that massive allograft reconstruction achieved desirable functions of the salvaged limbs. Massive allograft is a feasible, safe, effective material for the reconstruction of bone defects after resection of extremity osteosarcomas.

## Ethical approval

This study was approved by the Institutional Review Board of General Hospital of Chinese PLA.

## Funding

None.

## Author contribution

Study concepts: Gang Han, Yan Wang.  
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Quality control of data and algorithms: Jinpeng Jia.  
Statistical analysis: Meng Xu, Xiaoque Zheng.  
Manuscript preparation: Gang Han, Lina Mei.  
Manuscript editing: Gang Han, Mingyu Yang.  
Manuscript review: Yan Wang.

## Conflict of interest

The authors declare that they have no conflict of interest.

## Guarantor

Yan Wang.

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