Orthopaedic Surgery

CLINICAL ARTICLE

Clinical Outcome of Free Vascularized Fibula Graft in the Surgical Treatment of Extremity Osteosarcoma

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Objective: To determine the clinical outcome and complications associated with use of free vascularized fibular graft (FVFG) in the resection and reconstruction of extremity osteosarcoma (OS).

Methods: This is a retrospective study recruiting a consecutive series of 18 patients who had undergone resection of extremity OS between May 2009 and June 2017 in our clinic center. Reconstruction of the bone defect with FVFG was performed for each patient. Surgery-related complications and time of bone union were recorded at the follow-up visit. The functional outcome of the reconstructed limb was assessed with the musculoskeletal tumor society (MSTS) scoring system. Patients were further classified into low extremity group and upper extremity group according to the tumor location. The Student t-test was used to compare the surgical outcome between the two subgroups.

Results: There were 11 males and seven females with an average age of 25.9 ± 14.2 years. The mean length of the bone resection was 11.9 ± 4.1 cm. The mean follow-up duration was 3.1 ± 1.2 years. As for tumor location, six cases were located in the femur, five in the tibia, four in the humerus, two in the ulna, and one in the radius. All the patients had successful graft healing at an average of 4.9 months after surgery. At the 2-year follow-up, an excellent functional outcome was observed in 88.9% of the patients (n = 16). The mean score of MSTS was 27.0 ± 4.6. Screw loosening and autograft fracture were observed in one patient with femur tumor, who had a low MSTS score of 11. Besides, there were three cases with delayed incision healing. Patients with lower extremity OS were found to have significantly longer duration of hospital stay and more blood loss than those with upper extremity OS. The incidence of postoperative complication was higher in the lower extremity group but with marginal significance (0% *vs* 36.3%, $P = 0.1$). There was no significant difference regarding time to bone union and the functional outcome as indicated by MSTS score.

Conclusions: FVFG technique can be effectively applied to the reconstruction of bone defects after OS resection with satisfactory functional outcome and low incidence of complications.

Key words: Biological reconstruction; Free vascularized fibula graft; Osteosarcoma

Introduction

Patients with extremity osteosarcoma (OS) were routinely treated by amputation in the last century[1]. With the advances of adjuvant chemotherapy, supportive care, and multidisciplinary approach, the overall survival of OS patients has been greatly improved and limb salvage surgery was performed to preserve the extremities function[2–5]. In a recent systematic review of the literature which evaluated the outcomes of OS resection either with limb salvage or amputation, the authors supported limb salvage procedures where wide surgical margins can be achieved and a functional limb can still be retained[5]. However, the authors also noted that there were higher revision

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rates (31%) and more complications (52%) in the salvage groups[5]. Thereafter, reconstruction of long bone defects after tumor resection has become a great challenge for surgeons. Many reconstructive techniques are now available for the resection of extremity tumors, such as allografts, autografts, and prosthetic devices[6–9]. Compared with reconstruction by prosthesis, biologic reconstruction can result in improved long-term functionality, yet has a relatively high complication rate[10]. Strategy to employ which type of graft largely depends on tumor location, size, conditions of soft tissue, and cosmetic requirements.

The fibula graft is a popular way for the reconstruction of segmental defects after tumor resection[11,12]. The fibula can be used either as non-vascularized fibular graft or free vascularized fibular graft (FVFG). Currently, with the advance of microsurgical techniques, the transplantation of bony graft with nutritional vascular pedicle has been a feasible option. Compared with non-vascularized graft, vascularized autograft has been reported to enhance biologic incorporation[11,12], as the blood supply is preserved by the connection of the feeding artery of the graft to a host artery. FVFG was initially applied to reconstruction of large defects of tibia[13,14]. Innocenti *et al.*[13] investigated a cohort of 21 patients undergoing excision of bone tumor of the proximal tibia and described the outcome of FVFG in the reconstruction of bone defect. Good long-term results were observed as indicated by a mean musculoskeletal tumor society (MSTS) score of 27.3 at the final follow-up. In another consecutive case of FVFG for the reconstruction of extensive tibia defects, Lee *et al.*[14] reported that bony union was achieved in 96% of patients at an average of 3.74 months after the operation. They therefore recommended FVFG as a useful therapeutic option for the reconstruction of large tibia defects combined with soft tissue injury. Gradually, FVFG was further used for segmental bone defects in the upper limb[15]. Gebert *et al.*[15] reviewed the clinical and radiological results of 21 patients who had FVFG for diaphyseal defect reconstruction of the upper extremity. The authors concluded that FVFG had broader structural application as well as lower donor site morbidity[15].

Postoperative complications of FVFG remain relatively high, commonly including nonunion, fracture, infection, and the need for reoperation[13–15]. To date, few studies have specifically analyzed the outcomes of FVFG in series of patients with extremity OS. It was important to have a good understanding of the long-term effectiveness of FVFG in the reconstruction of bone defects due to extremity OS. In this study, a consecutive of 18 OS patients who received FVFG after resection of extremity OS were retrospectively reviewed. Our purposes were: (i) to determine the clinical outcome of FVFG in the reconstruction of bone defect for OS patients; (ii) to clarify the related complications associated with the application of FVFG; and (iii) to investigate whether the efficacy of FVFG was the same when applied to the upper extremity or the lower extremity.

Methods

Subjects

We retrospectively reviewed medical records of patients who had undergone resection of extremity OS between May 2009 and June 2017. The inclusion criteria were as follows: (i) reconstruction of the bone defect with FVFG; (ii) histologically diagnosed as OS; and (iii) a minimum of 2-year follow-up. A consecutive series of 18 patients were finally included in the study. All the patients had received two circles of neo-adjuvant chemotherapy before surgery and four circles after surgery. The chemotherapy protocol was composed of cisplatin (100 mg/m^2), doxorubicin (80 mg/m^2), and methotrexate (10 g/m^2). The demographic data were recorded for each patient, including gender, age at surgery, Enneking stage, tumor location, and length of bone resection.

Surgical Procedures

After anesthesia and position, the bone tumor was exposed with routine approach. Tumor resection was performed by an experienced surgeon (S.W.). The length of tumor resection was evaluated on magnetic resonance imaging (MRI) images prior to surgery. The tumor was removed as a block with an adequate margin of healthy tissue. During the tumor resection, another microsurgical team harvested the free fibular graft using lateral approach as previously reported[16]. Briefly, the fibula was dissected together with the peroneal artery and veins. The proximal osteotomy site was located at the neck of the fibula. For the distal osteotomized site, a minimum of 6 cm was retained for the stability of ankle joint. Generally, the fibular graft was longer than the resection length by 4–5 cm, to ensure that the graft can be inserted into both the proximal and the distal end of the bone defect. Using routine microsurgical techniques, the graft's vascular pedicle was anastomosed to a branch of the artery. Specifically, for the reconstruction of femoral or tibial defects, a cortical allograft was used to support the fibular graft, placed in the medullary canal of the allograft. One locking plate spanning the whole construct was used, with at least three bicortical locking screws in the host bone. A diagram was used to illustrate the surgical procedures mentioned above (Fig. 1).

Assessment of Surgical Outcome

Surgery-related complications were recorded for each patient. Reconstructed limbs were immobilized with a cast for 3 months. During the follow-up, plain radiographs were routinely performed for the evaluation of surgical outcomes. Partial weight-bearing was allowed when X-ray radiographs indicated callus formation and primary healing between the graft and the host bone. The time of bone union was recorded and full weight-bearing was then allowed. The functional outcome of the reconstructed limb was assessed with the MSTS scoring system.

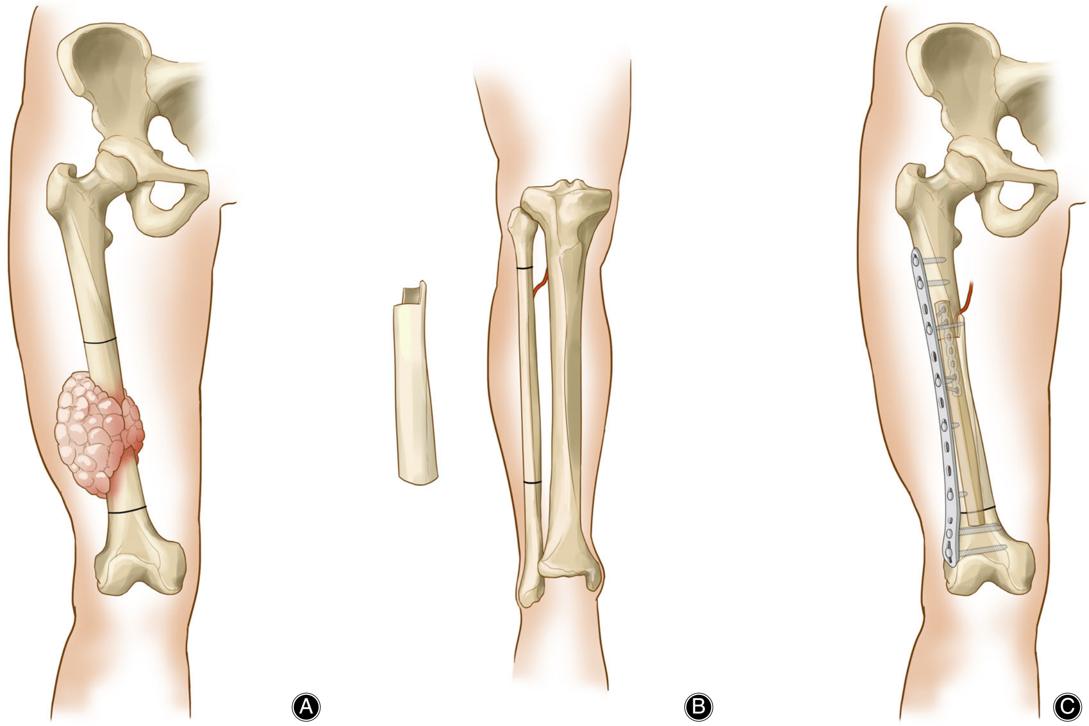

Fig. 1 Schematic diagram illustrating the surgical procedures. (A) En-block resection of the tumor located in the femur; (B) Preparation of the free vascularized fibula graft together with the peroneal artery and veins; (C) Reconstruction of the femoral defects with the fibular graft placed in the medullary canal of a cortical allograft.

MSTS Scoring System

The MSTS score measures six domains including pain, function, emotional acceptance, supports, walking ability, and gait. A 5-point scale was used for each domain, producing a maximum score of 30 points.

Statistical Analysis

SPSS 22.0 (SPSS Inc., Chicago, IL) was used for data analyses. The descriptive variables are reported as means ± standard deviation. Patients were classified into low extremity group and upper extremity group according to the tumor location. The Student t-test was used to compare the surgical outcome between the two subgroups. The Chi-square test was used to compare the categorical variable. The significance level was set at $P < 0.05$.

TABLE 1 demographic data of the patients

	Mean ± SD	Range
Gender		
Male	11	N/A
Female	7	N/A
Age (years)	26.6 ± 15.6	8–62
Tumor location		
Upper extremity	7	N/A
Lower extremity	11	N/A
Bone defect (cm)	11.9 ± 4.1	5–20
Time to bone union (months)	4.9 ± 1.6	3–8
Blood loss (mL)	647.5 ± 307.8	100–1080
Duration of hospital-stay (d)	32.2 ± 31.2	10–140
Follow-up period (years)	3.1 ± 1.2	2–8
MSTS score	27.0 ± 4.6	11–30

Results

Summary of Demographic Data

Baseline characteristics were summarized in Table 1. There were 11 males and seven females with an average age of 25.9 ± 15.6 years, ranging from 8 to 62 years. As for tumor location, six cases were located in the femur, five in the tibia, four in the humerus, two in the ulna, and one in the radius. There were 15 cases of high-grade OS (Anneking stage IIB) and three cases of low-grade OS (Anneking stage IB). The mean length of the bone resection was 11.9 ± 4.1 cm (5–20 cm). FVFG combined with segmental allografts were used in 11 patients (Figs 2 and 3). For the other seven patients, FVFG was applied directly for the reconstruction of bone defect (Fig. 4). The mean blood loss was 647.5 ± 307.8 mL (range 100–1080 mL). The mean duration of hospital stay was 32.2 ± 31.2 days.

Clinical Outcomes

The mean follow-up duration was 3.1 ± 1.2 years. All the patients had successful graft healing at an average of

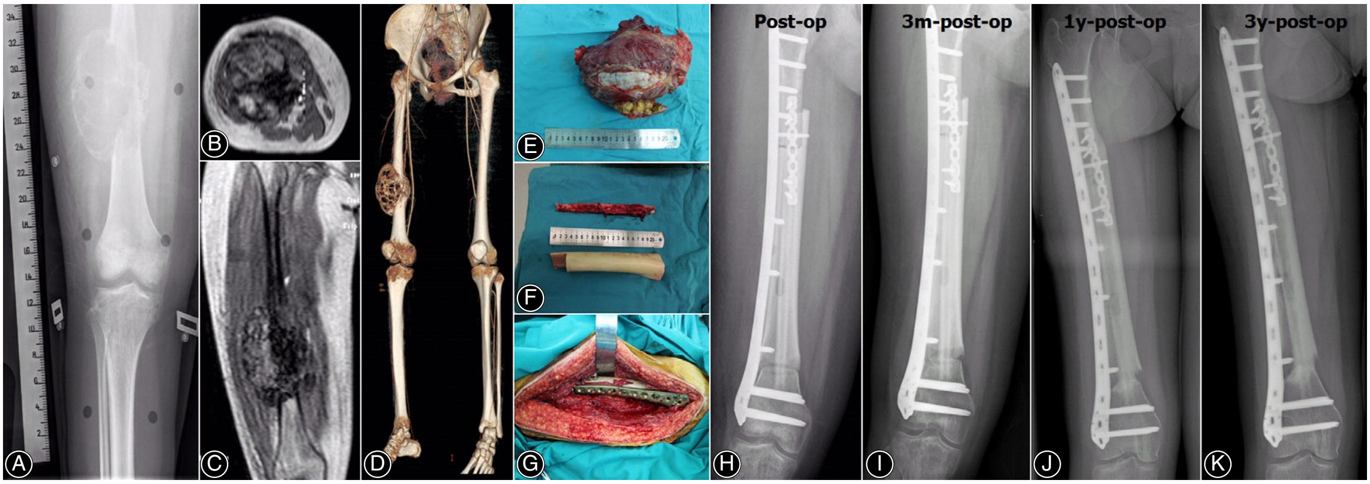

Fig. 2 A patient undergoing biological reconstruction of femur defect with 3 year follow-up. (A–D) A Female patient, aged 18 years, was histologically diagnosed as osteosarcoma located in the femur. Radiographic features of osteosarcoma were supported by both MRI image and CT scanning; (E–H) The tumor was resected, leaving a bone defect of 17 cm. Free vascularized fibula graft combined with segmental allografts was applied to the reconstruction of the bone defect; (I) At 3 month after surgery, graft union can be observed in the distal femur; (J) At the 1 year-follow-up, the radiograph indicated complete bone union; (K) At the 3 year-follow-up, the whole construct was maintained well with no complication reported. The patient had an excellent functional outcome with a MSTS score of 30.

4.9 months after surgery (range 3–8 months). At the 2-year follow-up, an excellent functional outcome was observed in 88.9% of the patients (n = 16). The mean score of MSTS was 27.0 ± 4.6 (range 11–30).

The Relationship between Tumor Location and Surgical Outcomes

Inter-group comparison showed that the two subgroups were matched in terms of age and gender (Table 2). Patients with

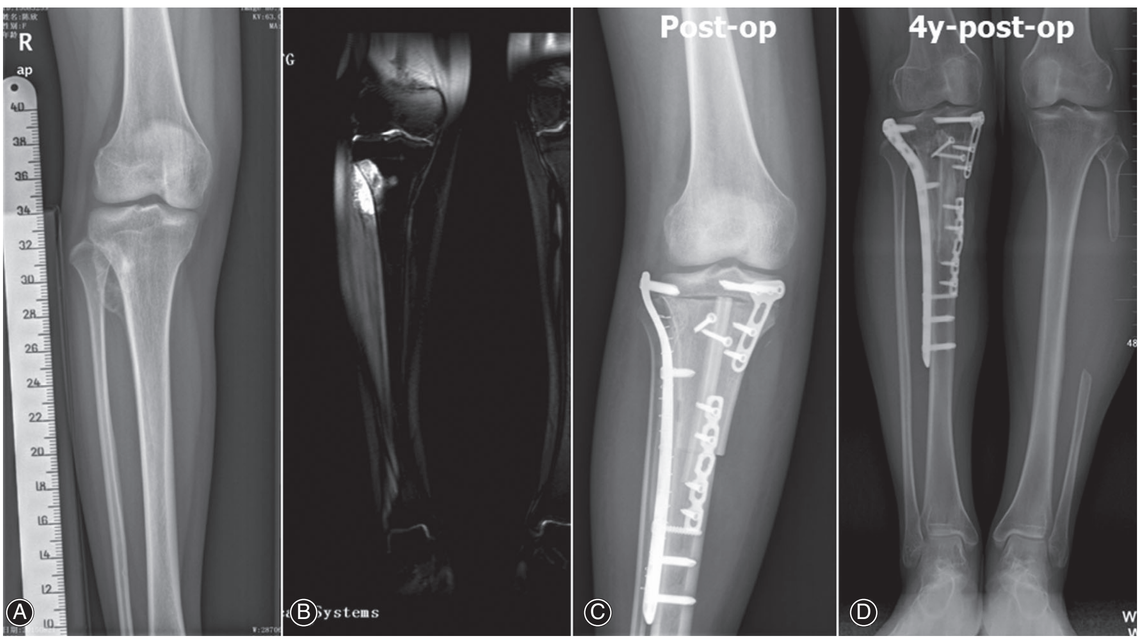

Fig. 3 A patient undergoing biological reconstruction of tibia defect with 4 year follow-up. (A, B) A Female patient, aged 19 years, was histologically diagnosed as osteosarcoma located in the tibia; (C) Free vascularized fibula graft combined with with segmental allografts was used for the reconstruction of the bone defect; (D) At the 4 year-follow-up, complete bone union was observed in the tibia. There was no surgery-related complication. The MSTS score was 25.

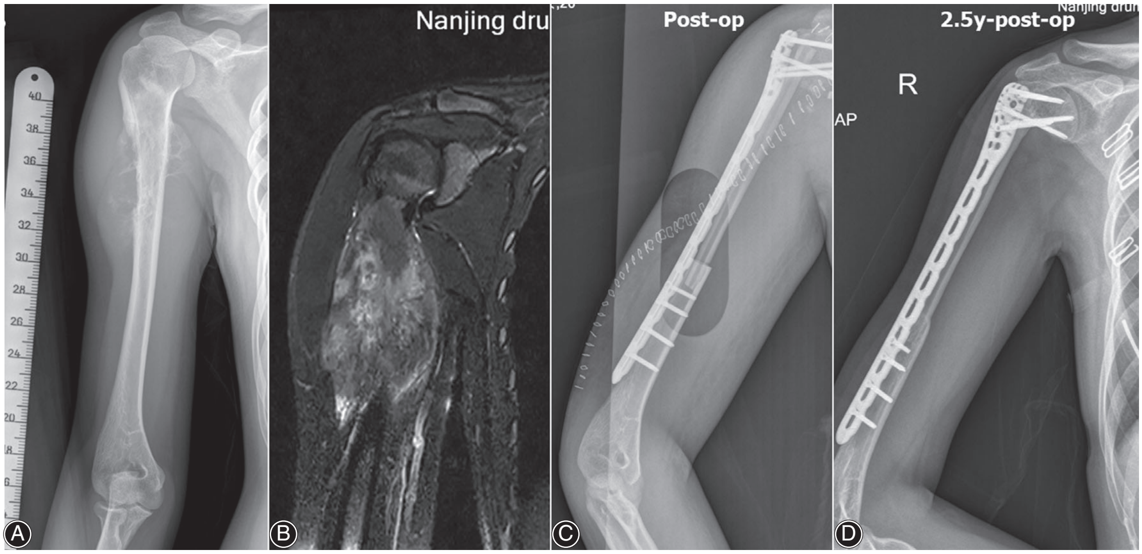

Fig. 4 A patient undergoing biological reconstruction of humerus defect with 2.5 year follow-up. (A, B) A Female patient, aged 26 years, was histologically diagnosed as osteosarcoma located in the humerus; (C) Free vascularized fibula graft was directly applied to the reconstruction of the bone defect; (D) At the 2.5 year-follow-up, the radiograph indicated complete bone union. No complication was reported. The patient had an excellent functional outcome with a MSTS score of 27.

lower extremity OS were found to have significantly longer duration of hospital stay and more blood loss than those with upper extremity OS. The incidence of postoperative complication was higher in the lower extremity group but with marginal significance (0% *vs* 36.3%, $P = 0.11$). There was no significant difference regarding time to bone union and the functional outcome as indicated by MSTS score.

Complications

Screw loosening and autograft fracture were observed in one patient with femur tumor, who had a low MSTS score of 11.

TABLE 2 Comparison between the upper extremity tumor group and the lower extremity tumor group

	Upper extremity tumor group (n = 7)	Lower extremity tumor group (n = 11)	*P*
Gender			0.63
Male	5	6	
Female	2	5	
Age (years)	16.4 ± 6.2	14.2 ± 4.3	0.16
Bone defect (cm)	11.1 ± 4.3	12.5 ± 4.1	0.35
Blood loss (mL)	371.5 ± 180.2	823.6 ± 232.5	<0.001
Duration of hospital-stay (d)	15.2 ± 8.5	43.0 ± 35.9	0.04
Time to bone union (months)	4.8 ± 1.7	5.1 ± 1.6	0.85
Follow-up period (years)	2.8 ± 0.9	3.3 ± 1.1	0.69
MSTS score	27.6 ± 2.1	26.7 ± 6.1	0.71
Incidence of complication (%)	0	36.3%	0.1

A revision surgery was then performed. Other complication included three cases of delayed healing of incision due to superficial infection. No intraoperative complications, donor site morbidity, or venous thrombosis was observed.

Discussion

The Clinical Outcome of FVFG in OS

Reconstruction of large bone defects following resection of bone tumors has always been complicated and become a challenge in modern orthopaedic practice. In the last century, Taylor *et al.*[17] first introduced free vascularized fibular autograft to the restoration of large long bone defects. It was reported that a graft of up to 26 cm long can be acquired from fibula[18]. With a straight shape, FVFG is thus considered as an optimal applicant option restoration of bone defects in both upper and lower extremities. With the development of current microsurgical technique, transfer of the fibula to recipient sites has been more feasible, which, in turn, increased the graft survival.

In this study, we presented a series of OS patients who underwent biological reconstruction using FVFG after tumor resection. The data gathered here suggested that FVFG could yield acceptable overall outcomes with high union rate and patient satisfaction. Our overall union rate was 94.4% and the average time to union was 4.9 months. Comparably, as shown in previous studies, bone union takes about 4 to 5 months on average after the vascularized fibular transfer[19]. Soucacos *et al.*[20] reviewed the clinical and radiographic results of 18 patients who underwent reconstruction of large bone defects with FVFG. Graft healing was achieved in 92%

of the patients in an average of 3 months[20]. With regard to the functional outcome, the median MSTS score of our patients was 90.0%, which is significantly higher than those undergoing amputation. Fuchs *et al.*[21] reported 21 patients who underwent tumor resection using FVFG. The mean MSTS score was 23 points (range, 17 to 26 points)[21], which was comparable with that of the patients in the present series.

An Overview of FVFG-Related Complications

In the current study, the overall complication rate of FVFG was 22.2%. The most severe complication was a case of screw loosening leading to graft fracture. In earlier literature, the average proportion of patients experiencing fracture was 11.7% for upper extremity reconstructions and 25% for lower extremity reconstructions[19]. By contrast, the rate of allograft fracture has been reported as 49% which ended in reconstruction failure[22]. In addition, there were three cases (16.7%) with delayed incision healing due to infection, the rate of which was lower than that reported in allograft (30%)[23]. Progressive valgus deformity of the ankle is a rare complication after FVFG. In our study, all the patients were confirmed to have stable ankle joint at the follow-up visit. It was recommended to preserve 5 to 6 cm of the distal fibula to protect the stability and function of the ankle joint. To summarize, the low rate of complications accentuates a substantial advantage of FVFG over allograft.

The Efficacy of FVFG in Upper Extremity and in Lower Extremity

For the first time, we compared the outcome of FVFG between patients with upper extremity OS and those with lower extremity OS. Obviously, patients with lower extremity OS tended to have more blood loss and higher incidence of postoperative complications. It was probable that the graft fracture in the lower limb was related to excessive loading. Considering low initial mechanical strength of the transferred fibula, the operated limb should be protected until hypertrophy surrounding the graft and the host bone is confirmed.

The primary limitation is that, as this is a small retrospective case series, the incidence of OS was quite low. It is noteworthy that all grafting procedures were carried out by a single surgeon (H.M.) who was experienced in microvascular techniques. All the reconstruction procedures were performed with the same protocol. Therefore, variations of surgical technique were minimized. Second, no control group was included in this study. In future study, other reconstruction techniques such as allograft or prosthetic devices can be applied to better clarify the effectiveness of FVFG.

Conclusions

FVFG technique can be effectively applied to the reconstruction of bone defects after OS resection. The long-term assessment indicated satisfactory functional outcome and low incidence of previously known complications. It was necessary to further validate its efficacy in limb-salvage therapy in the setting of malignant extremity tumor resection.

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