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Vascularized and Non-vascularized Fibula Grafts in Tumour Reconstruction: Single Centre Experience With Mid to Long-term Results

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Abstract. *Background/Aim: Vascularized (VFG) and non-vascularized fibula grafts (NVFG) are used in reconstruction of bone defects after tumour resection. This study compared both autografts and their results, risk factors, and complications. Patients and Methods: Tumour resection and reconstruction by using VFG (n=17) and NVFG (n=36) were performed in 53 patients at our institute (range=3-65 years of age, mean: 21.2 ± 13.2 years) of which 24 were female. Malignant tumours were diagnosed in 26 patients (VFG=16 patients–94%). The mean follow-up was 14.9 years (range=1.5-43 years). Factors like consolidation, functional and oncologic outcomes, and complications were analysed. Results: In total, 75 struts of fibula were obtained. The mean length of the fibula was 16.3 cm (16 in NVFG and 16.5 in VFG). The mean union time was 13 months (6 to 25 months) overall. Hypertrophy was found in 65 of 75 grafts (86.7%) and consolidation was found in 69 (92%). Hypertrophy was similar in VFG (85.3%) and NVFG (87.1%). Complication rate in VFG was 41% and in NVFG 25%. Fractures were found in 7 (13%), infections in 4 (7.5%), and non-union in 5 (9.4%) patients. Chemotherapy was the only negative prognostic factor for union time (p=0.021). Conclusion: Both VFG and NVFG are used with successful results in the reconstruction of segmental bone tumour defects. With lower complication rates, NVFG showed comparable results to VFG but is limited in indication by size for greater defects, and malignant tumours. Chemotherapy is an adverse factor leading to prolonged union time in both techniques.*

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Reconstruction of the extremities continues to be a major challenge in patients with bone tumours with regard to limb length preservation, function, and cosmesis. Many techniques are available, however, since survival rates of patients with bone tumours have improved, reconstructive interventions are adapting to increasingly biological procedures that can be classified into two general groups: vascularized *versus* non-vascularized autologous bone grafting. Thus, one of the most commonly employed reconstructive procedure is the use of fibular autografts. Since the first bone transfer was described by Taylor *et al*. in 1975 (1), vascularized fibular grafts have been used more frequently for defect reconstructions of long bone defects (2, 3). However, conventional non-vascularized bone grafting is still widely performed. Conventional fibular grafts show relatively satisfactory results (4) and are technically easier to perform compared to vascularized fibular grafts, which require microsurgical techniques. While various reconstructive options are evaluated, individual treatment modalities of patients remain subject to controversial discussions. To date, literature demonstrating a direct comparison of vascularized *versus* non-vascularized fibular grafts for the treatment of long bone defects following tumour resection is limited. Therefore, we present a retrospective analysis of 53 patients treated with autologous fibular grafts in a single centre over a 42-year period. Function and radiological outcomes were analysed in order to improve individualized indications and surgical therapy.

Patients and Methods

Between 1976 and 2018, 53 patients (29 male, 24 female) underwent bone graft reconstruction, 17 (32%) with a vascularized graft (VFG) and 36 (68%) with a non-vascularized graft (NVFG). Their mean age was 21.2 years (range=3-65 years). The mean follow-up was 14.9 years (range=1.5-43 years). Patient details are summarized in Table I. A total of 29 patients were diagnosed with a malignant bone tumour (16 with VFG, 13 with NVFG). There were 41 lower extremity and 12 upper extremity reconstructions. A posterolateral approach was used to harvest both NVFG and VFG. To maintain knee and ankle

Table I. *Demographic and clinical characteristics.*

Characteristic	Total (n=53)	VFG (n=17)	NVFG (n=36)
Age at index surgery	19.8 (range=3-68)	15.8 (range=3-39)	23.7 (range=5.5-68)
Sex			
Female	24 (45%)	8 (47%)	16 (44%)
Male	29 (55%)	9 (53%)	20 (56%)
Diagnosis			
Benign	24 (45%)	1 (6%)	23 (64%)
Malignant	29 (55%)	16 (94%)	13 (36%)
Site			
Upper extremity	12 (23%)	3 (18%)	9 (25%)
Lower extremity	41 (77%)	14 (82%)	27 (75%)
Defect length	13.3 (5-28)	15.5 (7-28)	11 (5-24)
Graft length	16.3 (6.5-30)	16.5 (8-27.5)	16 (6.5-30)
Neoadjuvant Tx		14 (82%)	4 (11%)
Adjuvant Tx		14 (82%)	5 (14%)

Tx: Treatment; VFG: vascularized fibula grafts; NVFG: non-vascularized fibula grafts.

joint stability, 4 cm of the proximal and 8 cm of the distal fibula were preserved. Postoperatively, patients were monitored in our outpatient clinic. Conventional radiographs were taken to evaluate bony union every 6 to 12 weeks. After consolidation, further follow-up appointments were organized twice a year to monitor biological activity, recurrence and complications. Biological activity was validated as periosteal hypertrophy according to the De Boer and Wood index (5). We considered a hypertrophy index of ≥20% as significant, an index between 0 and 19% as a biological active graft, whereas an index <0% was recorded as atrophy. The Musculoskeletal Tumor Society Rating Scale (MSTS) (6) was used to evaluate functional outcome. Additional chemo- and radiotherapy as well as any postoperative complications were also analysed in this series.

Statistical analysis. All analyses were performed using SPSS software, version 23.0 (SPSS Inc., Chicago, IL, USA). Continuous endpoints were expressed as medians with interquartile ranges (IQR) and as means with standard deviations (SD). Binary endpoints were recorded as absolute and relative numbers of patients and grafts. Complications were compared using Fisher's exact test. Significance level was defined as α=0.05.

Results

Clinical findings. Mean defect size after tumour resection was 13.3 cm [range=5-28 cm, standard deviation (SD)=5 cm], and the mean length of the harvested NVFGs was 16 cm (range=6.5-30 cm, SD=6 cm) and 16.5 cm (range=8-27.5 cm, SD=6 cm) for VFG. In total, 20 patients received neo-/adjuvant treatment. The average follow-up period was 14.9 years (range=1.5-43 years) and none of the patients were lost during follow-up.

Consolidation and hypertrophy. Osseous consolidation was predominantly achieved in both groups. Primary union was seen in 94.6% (n=104 junctions) of NVFGs after a mean of 23.4 weeks (7.4-47 weeks, SD 9 weeks), whereas 82.4% (n=28 junctions) in the vascularized bone graft group showed uneventful osseous consolidation after a mean of 10.6 weeks (3-30 weeks, SD 6 weeks) (Figure 1). Delayed union (>12 months) was recorded in 2% and non-union in 4% of segmental reconstructions in NVFGs. In case of VFG, delayed union (>12 months) was recorded in 17% (1 proximal and 5 distal junctions) and healed after a mean of 72 weeks (range=12-120 weeks). Adjuvant chemo- and/or radiotherapy was applied in all cases with delayed union (p=0.021). Once osseous consolidation was achieved, periosteal hypertrophy was seen in 87.1% of NVFGs and in 85.3% of VFGs, and significant hypertrophy (>20%) was detected in 52% of the NVFG and 56% of VFG cases. Mean hypertrophy of NVFG was 33% (range=7-69%) within 37.8 months on average (range=22-76 months) and 42.2% for the VFG (range=6-100%) within 26.5 months on average (range=24-27 months).

Function. Functional results were evaluated in 50 patients (34 NVFGs, 16 VFGs) using the MSTS (5). At final follow-up, the median functional index was 86% (range=37-100%, SD=13%) in the NVFG group and 87% (range=56-100%, SD=12.5%) in the VFG group. Overall, excellent or good results were seen in 43 patients (86%) and 7 patients (14%) showed a fair result.

Complications. Overall, 17 patients (32%) required revision surgery for graft fracture, wound or infectious complications. In the NVFG group, fatigue fractures were seen in 5 grafts (9%) among 5 different patients (14%). One patient was treated conservatively, whereas in the other four patients reosteosynthesis (Figure 2) was performed. Four fractures occurred in bone defects greater than 12 cm, which was significant (p=0.013) for mechanical complications. In

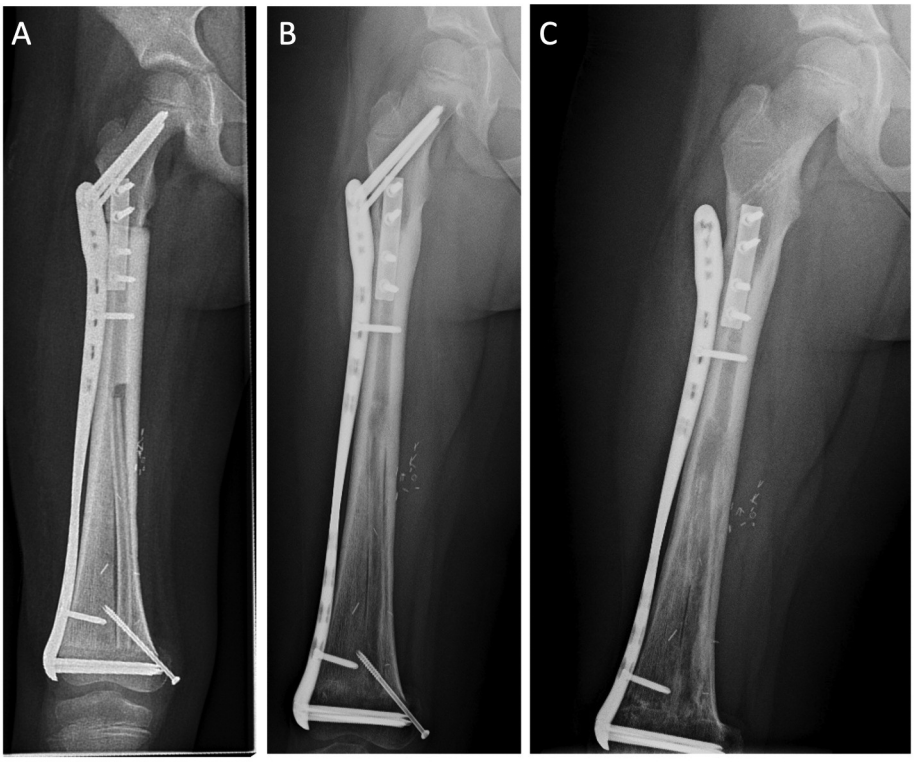

Figure 1. *Ewing sarcoma of the distal femur in a 5-year-old female patient. After R0 resection, reconstruction was performed with a vascularized fibula graft. Conventional antero-posterior view after index surgery (A), 12 months postoperatively (B) and at last follow up 3.5 years after partial screw-removal (C).*

addition, segmental reconstructions (p=0.013) and patients with adjuvant therapy (p=0.006) showed a significantly higher mechanical complication rate.

In the VFG group, fatigue fractures occurred in 7 patients (41%). Reosteosynthesis was performed in 5 patients, while 2 patients were treated conservatively. Adjuvant chemotherapy, which was statistically significant for delayed bone healing, was applied in 6 patients.

In case of donor site complications, 2 patients of the NVFG group showed transient peroneal nerve palsy, whereas 1 case of painful flexion contracture of the toes occurred in the VFG group. There were no instances of instability or restriction in range of motion of the knee or ankle joint and all patients showed good aesthetic results.

Discussion

The objective of bone tumour reconstruction includes symmetrical extremities with complete bony union and good function. This study highlights that similar results can be obtained with NVFG and VFG for bone tumour reconstruction, even though NVFGs have a limited indication for malignant bone tumours. Conventional fibular grafts are widely applied in bone tumour patients, providing relatively large grafts to bridge osseus defects after wide tumour resection, are relatively easy to harvest and have favourable biomechanical properties (4). Nevertheless, conventional grafts have limited indications compared to VFG. Vascularized bone grafts from the fibula, on the other hand, have a preserved vascular supply and therefore increase the likelihood of bony consolidation, particularly in patients with substantial bone defects (>12 cm) and a concomitant use of chemo- and radiotherapy (7).

In literature, studies are focusing on either VFG or NVFG following bone tumour resection (6, 8, 9); however, there are only few studies comparing vascularized and conventional grafts for bone tumour reconstruction. Thus, the purpose of this study was to compare practicability and reliability of VFG and NVFG for reconstruction of bone defects following tumour resection and to establish an algorithm for each procedure.

In this study, the overall union rate, whether VFG or NVFG, was 92%. The union rate was quicker in VFG compared to NVFG (p=0.04). For VFG, union rates vary between 67-100% according to literature (3, 10-12). Patients in the VFG group showed bony union in 86% at the proximal osteotomy, and in 64% at the distal osteotomy sites.

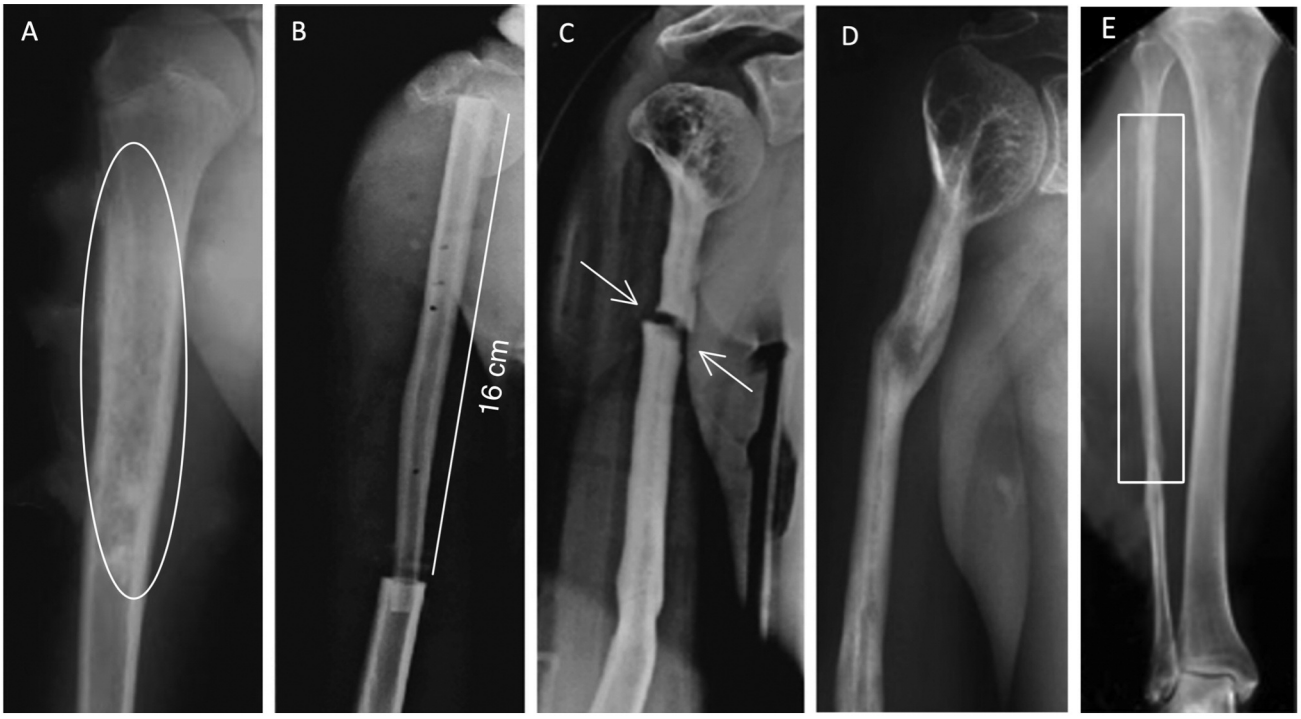

Figure 2. *Chondrosarcoma of the proximal humerus in a 16-year-old male patient. Preoperative (A), and postoperative conventional X-rays after R0 resection and reconstruction with a non-vascularized fibula graft (NVFG) (B). The patient experienced a traumatic fracture 6 years postoperatively (C), which was treated conservatively. At final follow-up 26 years postoperatively, the NVFG showed complete integration and remodeling of the resected segments at the donor- and host sites (D, E).*

As previously shown in our outcome analysis of vascularized bone graft reconstruction in bone tumour patients (7), delayed union was primarily influenced by the concomitant use of radio- and chemotherapy, which is a detrimental effect on bony union. Additionally, we believe that the poor vascular supply at the distal part of the tibia could also determine the delayed union at the distal osteotomy sites (13). In this study, two patients underwent revision surgery due to non-union, both of which were in the NVFG group. One patient healed after reosteosynthesis and grafting with autologous iliac crest. The other patient refused further reconstructive surgery, thus the fibular graft was just removed and replaced by a spacer. Morbidity of the donor site was rather low in both groups and occurred in 6%. Although our series has a small number of patients, we support the idea that this risk is acceptable, at least in NVFG offering bone remodelling at the donor site (Figure 2E), which was shown by Lenze *et al*. (4).

Functional results are in line with those reported for endoprosthetic reconstruction (14). However, long-term results are associated with a life-long risk of aseptic loosening and infectious complications, which is usually treated by removal of the device or even amputation of the affected limb. As bone sarcomas are more common in young patients, we consequently do prefer autologous reconstruction in this population. MSTS scores in this study reveal similar functional outcomes in both groups. Our findings are in line with those reported by Schuh *et al*. who reported MSTS scores of 77.9% in the use of VFG and 75.8% in NVFG reconstructions (15).

There were several limitations to this study. It is a retrospective, single-centre study with a small number of patients. However, autologous bone tumour reconstructions are rare and studies with high numbers of patients are scarce. Additionally, the included patients were heterogeneous, and there was a lack of control group. Both reconstructive procedures have been performed equally over the whole study; however, preference of vascularisation was mainly the result of an interdisciplinary approach.

In conclusion, similar union rates and functional outcomes can be accomplished with VFG as well as NVFG for bone tumour reconstruction in this retrospective study. A disease-specific algorithm for surgeons should include vascularized fibulas to be preferred for patients with malignant bone tumours at any site and segmental defects >12 cm to benefit from the preserved vascular supply. In contrast, NVFG should be preferred in patients with benign tumours or malignant bone tumours with one preserved cortex without adjuvant therapy and a defect size of <12 cm.

Conflicts of Interest

The Authors declare no potential conflicts of interest with respect to this article.

Authors' Contributions

All surgeries were performed by AHK and MH. Data were collected by SMG and UL, SMG analysed the data and wrote the article. CD critically revised the manuscript. AHK, SMG and UL finalized the publication.

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