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Long-term Outcomes of Biological Reconstruction for Primary Bone Sarcoma of the Humerus

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Abstract

Background/Aim: Options for the reconstruction of bone defects following resection of primary bone sarcomas of the humerus include massive endoprostheses or biological reconstruction. We report the oncological, clinical, and functional outcomes in patients treated with biological reconstructions.

Patients and Methods: This study included 23 consecutive patients with primary bone sarcoma of humerus who underwent *en-bloc* resection and biological reconstructions at a single institution. Four groups of patients were identified. Group A: twelve patients with vascularized fibula epiphyseal transfer. Group B: four patients with structural grafts with vascularized fibula. Group C: four patients with structural grafts with non-vascularized fibula. Group D: three patients with only structural grafts (allograft or reimplanted bone only). The postoperative oncological outcomes, complications, reoperation rates, and postoperative limb function using the Musculoskeletal Tumor Society (MSTS) scores were evaluated.

Results: The median age at diagnosis was 8 years (range=3-54 years). The median follow-up was 87 months (range=6-172 months). Graft complications at recipient sites occurred in 13 patients including fracture in seven, non-union in four, and avascular necrosis in two. Donor site peroneal nerve palsy occurred in seven patients. Local recurrence and metastases occurred in one and two patients, respectively. At the last follow-up, twenty-two patients were alive (21 continuously disease-free for a median of 87 months, and one with no evidence of disease), and one patient died of disease. The mean MSTS scores for all patients was 78.9%, and this was similar in the four groups: 77.5%, 72.5%, 85.8%, and 83.3% in Groups A, B, C, and D, respectively.

Conclusion: Biological reconstruction of the humerus is a complex procedure with a risk of complications but has good oncological and functional outcomes.

Keywords: Biological reconstruction, primary bone sarcoma, humerus.

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Introduction

The humerus is a common site for primary bone sarcoma and metastatic malignant bone tumors (1, 2). The standard treatment for primary bone sarcoma of the humerus is limb preservation with *en-bloc* resection and reconstruction (3). The options for reconstruction of defects after removal of the tumors of the humerus include biological reconstruction with allografts or autografts or in combination, endoprosthetic replacement or allograft prosthetic composite (4). Biological options may include vascularized fibula epiphyseal transfers (VFET) for the growing bones in pediatric patients, or free vascularized or non-vascularized fibula diaphyseal grafts with or without structural allografts or allografts alone (5). However, the optimal method for reconstruction after proximal humerus resection remains controversial. Liu *et al.* reported that revision rates were higher for endoprostheses than biological reconstruction (6). Furthermore, VFET provides a functional advantage for pediatric limb-salvage by preserving growth potential and an articular surface for remodeling (7). Extracorporeal irradiation (ECI) and reimplantation is reportedly a safe and inexpensive technique to save the limbs in diaphyseal sarcomas with good functional outcomes (8).

When deciding on whether to vascularize a graft for long-bone reconstructions, it is essential to weigh the benefits and risks carefully (9, 10). Vascularized grafts are reported to be superior to non-vascularized grafts in the case of large segmental defects (11). In practice, there is a general perception that a vascular supply should be used when large pieces of bone graft are used, particularly those greater than 6 cm in length for long-bone and large-joint reconstructions, or when the biological integrity of the surrounding bone is compromised, particularly after radiotherapy. However, Allsopp *et al*. found no compelling evidence to justify the 6 cm rule for vascularized bone grafts (12) and suggested that vascularized grafts may increase the risk of complications without improving union rates or the time to union. Consensus is needed in the literature to determine the most successful graft type in reconstructive procedures. Conversely, there are reports of frequent complications associated with using allografts alone (13).

Reconstruction of the humeral bone defects may involve a combination of the above reconstructions. Reports of outcomes of biological reconstruction of the humerus are limited because of the rarity of biological reconstruction of the humerus following sarcoma resection. There is no consensus on when or which biological reconstruction should be used. The current study aimed to summarize the oncological, clinical, and functional outcomes in patients treated with biological reconstructions.

Patients and Methods

Study design and patients. Institutional approval was obtained for the study. We retrospectively searched our institution's database to identify patients who underwent surgical treatment for bone sarcoma of the humerus between January 2000 and December 2023. We identified a total of 265 patients from our institution. Table I presents the demographics for all the patients with primary humeral bone sarcomas, including sex, age at surgery, tumor location, histology, and surgical technique. Of these patients, 23 underwent *en-bloc* resection and biological reconstruction. Table II presents the patient demographics of these 23 patients, including sex, age at surgery, follow-up period after surgery, tumor location, histology, surgical technique, tumor size, tumor stage, adjuvant therapies, bone defect length, bone union, time to bone union, surgical margin, local recurrence, distant metastasis, and oncological outcome.

Surgical procedure. The tumor, along with the surrounding soft tissue and the biopsy tract, was resected *en-bloc*. The humeral osteotomy was precisely planned to be at least 10 mm above and below the maximum extent of the tumor on MRI scans.

In the VFET, an anterolateral incision was made on the lower leg; the anterior tibial vessels, common peroneal nerve, and their branches were dissected free. The proximal tibial fibula joint was disarticulated, and the fibula was

Table I. *Demographics and disease characteristics of all patients treated for primary bone sarcomas of the humerus.*

Characteristics		N or Median (Range or %)
Sex	Male	132 (49.8%)
	Female	133 (50.2%)
Age at surgery (years)		25 (3-85)
Tumor location	Proximal	219 (82.6%)
	Mid-shaft	18 (6.8%)
	Distal	28 (10.6%)
Histology	Osteosarcoma	113 (42.6%)
	Chondrosarcoma	88 (33.2%)
	Ewing sarcoma	49(18.5%)
	Others	15 (5.7%)
Surgical technique	Excision+EPR	186 (70.2%)
	Amputation	40 (15.1%)
	Excision+Biological reconstruction	23 (8.7%)
	Others	16 (6%)

EPR: Endoprosthetic replacement.

mobilized, preserving the osteoperiosteal and anterior tibial vessels. The popliteal vessels were dissected, and the anterior tibial vessels were resected at the necessary proximal length of the fibula. The biceps femoris tendon and the lateral collateral ligament were re-attached to the tibial epiphysis, stabilizing the knee joint. The harvested fibula was impacted into the remnant humerus producing a good fixation, which was further secured with screws or plate. The soft tissues were reconstructed around the proximal fibula, and vascular anastomosis was performed between the anterior tibial artery and axillary artery. Venous drainage was between the anterior tibial vein and the axillary vein. Good reconstruction and flow were achieved. Prior to the reimplantation of the humerus, the tumor-containing bone segment was removed and cleaned on separate tables. The muscles were stripped off the tumor, and all the cancellous bone was removed and washed. Intraoperative radiotherapy was performed with a dose of 90 Gy for the resected humerus. The irradiated humerus was fixed with or without the harvested vascularized or non-vascularized fibula.

In vascularized or non-vascularized fibula grafts, the length of the fibula was determined based on the defect size. A sufficient distal fibula was maintained for fibular

Table II. *Demographics and disease characteristics of patients treated with biological reconstruction.*

Characteristics		N or Median (Range or %)
Sex	Male	12 (52.2%)
	Female	11 (47.8%)
Age at surgery (years)		8 (3-54)
Follow-up period after surgery (months)		87 (6-172)
Tumor location	Proximal	17 (73.9%)
	Mid-shaft	4 (17.4%)
	Distal	2 (8.7%)
Histology	Osteosarcoma	11 (47.8%)
	Ewing sarcoma	8 (34.8%)
	Chondrosarcoma	4 (17.4%)
Surgical technique	Vascularized fibular epiphyseal transfer	12 (52.2%)
	Reimplantation alone	1 (4.3%)
	Reimplantation+ vascularized fibula	1 (4.3%)
	Reimplantation+ non-vascularized fibula	3 (13%)
	Vascularized fibula alone	2 (8.7%)
	Vascularized fibula+ allograft	1 (4.3%)
	Non-vascularized fibula+allograft	1 (4.3%)
	Allograft alone	2 (8.7%)
Tumor size (cm)		9 (4-19)
Tumor stage	IIA	7 (30.4%)
	IIB	13 (56.5%)
	III	3 (13%)
Adjuvant therapies	Perioperative chemotherapy	15 (65.2%)
	Perioperative chemotherapy+ Preoperative radiotherapy	2 (8.7%)
	None	4 (17.4%)
	Not available	2(8.7%)
Bone defect length (cm)		11 (7-22)
Bone union	Union	18 (78.3%)
	Nonunion	4 (17.4%)
	Not available	1 (4.3%)
Time to bone union (months)		6 (3-15)
Surgical margin	R0	23 (100%)
	R1	0 (0%)
Local recurrence		1 (4.3%)
Distant metastasis		2 (8.7%)
Oncological outcome	Continuously disease-free	21 (91.3%)
	No evidence of disease	1 (4.3%)
	Died of disease	1 (4.3%)

osteotomy to prevent ankle instability. When a vascularized fibula was utilized, the vascular pedicle of the graft was anastomosed to a branch of the brachial artery. Allografts were obtained from a commercial bone bank, trimmed to fit the defect size, and secured with plates and screws.

Postoperative management included intravenous antibiotics for 24 to 48 h and a shoulder-supporting sling with abduction restriction for six weeks. Only shoulder shrugging exercises were allowed for six weeks postoperatively. Gentle passive abduction, flexion, and circumduction exercises were permitted after six weeks, with progression to active assisted exercises and then active exercises after three months.

Parameters for investigation. Malignant tumors were classified according to the 8th edition of the American Joint Committee on Cancer (AJCC) cancer staging system. The surgical margin was categorized microscopically as either positive (R1 resection) if tumor cells were present at the closest margin or negative (R0 resection) if no tumor cells were detected at the margin. The Musculoskeletal Tumour Society (MSTS) score was used to evaluate limb salvage outcomes. It was based on six factors: pain, function, emotional acceptance, positioning of the hand, manual dexterity, and lifting ability. The maximum score was 5 for each factor, resulting in a total possible score of 30 points. The sum of all scores was calculated as a percentage of the total 30 points.

Statistical analysis. Patient data were prospectively entered into our database. All data were collected from central electronic medical records at our institution. MSTS score is expressed as mean±standard deviation (SD). All analyses were performed using SAS software, version 14.2 (SAS Institute, Inc., Cary, NC, USA).

Results

Demographics and disease characteristics of all patients. Data regarding patient demographics and disease characteristics of patients who underwent surgery for the humerus are presented in Table I. One hundred thirty-two patients were male, and 133 patients were female. The median age at surgery was 25 years (range=3-85 years). The tumors were located in the proximal region (219 patients), mid-shaft (18 patients), and distal region (28 patients). The histological tumor subtypes were osteosarcoma (113 patients), chondrosarcoma (88 patients), and Ewing sarcoma (49 patients). Surgical techniques were excision with endoprosthetic replacement (EPR) (186 patients), amputation (40 patients), and excision with biological reconstruction (23 patients).

Demographics and disease characteristics of patients who underwent biological reconstruction. Data regarding patient demographics and disease characteristics of the patients who underwent biological reconstruction of the humerus are presented in Table II. Twelve patients were male, and eleven patients were female. The median age at the time of surgery was eight years (range=3-54 years). The median follow-up was 87 months (range=6-172 months). The tumors were in the proximal (seventeen patients), mid-shaft (four patients), and distal humerus (two patients). The histological tumor subtypes were osteosarcoma (eleven patients), Ewing sarcoma (eight patients), and chondrosarcoma (four patients). Surgical techniques were VFET (twelve patients), reimplantation alone (one patient), reimplantation with vascularized fibula (one patient), reimplantation with non-vascularized fibula (three patients), vascularized fibula alone (two patients), vascularized fibula with allograft (one patient), non-vascularized fibula with allograft (one patient), and allograft alone (two patients). The median tumor size was 9 cm (range=4-19 cm). Tumor stages were IIA (seven patients), IIB (thirteen patients), and III (three patients). Fifteen patients had perioperative chemotherapy, and two patients had perioperative chemotherapy with preoperative radiotherapy. The median length of bone defects was 11 cm (range=7-22 cm). Eighteen patients had a bony union at the osteotomy sites, while four patients developed nonunion requiring further surgical interventions. The median time to bone union was six months (range=3-15 months). All

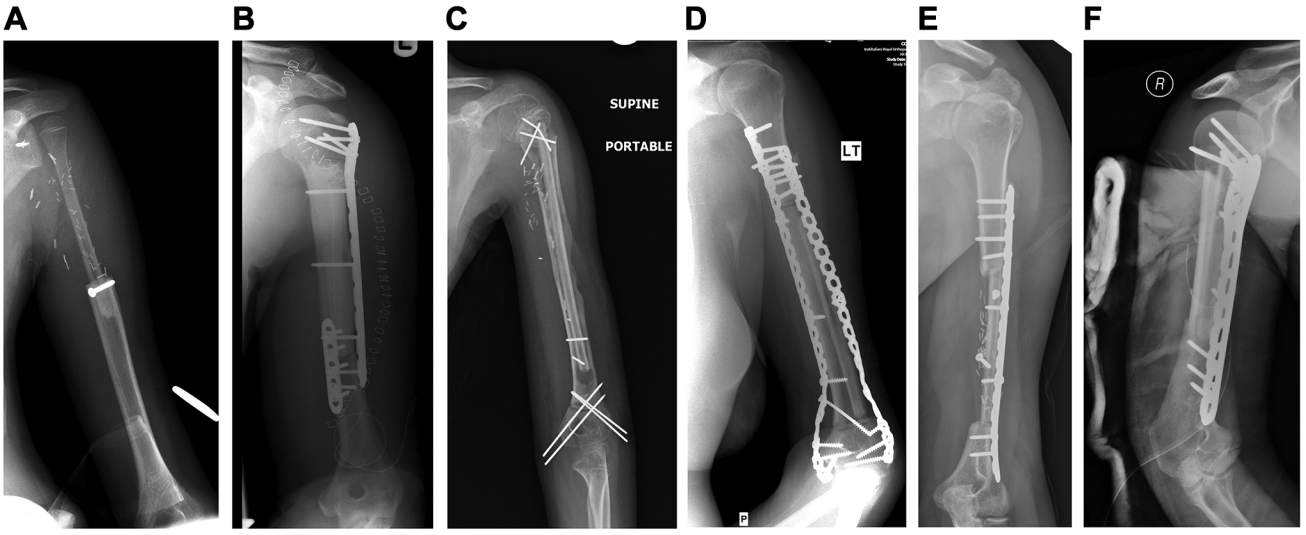

Figure 1. *Representative postoperative radiographs. (A) Vascularized fibula epiphyseal transfers, (B) Reimplantation alone, (C) Reimplantation + vascularized fibula, (D) Reimplantation+non-vascularized fibula, (E) Vascularized fibula alone, (F) Vascularized fibula+allograft.*

Table III. *Postoperative rates of complications and reoperation in four groups.*

	Donor/Recipient	Complications N (%)	Reoperation due to complications N (%)
Group A	Donor-site	7 (58.3%)	2 (16.7%)
(12 patients)		Transient peroneal nerve palsy: 6 patients	Tendon transfer for the foot drop: 1 patient
		Permanent peroneal nerve palsy: 1 patient	Fixation for fibula epiphysis slipping: 1 patient
	Recipient-site	9 (75%)	
		Fracture: 7 patients	
		Avascular necrosis: 2 patients	
Group B	Donor-site	0 (0%)	1 (25%)
(4 patients)	Recipient-site	1 (25%)	Bone grafting: 1 patient
		Infection/Nonunion: 1 patient	
Group C	Donor-site	0 (0%)	2 (50%)
(4 patients)	Recipient-site	2 (50%)	Bone grafting: 2 patients
		Nonunion: 2 patients	
Group D	Donor-site	NA	1 (33.3%)
(3 patients)	Recipient-site	1 (33.3%)	Bone grafting: 1 patient
		Nonunion: 1 patient	

NA: Not available. Group A: Patients with vascularized fibula epiphyseal transfer. Group B: Patients with structural grafts with the vascularized fibula. Group C: Patients with structural grafts with non-vascularized fibula. Group D: Patients with only structural grafts.

surgical margins were R0. One patient had local recurrence, and two patients developed distant metastasis. At the study's end, the disease status was continuously disease-free for 21 patients (91%); one patient was alive with no evidence of disease (4%) and one patient had died of disease (4%).

Postoperative clinical course and complications. Figure 1 shows the representative postoperative radiographs of each surgical procedure. Table III indicates postoperative complications. We divided the 23 cases of biological reconstruction of the humerus into four groups. Group A (12 patients) - the VFET group. Group B (4 patients) - the

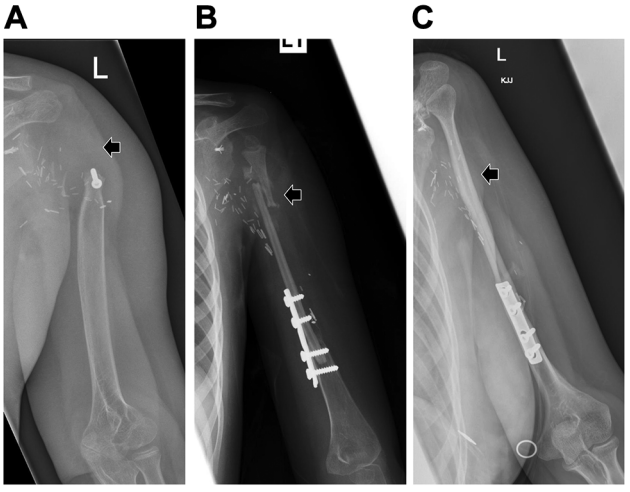

Figure 2. *Representative complication radiographs. (A) Avascular necrosis of the fibula postoperatively. (B) The vascularized fibular epiphyseal transfer had a postoperative fracture, improving bone union in six months. (C) Radiographs are from the same patients' final follow-up as in (B).*

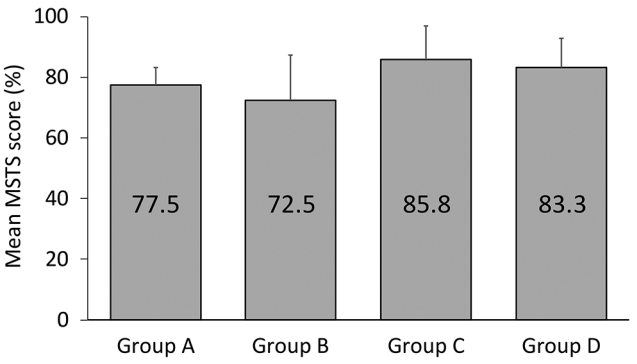

Figure 3. *The evaluation of postoperative limb function with the Musculoskeletal Tumour Society (MSTS) score in four groups. In Groups A, B, C, and D, the mean MSTS scores were 77.5%, 72.5%, 85.8%, and 83.3%, respectively. Group A: Patients with vascularized fibula epiphyseal transfer. Group B: Patients with structural grafts with the vascularized fibula. Group C: Patients with structural grafts with non-vascularized fibula. Group D: Patients with only structural grafts.*

vascularized fibula-based group, which includes the vascularized fibula±allograft or reimplantation. Group C (4 patients) was the non-vascularized fibula-based group, which is non-vascularized fibula+allograft or reimplantation, and Group D (3 patients) comprising the non-fibula structural grafts. In Group A, six patients had a transient peroneal nerve palsy at the donor site and one patient had a permanent peroneal nerve palsy. Graft recipient site complications occurred in nine patients (75%), including graft fracture in seven and avascular necrosis in two patients. However, only two patients out of these required reoperations; one underwent a tendon transfer for foot drop and the other underwent fixation for fibula epiphysis slipping. All the fractures united with conservative management. In Group B, no patient developed donor site complications, but recipient site complications occurred in one patient who developed a superficial infection and later nonunion, which was treated with supplemental bone grafting. There was no donor site complication in Group C, but two patients developed nonunion at the graft recipient site. Both of these required supplemental bone grafting, after which the osteotomy sites united. In Group D, recipient site complications occurred in one patient who developed a nonunion, which was treated with supplemental bone grafting. Figure 2 shows the representative radiographs of the complications, including avascular necrosis of the transferred fibula (Figure 2A) and another patient who developed a fracture after VFET (Figure 2B). This fracture was healed without surgical intervention and with a good limb function of 80% of the MSTS score (Figure 2C). The mean MSTS scores were 77.5%, 72.5%, 85.8%, and 83.3% in Groups A, B, C, and D, respectively (Figure 3).

Discussion

This study presents the clinical, oncological, and functional outcomes of excision and reconstruction of massive bone defects after excision of primary bone sarcoma in the humerus at a single institution. This is an uncommon procedure with limited reports in the literature. We hope this will be of benefit to surgeons when considering this form of reconstruction.

Surgery for humeral sarcoma often involves removal of a large portion of the humerus bone with or without the articular surface depending on the location of the tumor. Reconstruction therefore often requires either an artificial

Table IV. *Comparison with previous literature on postoperative outcomes of several biological reconstructions.*

Study	Surgically technique	Number of patients	Median age (Range) (years)	Median follow-up duration (months)	Complications	Reoperation due to complications	Local recurrence rate	Mean MSTS score
Tang *et al.* (15)	Recycled pasteurized autograft combined with non-vascularized fibula autograft	16	32 (21-45)	63	Nonunion, Fracture	31.3%	12.5%	63%
Wada *et al.* (16)	VFET	8	25 (10-47)	76	Absorption, Fracture	0%	0%	79%
Zhaohui *et al.* (17)	Vascularized fibula or non-vascularized fibula with allograft or devitalized autograft	26	42* (8-64)	72	Infection, Nonunion	15.4%	NA	90.7%
Kinoshita *et al.* (18)	Clavicula Pro Humero reconstruction	8	39* (10-69)	35*	Nonunion, Fracture	25%	12.5%	69.3%
Tsuchiya *et al.* (19)	VFET	19	20 (4-70)	63	Fracture, Infection, Absorption, Peroneal nerve palsy	10.5%	NA	66.9%
Present study	VFET, Reimplantation, Vascularized fibula, or Non-vascularized fibula	23	8 (4-54)	87	Fracture, Infection, Absorption, Peroneal nerve palsy	26%	4.3%	78.9%

VFET: Vascularized fibula epiphyseal transfers; NA: not available; MSTS: Musculoskeletal Tumour Society; *Mean.

joint or biological reconstruction (14). The decision to choose between these options will depend on the location of the tumor, age of the patient, expected prognosis, and the surgical expertise available at the particular institution. In the present study, we primarily focused on the postoperative oncological outcomes and limb function of VFET, reimplantation, vascularized fibula, and non-vascularized fibula. Table IV presents the comparison with previous literature on postoperative outcomes of biological reconstructions (15-19).

Maintaining limb growth after limb-salvage surgery of the humerus in children is difficult. However, VFET can offer quick biological integration with the potential for growth and longevity (7). However, several reports of complications are associated with VFET. In our study, postoperatively transplanted fibulas experienced absorption due to avascular necrosis. Wada *et al.* reported that among eight cases, four experienced absorption complications (16). Additionally, scattered reports of fractures occur in transplanted fibulas due to their slender shafts (18, 19). In our study, seven cases experienced a fracture in the VFET group; however, the fracture healed without any surgical intervention or functional loss due to the vascularity of the transplanted fibula. Among the nine patients who experienced postoperative complications in the recipient site, only one patient required surgery for the complication. Previous literature also reports cases of good limb function without additional surgery in instances of bone absorption or fracture (16, 19). Moreover, peripheral fibula nerve palsy on the donor side is a notable complication. In our study, peripheral fibula nerve palsy occurred in seven cases postoperatively; six cases were transient, and one case required tendon transfer. Previous reports also indicate that the palsy tends to be transient as long as the fibula nerve is not excised during surgery (19).

Extracorporeal irradiation (ECI) and reimplantation are surgical techniques that have been used for limb

salvage in patients with malignant tumors of diaphyseal ones where the joint surface can be preserved. This method offers several advantages over replacement with a megaprosthesis, including biological reconstruction, preservation of bone stock, and ready availability (20). Zhang *et al.* conducted a study on patients who underwent wide resection and ECI and reimplantation, evaluating the postoperative oncological outcomes and limb function. They found a local recurrence rate of 13%, with early and late postoperative complications at 47.8%. Most patients demonstrated bone union, and the average MSTS score was 78.8%, indicating good outcomes. Despite the high complication rate (47.8%) and reoperation rate (39.1%), the study concluded that ECI and reimplantation are useful and cost-effective techniques for limb preservation in appropriately selected patients after *en-bloc* resection.

There is no consensus on whether vascularized structural grafts are better or not compared to non-vascularized structural grafts. Previous literature showed evidence that vascularized grafts do not improve union rates or time to union and may increase the risk of complications (12). However, in a study comparing two surgical techniques for treating osteonecrosis of the femoral head, it was found that although there was no significant radiological difference in the early results, the clinical results of vascularized fibular grafting were significantly better than those of non-vascularized fibular grafting (21). Furthermore, vascularized free-fibula transfer offers the potential for fast autograft incorporation in areas that have been affected by radiation, chemotherapy, and resection (22). In our study, postoperative complications in transplanted fibulas were observed to be 25% in the vascularized fibula-based group and 50% in the non-vascularized fibula-based group, with corresponding rates of additional surgeries at 25% and 50%, respectively. We are unable to make a definitive conclusion about the benefit of vascularized grafts because of the small number of patients in the two groups and therefore, believe that further studies are warranted to examine these thoroughly.

The postoperative mean MSTS scores were 77.5%, 72.5%, 85.8%, and 83.3% for the VFEF, vascularized, non-vascularized fibula groups, and non-fibula structural grafts, respectively. The slightly lower score in the vascularized fibula group is due to a patient whose sarcoma was close to the nerves, requiring severance of the radial nerve. These scores compare favorably with various reports of biological reconstruction for humeral sarcoma in the past (Table IV), suggesting excellent postoperative limb function.

The present study represents one of the few reports on biological reconstruction with long-term follow-up. However, there are several limitations to consider. Firstly, this was a retrospective study with a small number of cases and secondly, we could not compare the results by group due to the small number of patients.

In conclusion, biological reconstruction of the humerus is a complex procedure with a risk of complication but good oncological and functional outcomes.

Conflicts of Interest

The Authors received no financial or material support for the research, authorship, and/or publication of this article.

Authors' Contributions

H. Kinoshita collected and analyzed all the data and wrote the article. A. Abudu designed the research and conceptual advice. J. Stevenson, G. Morris, V. Kurisunkal, and B. Shreemal provided technical support and conceptual advice.

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