



Does intramedullary nailing improve the union rate or decrease mechanical complications for patients with extremity sarcoma after biological reconstruction?

Jun Wang, Yi Yang, Rongli Yang, Xiaodong Tang, Wei Guo*

Peking University People's Hospital, Musculoskeletal Tumor Center, No. 11 Xizhimen South Street, 100044 Beijing, China

ARTICLE INFO

Keywords:

Extremity sarcoma
Biological reconstruction
Intramedullary nailing
Plate
Outcome

ABSTRACT

Introduction: This is a retrospective study that evaluate the outcome of patients with extremity sarcoma between extramedullary plate and intramedullary nailing for the biological reconstruction after tumor resection.

Methods: 58 patients (40 treated with plate fixation and 18 with intramedullary nailing, IM group) with sarcomas of the lower and upper extremity who received biological reconstruction at our bone tumor center from November 2003 to November 2015 were reviewed for the study. There were 29 male and 29 female patients with a mean age of 20.8 years (range, 5–72 years). The mean follow-up duration was 90.8 months (range, 12.2–244.4 months). All data were obtained from the clinical, radiograph records and follow-up information. The analysis of outcome, survival, local recurrence, function and complications of patients in the plate group and IM group was performed.

Results: 28 cases in the plate group lived at the last follow-up, of which 26 had no evidence of disease, 2 lived with the pulmonary metastasis, whereas 15 in the IM group lived at the last follow-up, of which all had no evidence of disease and no lived with the pulmonary metastasis. There was no significant difference between the two groups for the prognosis. Meanwhile, there was no significant difference of incidence of nonunion, graft fracture and fixation breakage between the two groups, whereas the time to diaphysis union in the plate group (11.6 ± 2.7 months) was shorter than that in IM group (14.7 ± 4.8 months, $P = 0.015$). It had the tendency that the time to mechanical complications in the intramedullary nailing group (38.1 ± 39.6 months) was longer than that in the plate group (15.7 ± 13.4 months, $P = 0.058$, 95% CI, -45.6–0.8). Furthermore, the infection occurred in 12 cases and five grafts of them developed the deep infection and the mean time to deep infection was 14.8 ± 20.5 months. Furthermore, the incidence of local recurrence for the patients who had plate fixation was similar to the incidence of patients who had nailing fixation. At the last follow-up, the functional evaluation was performed for 39 patients. There was no significant difference in MSTs and VAS functional score for patients between in the plate group ($n = 32$) and IM group ($n = 7$).

Conclusions: The findings of the present study showed that intramedullary nailing does not improve the union rate or decrease the incidence of mechanical complications for patients with extremity sarcoma after biological reconstruction. However, intramedullary nailing may have potential advantages on the service life for the biological reconstruction after extremity sarcoma resection.

© 2019 Elsevier Ltd. All rights reserved.

Introduction

Segmental resection of a tumor in the long bones can be treated with biological reconstruction including allograft or inactivated autograft. Allografts and inactivated autograft have been most

successful in intercalary and intraarticular reconstructions, with the advantages over prosthetic reconstruction in that it restores bone stock, avoids the prosthetic complication and provides possibly a lifelong biologic reconstruction. The structural allograft and inactivated autograft are appropriate alternatives in limb reconstruction after massive resection of involved tissues in malignant bone tumors and both can acquire satisfactory outcome in the previous studies [1–9]. Allografts and inactivated autograft need internal fixation to restore the limb stability for the biological reconstruction. However, it is unclear which fixation is better for

* Corresponding author.

E-mail addresses: pkujw2010@163.com (J. Wang), bonetumor@163.com (W. Guo).

biological reconstruction after resection of extremity sarcoma, intramedullary nailing or extramedullary plate.

Many studies in the literature have advocated the use of intramedullary nailing as the current treatment of choice in patients with the malignant bone tumor in the extremity due to the biomechanical superiority, which can enhance callus formation and decrease the mechanical complication [10–12]. However, the plating fixation has been reported to have good surgical outcomes for the treatment of limb bone tumor [1,3,13,14]. Although orthopedic surgeons should contemplate many factors to select the fixation method, it is still debatable whether intramedullary nailing or extramedullary plate is more appropriate for the surgical management of extremity malignant bone tumor for the biological reconstruction. Nevertheless, little is known that the intramedullary nailing improve the union rate or decrease mechanical complications for patients with extremity sarcoma after biological reconstruction. Thus, the objective of this study is to evaluate the outcome of patients with extremity sarcoma between extramedullary plate and intramedullary nailing for the biological reconstruction after extremity tumor resection.

Patients and methods

We retrospectively reviewed 58 patients (40 treated with plate fixation and 18 with intramedullary nailing, IM group) with sarcomas of the lower and upper extremity which had the intact clinical and follow-up information and who received biological reconstruction at our bone tumor center from November 2003 to November 2015. There were 29 male and 29 female patients with a mean age of 20.8 years (range, 5–72 years). The histological diagnoses were osteosarcoma (43 patients), Ewing's sarcoma (10 patients) and chondrosarcoma (5 patients). The tumors were located in the femur (28 patients), tibia (26 patients), humerus (2 patients) and fibula (2 patients). The clinical characteristics was shown in Table 1. The mean follow-up duration was 90.8 months (range, 12.2–244.4 months). The inclusion criteria for the present study were as follows: (1) diagnosis as sarcoma including osteosarcoma, Ewing sarcoma and chondrosarcoma, (2) with the intact clinical and follow-up data including basic characteristics, radiological data, function assessment and oncological/non-oncological evaluation at the last follow-up, (3) fixation method using any intramedullary nail device or plate. The exclusion criteria were as follows: (1) incomplete medical records, (2) inadequate follow-up, (3) fixation with the intramedullary nailing combined with the plate. 58 patients were divided into two groups (plate group and IM group), according to the fixation method (Figs. 1–3).

All patients which were included in the present study were gave written informed consent for their data to be included in this study during the follow-up. All data were obtained from the clinical and radiograph records. This study was approved by the Institutional Review Board/Ethics Committee of the authors' institution. For the initial clinical evaluation and diagnosis, all patients received plain

radiographs, CT, MRI and bone scanning. After imaging, we performed the needle biopsy to clarify the diagnosis and all patients were staged according to the surgical staging system of the MSTs. The routine follow-up including clinical examination, radiographs of the extremity and chest were performed every 3 months for the first 6 months, every 6 months for the first 3 years, and then annually. The chest CT scanning was performed every 6 months for the first 3 years, and then annually.

Surgical technique

We determined the limb salvage for the patient with extremity sarcoma that did not involve the major vessels as evaluated by preoperative radiological image and intraoperative finding. Limb salvage was planned to include the preoperative biopsy site, resect the tumor with a normal muscle cuff in all directions and resect the bone 2 cm–3 cm beyond abnormal uptake according to standard oncology principles.

After tumor resection, we performed the allograft or the inactivated autograft reconstruction following the preoperative surgical plan. For the devitalization of the bone, the surrounding soft tissue and any tumor mass protruding out of the bone were resected and the tumor in the medullary cavity and the eroded cortex bone were removed. The bony segment was then incubated in 20% sterile saline at 65 °C for 30 min. The recycled bone was prepared to be implanted after washing in normal saline at 37 °C. The osteosynthesis was performed according to the surgeons' preference with plates or the intramedullary nailing. Intercalary resection and biological reconstruction were performed for tumors 2 cm or greater from the articular surface. Meanwhile, intraarticular resection were performed for tumors less than 2 cm from the adjacent joint.

Assessment of outcome measures

Following data were collected to compare preoperative details between two groups in the present study: age, gender, affected side, anatomical site including femur, tibia, fibula and humerus, pathology type, pulmonary and other metastasis at presentation and follow-up period. Complications, local recurrence, metastasis and death were recorded from the clinical and follow-up files. Furthermore, the mechanical complications included allograft and inactivated graft fracture and fixation breakage. The oncological complications composed of recurrence and pulmonary and multiple metastasis. Meanwhile, the non-oncological complications included infection, nonunion, graft fracture and fixation breakage. We classified patients as having no evidence of disease (NED), live with disease (LWD) and dead with disease (DWD). We evaluated their function using the MSTs functional scoring system and VAS evaluation. We presumed that the union of allograft or inactivated autograft was achieved when continuous external bone borders between the graft and the recipient

Table 1
Comparison of the clinical characteristics between plate group and IM group.

	plate group (n = 40)	IM group (n = 18)	statistical significance
Gender male/ female	20/20	9/9	1.000
Age	18.2 ± 11.7	26.6 ± 19.7	0.106,95% CI, -18.7–1.9
Site femur/tibia/humerus/fibula	18/19/1/2	10/7/1/0	0.631
Side left/right	23/17	13/5	0.285
Graft-host junction diaphysis/metaphysis	23/26	15/12	0.726
Histological type OS/ES/CS	29/10/1	14/0/4	0.006
reconstruction method allograft/inactivated autograft	26/14	7/11	0.063
Pulmonary and other metastasis at presentation	2	3	0.143
Follow-up duration (m)	75.3 ± 41.5	125.3 ± 77.4	0.002,95% CI, -81.2--18.8

OS, osteosarcoma; ES, Ewing sarcoma; CS, chondrosarcoma.

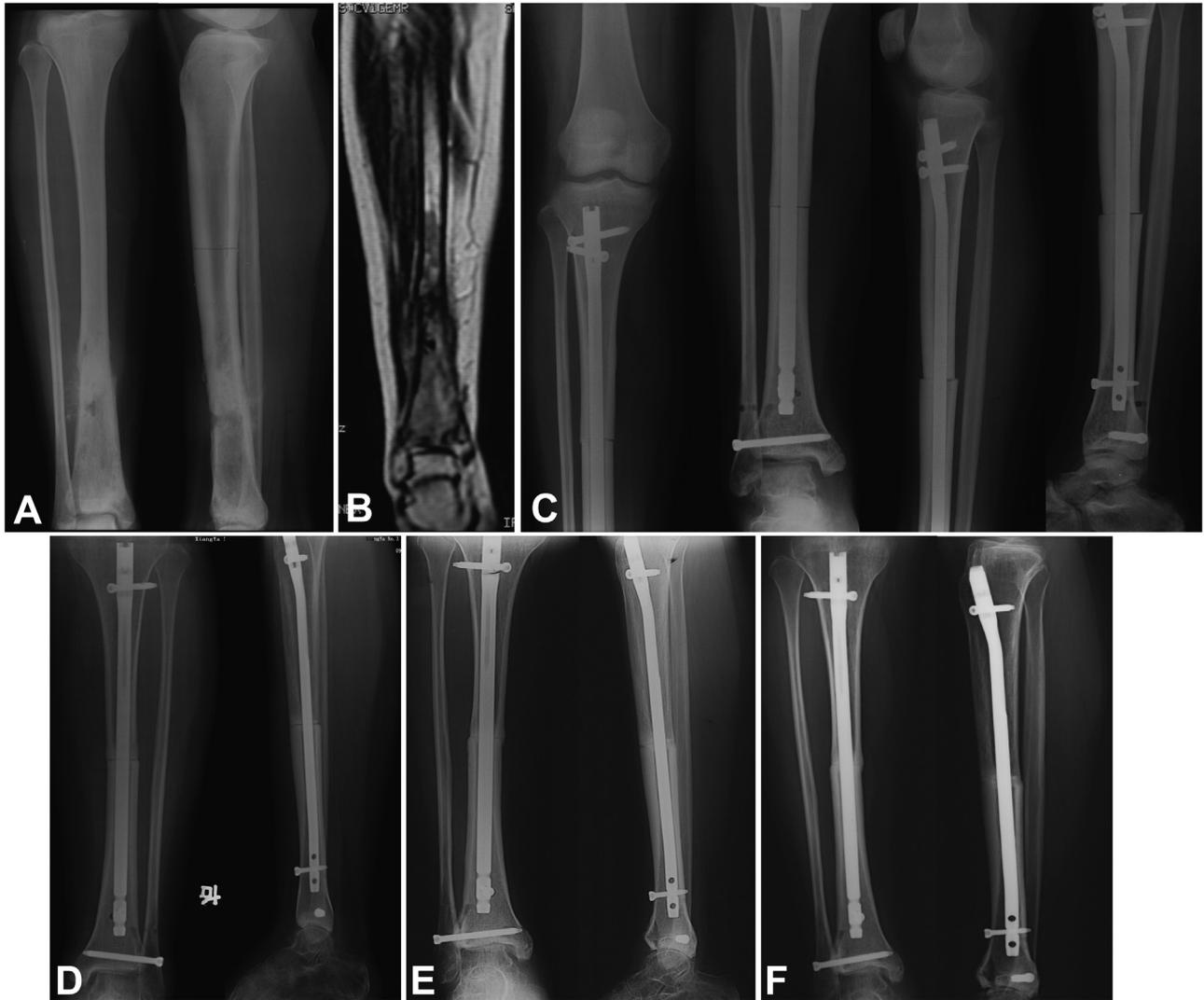


Fig. 1. A 21-year-old female patient with an osteosarcoma in the distal part of the right tibia reconstructed with the allograft bone and intramedullary nailing fixation after resection of the extremity sarcoma. A&B X ray and MRI showed a osteogenic lesion in the metaphysal region of the right distal tibia. C Postoperative X ray showed the allograft bone restored the limb defect perfectly and was fixed by the intramedullary nailing. D X ray at the 1 year after the operation. E X ray at the 1.5 years after the operation revealed continuous callus at the junction. F The perfect union at the junction were observed two years after the reconstruction in the X ray.

bone with obscured or absent osteotomy lines. Union and time to union were evaluated to assess radiological outcomes. Oncological and non-oncological reoperation numbers were calculated. Oncological reoperation was aiming to solve the recurrence and multiple metastasis. Simultaneously, non-oncological reoperation was designed to cure the nonunion, infection, graft fracture and fixation breakage.

Statistical analysis

The Student's *t*-test or the Mann-Whitney U test were used to compare preoperative details including age, follow-up time, time to union/fracture/fixation breakage /infection/reoperation number and MSTs/VAS analysis. The chi-square test was used to compare variables between two groups as follows: gender, affected side, anatomical site, pathology type, pulmonary and other metastasis at presentation, whether union, fracture, fixation breakage, mechanical complication, infection or not. The SPSS software (version 19.0; SPSS Inc, Chicago, IL, USA) was used for all statistical analyses. $P \leq 0.05$ indicated a statistically significant difference.

Results

The clinical characteristics of patients was shown in the [Table 1](#). The mean follow-up duration was 90.8 months (range, 12.2–244.4 months). 41 patients were free of disease, 15 had died of disease at the mean 32.7 months postoperatively and 2 lived with the pulmonary metastasis at the last follow-up. 28 cases in the plate group lived at the last follow-up, of which 26 had no evidence of disease, 2 lived with the pulmonary metastasis, whereas 15 in the IM group lived at the last follow-up, of which all had no evidence of disease and no lived with the pulmonary metastasis. However, there was no significant difference between the two groups for the prognosis ($P > 0.05$) ([Table 3](#)).

27 out of 58 patients had the non-oncological complications that required second surgery. 20 of 40 patients in the plate group had the second surgery due to the non-oncological complications compared to 7 of 18 patients in the IM group ($P = 0.433$). The mechanical complications included the nonunion, graft fracture and fixation breakage. There was no significant difference of incidence of nonunion, graft fracture and fixation breakage

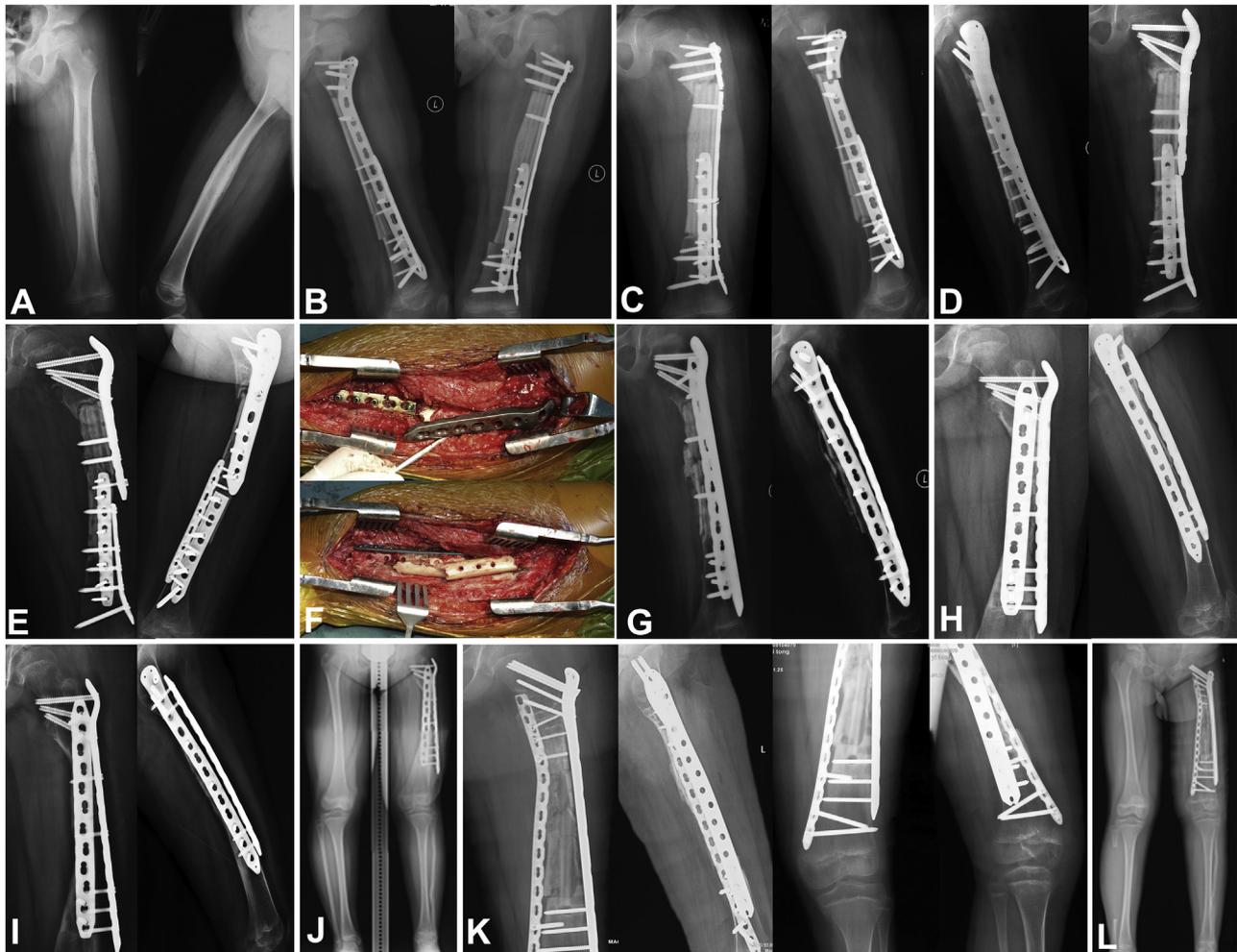


Fig. 2. A 5-year-old female patient with an Ewing sarcoma in the diaphysis of the left femur reconstructed with the allograft bone and plate fixation after resection of the limb tumor. A X ray showed a osteogenic mass in the middle part of the left femur. B The perfect biological reconstruction with the allograft bone was showed in the postoperative X ray. C The plate breakage was observed at the half of one year after the initial surgery. D The lateral plate of the proximal femur was utilized after removal of the lateral plate at the second operation. E The nonunion was observed and the second mechanical failure occurred at the five months after the second surgery. F The intraoperative photo after removal of the failure fixation. G The longer plate was fixed at the third operation. H The follow-up at the 29 months after the third operation. I&J The follow-up at the 35 months after the third operation and the mechanical failure was observed in the X ray. K&L The longer double plates combined with free vascularised fibula was performed in the fourth operation.

between the two groups, whereas the time to diaphysis union in the plate group (11.6 ± 2.7 months) was shorter than that in IM group (14.7 ± 4.8 months, $P=0.015$). It had the tendency that the time to mechanical complications in the intramedullary nailing group (38.1 ± 39.6 months) was longer than that in the plate group (15.7 ± 13.4 months, $P=0.058$, 95% CI: -45.6–0.8). Furthermore, the infection occurred in 12 cases and five grafts of them developed the deep infection and the mean time to deep infection was 14.8 ± 20.5 months. Four graft infections in the plate group respectively occurred postoperatively at 49.5, 17.4, 2.7 and 0.4 months and one grafts in IM group at 3.9 months. All five grafts were removed to control the deep infection (Table 2).

19 out of 58 patients had the local recurrence that required surgery treatment. Ten of patients with local recurrence received the amputation, six of them had the prosthetic reconstruction, two had the resection of the recurred soft tumor, one was performed the arterial infusion chemotherapy and the other one rejected the operation. Furthermore, the incidence of local recurrence for the patients who had plate fixation (37.5%, 15/40) was similar to the incidence for patients who had nailing fixation (22.2%, 4/18). 15 of 40 patients in the plate group had the second surgery that solved the local recurrence compared to 4 of 18 patients in the IM group

($P=0.251$). Time to recurrence after operation in the plate group and IM group was respectively 35.3 ± 30.9 months and 46.2 ± 71.7 months and there was no statistical difference between the two group for the time to recurrence after first surgery ($P=0.642$, 95% CI: -59.8–37.9) (Table 3).

At the last follow-up, the functional evaluation was performed for 39 patients. There was no significant difference in MSTs functional score for patients between in the plate group ($n=32$) and IM group ($n=7$) (25.9 ± 4.3 vs 27.6 ± 2.2 , 95% CI: -5.1–1.7, $P=0.329$). Meanwhile, no statistical difference for VAS evaluation existed between the two groups (plate group: 0.3 ± 0.6 , IM group: 0.3 ± 0.5 , 95% CI: -0.5–0.5, $P=0.986$).

Discussion

The main purpose of the present study was to evaluate the outcome measures of patients with extremity sarcoma between extremedullary plate and intramedullary nailing for the biological reconstruction. Although plating and intramedullary nailing have been accepted as different fixation methods for the biological reconstruction after resection of the extremity sarcoma, there was no study in the literature which compared the outcome between

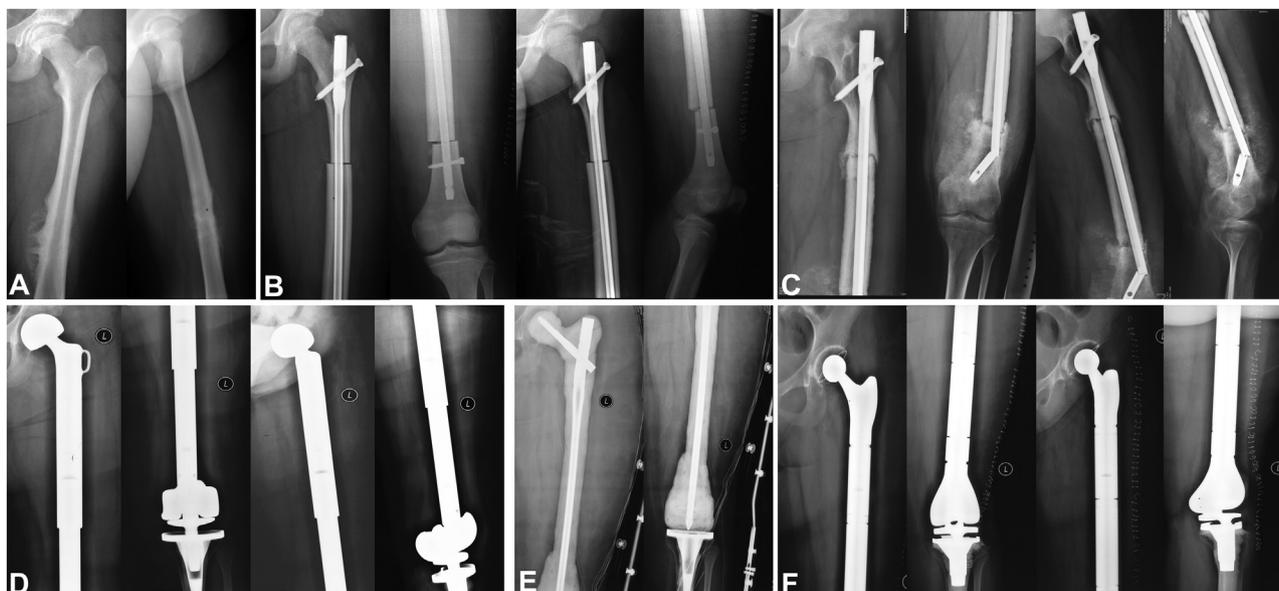


Fig. 3. A 12-year-old female patient with an osteosarcoma in the diaphysis of the left femur reconstructed with the allograft bone and intramedullary nailing fixation after resection of the extremity sarcoma. A X ray showed a mixture of the lytic and osteogenic lesion in the diaphysis of the left femur. B A 14-cm segmental bone was resected and the appropriate allograft bone was utilized, which was fixed by the intramedullary nailing. C The tumor recurrence was observed during the follow-up at the postoperative 21 months. D The total femoral prosthesis replacement was performed after resection of recurred tumor. E The infection occurred at the four years after the total femoral prosthesis replacement and the cement spacer was recruited for the control of infection. F The second total femoral prosthesis replacement was performed after the control of infection at the two years post the third surgery. G The second total femoral prosthesis replacement was performed after the control of infection at the two years post the third surgery.

Table 2
Comparison of the mechanical complications between plate group and IM group.

	plate group (n = 40)	IM group (n = 18)	statistical significance
Mechanical complication	17	4	0.137
Time to mechanical complication	15.7 ± 13.4	38.1 ± 39.6	0.058, 95% CI, -45.6–0.8
Nonunion	11	4	0.671
Time to union for diaphysis (m)	11.6 ± 2.7	14.7 ± 4.8	0.015, 95% CI, -5.6–0.6
Time to union for metaphysis (m)	8.4 ± 3.6	9.9 ± 3.7	0.244, 95% CI, -4.1–1.1
Graft fracture	7	1	0.222
Time to fracture after op (m)	21.3 ± 17.2	114.4	0.002
Fixation breakage	10	1	0.081
Time to breakage after op (m)	11.7 ± 8.0	19.6	0.375
Infection	9	3	0.612
Time to infection after op (m)	10.1 ± 16.0	25.7 ± 38.2	0.320
Oncological reoperation number	0.5 ± 0.6	0.2 ± 0.4	0.174, 95% CI, -0.1–0.6
Non-oncological reoperation number	0.8 ± 1.0	0.6 ± 0.8	0.429, 95% CI, -0.3–0.8
Total reoperation number	1.3 ± 1.0	0.8 ± 1.1	0.146, 95% CI, -0.2–1.0

Table 3
Comparison of the oncological prognosis between plate group and IM group.

	plate group (n = 40)	IM group (n = 18)	statistical significance
Local recurrence	15	4	0.251
Time to recurrence after operation	35.3 ± 30.9	46.2 ± 71.7	0.642
Outcome			
NED	26	15	0.310
DWD	12	3	
LWD	2	0	

NED, no evidence of disease; LWD, live with disease; DWD, dead with disease.

the two fixations [13–16]. Thus, we compared survival, local recurrence, function, and oncological/non-oncological complications of patients with extremity sarcoma reconstructed with intramedullary nailing or extramedullary plate. In the present study, the survival, local recurrence, function and complication incidence were similar and intramedullary nailing does not

improve the union rate or decrease the incidence of mechanical complications for patients with extremity sarcoma after biological reconstruction, but it had a tendency that the time to graft fracture of patients with intramedullary nailing fixation was longer than that with the plate fixation. However, the conclusions are tempered by the small case numbers.

Although many studies supported the opinion that intramedullary nailing may provide more advantages over extreme-dullary plate for the treatment of extremity fracture due to its mechanical advantage, no significant differences in union rates, graft fracture and fixation breakage were identified between the two groups in our study [17–21]. The mechanical complications included nonunion, graft fracture and fixation breakage in our study. Some studies showed that intramedullary nailing could stimulate the union of traumatic fracture due to its mechanical advantage, whereas other opinions revealed that the plate appeared to be advantageous over intramedullary nailing in terms of leading to a better anatomical and fixed reductions of the fracture and a lower rate of union complications [17,18,20–23]. But for the reconstruction with allograft or inactivated autograft after resection of extremity tumor, the bone bioactivity is the most remarkable factor which influences the union of host-graft site [7,8,24,25]. As a result of its compromised bioactivity, intramedullary nailing can not abstain from the delayed union or nonunion of host-graft site after resection of extremity sarcoma and our findings also supported this speculation. However, there are several interesting findings. For the patients with mechanical failure, the time to failure and graft fracture in the plate group was earlier than that in IM group. This result illustrated that it may have potential mechanical advantages for the biological reconstruction after extremity sarcoma resection, although the intramedullary nailing could not improve the union rate.

Based on our results, we believe that intramedullary nailing can not improve the union rate or decrease the occurrence of mechanical complications for patients with extremity sarcoma after biological reconstruction. Furthermore, our analysis showed that the time to diaphysis union after intramedullary nailing was obviously longer than that after extramedullary plate. Alternative to enhance graft union include autogenous bone grafting, bone morphogenic protein, bisphosphonate treatment and more other methods [26–28]. Plate fixation allows controlled compression of the host osteotomy site to the allograft or inactivated autograft bone. In comparison, fixation with intramedullary devices can induce distraction and fretting at the host allograft or inactivated autograft junction and it influences the graft union which is distinct from the treatment of traumatic fracture. The most important limitation of biological reconstructions using intramedullary devices is the inability to generate compression across host-graft junctions, resulting in gap formation and suboptimal healing conditions. Some studies revealed that the inferior allograft or inactivated graft healing rates associated with increasingly larger cortical displacement [29,30]. In an already compromised healing environment, a residual gap may be substantial and lead to bone graft delayed union or nonunion [31]. Thus, the compression effect of the plate can increase the graft union for the biological reconstruction after tumor resection compared to the intramedullary nailing.

Infection is also the common complication that may occur after allograft or inactivated autograft implantation for bone tumor resection. The infection of large segment allograft or inactivated autograft is extremely difficult to treat when it occurs and it may ultimately lead to limb amputation [22,32]. Meanwhile, due to malignant systemic diseases and chemotherapy in some patients, the immune system became compromised and the patient was thus predisposed to the site infection [8,32,33]. The rate of infection in our study was 20.7% (12 in 58 cases) and there was no significant difference between the two groups. It illustrated that the choice of fixation method did not influence the infection occurrence.

The present study had several limitations. Firstly, this was a retrospective study. All preoperative factors that may affect surgical outcomes between the two groups could not be randomly

controlled. Secondly, the preference for utilizing plates versus intramedullary nailing and the fact that surgeons performed the procedures without standardized training also made it difficult to accurately determine which fixation was better. Thirdly, the sample size was too small to show significant difference between the two fixation methods and in the future study, a larger sample size would be needed to show that which fixation is superior for the biological reconstruction after resection of extremity sarcoma.

In conclusion, the findings of the present study showed that intramedullary nailing does not improve the union rate or decrease the incidence of mechanical complications for patients with extremity sarcoma after biological reconstruction. However, intramedullary nailing may have potential advantages on the service life for the biological reconstruction after extremity sarcoma resection.

Competing interests

The authors declare that they have no competing interests.

Funding

This work was supported by the Natural Science Foundation of China (NO:81702657).

Ethical approval

This article does not contain any studies with human participants or animals performed by any of the authors.

Informed consent

Informed consent was obtained from all individual participants included in the study.

References

- [1] Erol B, Basci O, Topkar MO, Caypinar B, Basar H, Tetik C. Mid-term radiological and functional results of biological reconstructions of extremity-located bone sarcomas in children and young adults. *J Pediatr Orthop Part B* 2015;24:469–78.
- [2] Li J, Wang Z, Pei GX, Guo Z. Biological reconstruction using massive bone allograft with intramedullary vascularized fibular flap after intercalary resection of humeral malignancy. *J Surg Oncol* 2011;104:244–9.
- [3] Brunet O, Anract P, Bouabid S, Babinet A, Dumaine V, Tomeno B, et al. Intercalary defects reconstruction of the femur and tibia after primary malignant bone tumour resection. A series of 13 cases. *Orthop Traumatol Surg Res* 2011;97:512–9.
- [4] Gharedaghi M, Peivandi MT, Mazloomi M, Shoorin HR, Hasani M, Seyf P, et al. Evaluation of clinical results and complications of structural allograft reconstruction after bone tumor surgery. *Arch Bone Jt Surg* 2016;4:236–42.
- [5] Aponte-Tinao L, Farfalli GL, Ritacco LE, Ayerza MA, Muscolo DL. Intercalary femur allografts are an acceptable alternative after tumor resection. *Clin Orthop Relat Res* 2012;470:728–34.
- [6] Bullens PH, Minderhoud NM, de Waal Malefijt MC, Veth RP, Buma P, Schreuder HW. Survival of massive allografts in segmental oncological bone defect reconstructions. *Int Orthop* 2009;33:757–60.
- [7] Li J, Zhang F, Yang M, Liu S, Wang X, Yang Q, et al. Extracorporeally frozen tumour-bearing bone combined with free vascularised fibula for the intercalary reconstruction of femoral defect after resection of bony sarcoma. *J Plast Reconstr Aesthet Surg* 2016;69:856–63.
- [8] Yang J, Zhu B, Fu K, Yang Q. The long-term outcomes following the use of inactivated autograft in the treatment of primary malignant musculoskeletal tumor. *J Orthop Surg Res* 2015;10:177.
- [9] Qu H, Guo W, Yang R, Li D, Tang S, Yang Y, et al. Reconstruction of segmental bone defect of long bones after tumor resection by devitalized tumor-bearing bone. *World J Surg Oncol* 2015;13:282.
- [10] Moon B, Lin P, Satcher R, Bird J, Lewis V. Intramedullary nailing of femoral diaphyseal metastases: is it necessary to protect the femoral neck? *Clin Orthop Relat Res* 2015;473:1499–502.
- [11] Piccioli A, Rossi B, Scaramuzzo L, Spinelli MS, Yang Z, Maccauro G. Intramedullary nailing for treatment of pathologic femoral fractures due to metastases. *Injury* 2014;45:412–7.
- [12] Ward WG, Spang J, Howe D, Gordan S. Femoral recon nails for metastatic disease: indications, technique, and results. *Am J Orthop* 2000;29:34–42.

- [13] Kowalczyk B, Miklaszewski K, Felus J. Spontaneous healing of fractures and osteotomy within intercalary allograft reconstruction after distal femur osteosarcoma resection in a child. *J Pediatr Orthop Part B* 2016.
- [14] Rabitsch K, Maurer-Ertl W, Pirker-Fruhauf U, Wibmer C, Leithner A. Intercalary reconstructions with vascularised fibula and allograft after tumour resection in the lower limb. *Sarcoma* 2013;2013:160295.
- [15] Han G, Wang Y, Bi W, Jia J, Wang W, Xu M, et al. Reconstruction using massive allografts after resection of extremity osteosarcomas the study design: a retrospective cohort study. *Int J Surg* 2015;21:108–11.
- [16] Miller BJ, Virkus WW. Intercalary allograft reconstructions using a compressible intramedullary nail: a preliminary report. *Clin Orthop Relat Res* 2010;468:2507–13.
- [17] Zarkadis NJ, Eisenstein ED, Kusnezov NA, Dunn JC, Blair JA. Open reduction-internal fixation versus intramedullary nailing for humeral shaft fractures: an expected value decision analysis. *J Shoulder Elbow Surg/Am Shoulder Elbow Surg* 2018;27:204–10.
- [18] Bisaccia M, Cappiello A, Meccariello L, Rinonapoli G, Falzarano G, Medici A, et al. Nail or plate in the management of distal extra-articular tibial fracture, what is better? Valuation of outcomes. *Sicot-J* 2018;4:2.
- [19] Allende C, Vanoli F, Gentile L, Gutierrez N. Minimally invasive plate osteosynthesis in humerus nonunion after intramedullary nailing. *Int Orthop* 2018;42:2685–9.
- [20] Shin WC, Moon NH, Jang JH, Lee HJ, Suh KT. Comparative study between biologic plating and intramedullary nailing for the treatment of subtrochanteric fractures: Is biologic plating using LCP-DF superior to intramedullary nailing? *Injury* 2017;48:2207–13.
- [21] Ebraheim NA, Evans B, Liu X, Tanius M, Gillette M, Liu J. Comparison of intramedullary nail, plate, and external fixation in the treatment of distal tibia nonunions. *Int Orthop* 2017;41:1925–34.
- [22] Mauffrey C, Hak DJ, Giannoudis P, Alt V, Nau C, Marzi I, et al. Treatment of infection following intramedullary nailing of tibial shaft fractures—results of the ORS/ISFR expert group survey. *Int Orthop* 2018.
- [23] Lin L, Liu Y, Lin C, Zhou Y, Feng Y, Shui X, et al. Comparison of three fixation methods in treatment of tibial fracture in adolescents. *ANZ J Surg* 2018;88: E480–E5.
- [24] Han I, Kim JH, Cho HS, Kim HS. Low-heat treated autograft versus allograft for intercalary reconstruction of malignant bone tumors. *J Surg Oncol* 2014;110:823–7.
- [25] Piotrowski M, Pankowski R, Luczkiewicz P, Markowicz A. A comparison of the effect of autogenous vs. frozen homogenous grafts on the healing of non-union of forearm bones. *Ortop Traumatol Rehabil* 2008;10:146–51.
- [26] Fuchs B, Ossendorf C, Leerapun T, Sim FH. Intercalary segmental reconstruction after bone tumor resection. *Eur J Surg Oncol* 2008;34:1271–6.
- [27] Delloye C, Suratwala SJ, Cornu O, Lee FY. Treatment of allograft nonunions with recombinant human bone morphogenetic proteins (rhBMP). *Acta Orthop Belg* 2004;70:591–7.
- [28] DiResta GR, Manoso MW, Naqvi A, Zanzonico P, Smith-Jones P, Tyler W, et al. Bisphosphonate delivery to tubular bone allografts. *Clin Orthop Relat Res* 2008;466:1871–9.
- [29] Enneking WF, Campanacci DA. Retrieved human allografts: a clinicopathological study. *J Bone Joint Surg Am* 2001;83-A:971–86.
- [30] Vander Griend RA. The effect of internal fixation on the healing of large allografts. *J Bone Joint Surg Am* 1994;76:657–63.
- [31] Miller BJ, Virkus WW. Intercalary allograft reconstructions using a compressible intramedullary nail: a preliminary report. *Clin Orthop Relat Res* 2010;468:2507–13.
- [32] Angelini A, Drago G, Trovarelli G, Calabro T, Ruggieri P. Infection after surgical resection for pelvic bone tumors: an analysis of 270 patients from one institution. *Clin Orthop Relat Res* 2014;472:349–59.
- [33] Mavrogenis AF, Abati CN, Romagnoli C, Ruggieri P. Similar survival but better function for patients after limb salvage versus amputation for distal tibia osteosarcoma. *Clin Orthop Relat Res* 2012;470:1735–48.