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ORIGINAL STUDY

Vascularized fibular autograft as salvage technique in failure of allograft intercalary reconstructions after tumor resections

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Intercalary allografts after diaphyseal resections for bone tumors represent the most frequent option of reconstruction. Main complications are non-unions, fractures and infections. The purpose of the current study was to report our experience with the use of vascularized fibular autograft as rescue technique in failed previous reconstructions after intercalary bone tumor resection of the extremities. Twenty-eight patients were followed over time. Causes of failure were non-union, allograft fracture and infection. Vascularized fibular autograft was used with mechanical support of massive bone allograft in 13 cases. Functional results were excellent in 19 cases, good in 8 and fair in one patient. Among complications we reported 4 non-unions, 2 allograft fractures, 1 non-union with plate breakage, 1 plate breakage, 1 infection, 1 limb shortening and 1 knee varus deformity. The rationale of vascularized fibular autograft is to provide biologic support. The association with massive bone allograft provides mechanical strength and early stability.

Level of Evidence : Therapeutic Level IV.

Keywords : vascularized fibular autograft ; intercalary allograft ; salvage technique

INTRODUCTION

Nowadays, due to the advances in the fields of radiology, histopathology, surgery and chemotherapy, most of diaphyseal and metadiaphyseal malignant bone tumors can be treated with epiphyseal preservation, permitting conservation of the proximal and distal joint. These tumor resections originate in segmental bone defects that can be reconstructed with different options, such as endoprosthetic reconstructions, distraction osteogenesis and biologic reconstructions, each one with advantages and disadvantages *(3)*.

Endoprosthetic reconstructions allow patients early weight-bearing and function but they may have several complications, such as aseptic loosening, infection and mechanical failure. Besides, a large part of proximal and distant bone is needed to fix the stem prosthesis and frequently, in large resections, this is not possible *(1,21)*.

Distraction osteogenesis with bone transport by means of an external fixator is a valid reconstructive method with acceptable results (*7*). Nevertheless, according Tsuchiya et al. (*30*), this method should be reserved for segmental defects up to 15 centimeters in length, making the technique inappropriate for

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larger femoral defects commonly seen in diaphyseal sarcomas.

Biologic reconstructions include vascularized fibular autografts (VFA), allografts and extracorporeally irradiated autogenous bone grafts. VFA is a biologic method of reconstruction with the important advantage to restore bone stock, but may require a long time of non-weight-bearing to allow for union/graft hypertrophy (*10,23,32*). Extracorporeally irradiated autogenous bone grafts are suitable for larger defects but irradiated bone is brittle and takes a long time to revascularize and incorporate into surrounding bone, with consequently non-weight-bearing for a long time *(23)*. Fractures and non-unions are common complications.

Intercalary allografts after diaphyseal resections for bone tumors represent the most suitable option of reconstruction, almost of all in young, active and high-demanding patients. However, this type of reconstruction is characterized by common complications, such as fractures, infections and non-unions *(3,18)*.

VFA, alone or in association with massive bone allograft, has been used for reconstruction of intercalary defects of long bones *(8,9,11,14,19,20,28, 29,31)*. The first case of VFA in limb salvage surgery after trauma was reported by Taylor et al. in 1975 *(29)*, while Weiland et al. in 1977 described the first case after tumor resection *(31)*. The first description of VFA as salvage technique was reported by Duffy et al. *(12)* in the management of radiation-induced long bone fractures.

VFA has biologic properties that can induce fusion of the osteotomies ; with the combination of VFA and massive bone allograft we associate biologic properties and mechanical strength, diminishing the rate of complications, such as infections, fractures, non-unions and increasing the rate of internal repair of the allograft (*8*). The purpose of the current study was to investigate the results and the morbidity of VFA, alone or in association with massive bone allograft, as salvage technique in failed previous reconstructions after intercalary bone tumor resection of the extremities.

MATERIALS AND METHODS

A tumor registry review was conducted to identify all patients who underwent a reconstruction with a vascularized fibular graft for allograft reconstruction complications (non-union, allograft fracture or infection) following resection for primary malignant bone tumors between 1995 and 2011. We recorded general data, primary diagnosis, previous treatments, cause of failure, survivorship of the implant, adjuvant therapies, outcomes, complications and operative details. Twenty men and 8 women satisfied the criteria for this study. The average age at the time of the first diagnosis was of 24,2 years (9-44 years). The involved bones were the femur (twenty-two patients), tibia (three) and humerus (three). The initial diagnosis was in most cases osteosarcoma (OS, 20 cases), followed by Ewing's sarcoma (ES, 7 cases) and angiosarcoma (1 case). All patients underwent intercalary resection with an average resected specimen of 15,5 centimeters. Reconstructions were performed in 26 cases with plate (stainless steel plate in 21 cases, titanium plates in 5 cases). Only in 2 cases endomedullary nails were used. Twenty-five patients received neoadjuvant chemotherapy around the first surgical procedure. Two patients did not receive adjuvant therapies because they had low-grade OS ; 1 received post-operative radiotherapy. At histological examination of the specimen, surgical margins were wide in all cases.

Failure of the previous reconstruction occurred because of non-union in 18 cases, of which 9 with allograft fractures and 3with plate breakages. Other causes of failure were allograft fractures (5 cases), infections (4 cases) and 1 plate loosening. The average time of survivorship of the first reconstruction was 64 months (9-243 months). Eighteen patients underwent surgical procedures following the primary reconstruction and prior to VFA (Table 1).

In 27 cases we used a free VFA ; only 1 was a pedicle graft. VFA was used without allograft in 9 cases, with mechanical support of massive bone allograft in 13 cases and with cortical bone allograft in 6 cases. All cases had synthesis with stainless steel plates except one in which we used a titanium plate and 1 case treated with endomedullary nail. In 27 cases VFA was used as onlay graft (figures 1-4) ; only in 1 case we used VFA as inlay (intramedullary) graft (figures 5-7). We used controlateral fibula in 21 cases, omolateral fibula in 7 patients. The harvested fibula was at least 2 centimeters longer than the length of the bone defect to allow a minimum overlapping for each osteotomy. Patients were restricted from weight-bearing for 3 to 6 months after reconstructions based on radiographic evidence of healing. The functional evaluation was assessed with the scoring system of the Musculoskeletal Tumor Society (*13*). Implant outcome was assessed on serial radiology in all cases with minimum follow-up of 24 months.

RESULTS

Functional results were excellent in 19 cases, good in 8 cases and fair in one patient, a 30 year-old boy who suffered an osteosarcoma of the humerus and developed infection (case 21). No cases of failures of VFA were recorded. No donor site complications were reported. Among complications of VFA, we reported 4 non-unions, 2 allograft fractures, 1 non-union with plate breakage, 1 plate breakage, 1 infection, 1 limb shortening and 1

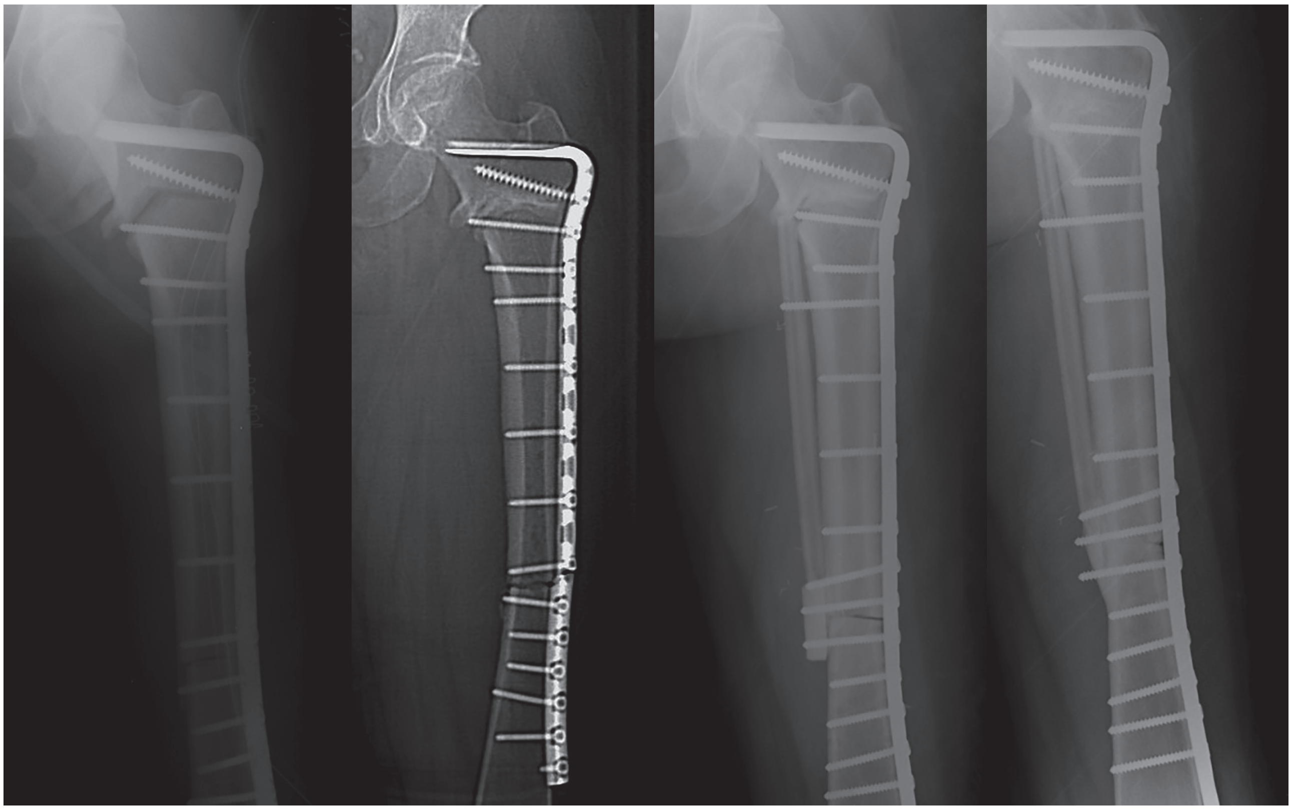

Fig. 1-2-3-4. — Case 27. Low-grade OS of the femoral diaphysis. After intercalary resection and reconstruction with massive bone allograft, the patient developed non-union of the distal osteotomy with hardware breakage. VFA was performed. At last follow-up union of both osteotomies with fibular integration was present.

Table 1. — General data, surgery details of primary and salvage reconstructions, complications of VFA, follow-up and outcomes of the 28 patients reported.

Case	Sex	Age	Diagnosis	Adjuvant therapies	Site	Primary reconstruction	Cause of failure	Treatments before VFA	VFA	Complications of VFA	Treatment of complications	F-U primary reconstruction (months)	F-U VFA (months)	Outcome
1	M	12	OS	Neoad chemo	F dia	Femoral intercalar recons+VFA	Allograft fracture	None	VFA+massive allograft	Allograft fracture	Implant removal+massive allograft+plate +VFA	42	240	Exc
2	M	29	OS	Neoad chemo	F dia	Femoral intercalar recons	Non-union-allograft fracture	Plate	VFA+cortical bone allograft	None	None	36	216	Exc
3	M	25	OS	Neoad chemo	F dia	Femoral intercalar recons	Non-union-allograft fracture	Autografts (1991), allograft+plate (1994), nail (1995)	VFA+massive allograft	None	None	92	177	Exc
4	F	38	OS	Neoad chemo	F dia	Femoral intercalar recons	Non-union-allograft fracture	Plate (1995), allograft+plate (1998), plate (2006), hardware removal (2007)	VFA+massive allograft	None	None	92	62	Exc
5	M	30	OS	Neoad chemo	F dia	Femoral intercalar recons + nail	Non-union	Synthesis with special plate	VFA+cortical bone allograft	None	None	174	120	Exc
6	F	13	OS	Neoad chemo	F dia	Femoral intercalar recons	Non-union-allograft fracture	Hardware removal	VFA	None	None	44	114	Good
7	M	16	OS	Neoad chemo	F dia	Femoral intercalar recons	Non-union-allograft fracture	Epiphysiodesis (2003), plate+cortical bone allograft	VFA+cortical bone allograft	None	None	81	108	Exc
8	F	36	ES	Neoad chemo	F dia	Femoral intercalar recons	Non-union	Autografts+hardware removal+cortical bone allograft	VFA+massive allograft	Non-union	Autografts+plate	84	111	Good
9	M	12	OS	Neoad chemo	Proximal T	Tibial intercalar recons	Infection	Synthesis (2003), surgical debridement+cement spacer (2004), spacer removal+ free microvascular latissimus dorsi flap (2005), Thiersch skin graft (2005)	VFA+massive allograft	Non-union	Autografts+plate	24	96	Exc
10	M	10	OS	Neoad chemo	H dia	Humeral intercalar recons	Non-union	None	VFA	None	None	36	93	Exc
11	F	17	OS	Neoad chemo	F dia	Femoral intercalar recons	Infection	Surgical debridement (2004), surgical debridement (2005), osteotomy revision+Thiersch skin graft (2005), allograft removal+cement spacer+nail (2006),new spacer (2006)	VFA+nail	Allograft fracture	Massive allograft+nail	25	86	Good
12	M	19	OS	Neoad chemo	F dia	Femoral intercalar recons	Non-union	Plate removal-allograft (2006), distal osteotomy revision (2007)	VFA+massive allograft	None	None	23	89	Good
13	M	17	OS	Neoad chemo	F dia	Femoral intercalar recons	Non-union	None	VFA+plate	None	None	14	48	Exc

14	M	29	ES	Neoad chemo	F dia	Femoral intercalar recons	Non-union-allograft fracture	Autografts	VFA+massive allograft	Hardware failure	Autografts+plate	154	100	Exc
15	M	32	OS	Neoad chemo	F dia	Femoral intercalar recons	Non-union-plate breakage	Autografts+cortical bone allograft+synthesis (2004), synthesis+autografts+plate (2004)	VFA+massive allograft	Non-union	Cortical bone allograft+plate	63	83	Good
16	M	44	ES	Neoad chemo	H dia	Humeral intercalar recons with cement	Plate loosening	None	VFA	None	None	243	79	Good
17	M	23	ES	Neoad chemo	F dia	Femoral intercalar recons	Allograft fracture	Cement spacer+plate (1997), new allograft+plate (2000)	VFA+massive allograft	None	None	126	92	Exc
18	M	16	OS	Neoad chemo	T dia	Tibial intercalar recons	Allograft fracture	None	VFA pedicled +massive allograft	Knee varus deformity	Corrective osteotomy	64	83	Good
19	F	33	Ang	Postoperative RXT	F dia	Femoral intercalar recons	Allograft fracture	None	VFA+cortical bone allograft	Non-union	Cortical bone allograft +synthesis with screws	9	72	Good
20	M	37	OS	Neoad chemo	F dia	Femoral intercalar recons	Non-union-allograft fracture	None	VFA+massive allograft	None	None	42	68	Exc
21	M	30	OS	Neoad chemo	O dia	Humeral intercalar recons	Infection	Implant removal+cement spacer (2008), spacer+nail (2008)	VFA	None	None	23	66	Fair
22	M	24	ES	Neoad chemo	F dia	Femoral intercalar recons	Non-union-plate breakage	Autografts	VFA+massive allograft	None	None	30	55	Exc
23	M	9	OS	Neoad chemo	F dia	Femoral intercalar recons	Non-union	Autografts	VFA+cortical bone allograft	Limb shortening	Expandable nail	20	59	Exc
24	F	17	OS	Neoad chemo	F dia	Femoral intercalar recons	Non-union-allograft fracture	None	VFA	None	None	40	60	Exc
25	M	42	ES	Neoad chemo	F dia	Femoral intercalar recons	Allograft fracture	Autografts	VFA	Infection	2 surgical debridements	76	57	Exc
26	M	17	ES	Neoad chemo	F dia	Femoral intercalar recons	Non-union-allograft fracture	N/A	VFA+massive allograft	Non-union/ hardware failure	New plate	N/A	58	Exc
27	F	37	Low-grade OS	None	F dia	Femoral intercalar recons	Non-union-plate brekage	N/A	VFA+cortical bone allograft	None	None	N/A	54	Exc
28	F	14	Low-grade OS	None	T dia	Tibial intercalar recons	Infection	Surgical debridement+free muscolar flap+Thiersch skin graf (2011), implant removal+cement spacer (2011)	VFA	None	None	9	46	Exc

Abbreviations: M : male; F : female; OS: osteosarcoma; ES : Ewing sarcoma ; Ang : angiosarcoma ; Neoad : neoadjuvant ; Chemo : chemotherapy ; F : femoral ; T : tibia ; H : humerus ; Dia : diaphysis ; RXT : radiotherapy ; Recons : reconstruction ; VFA : vascularized fibular autograft ; N/A : not available ; F-U : follow-up ; Exc : excellent.

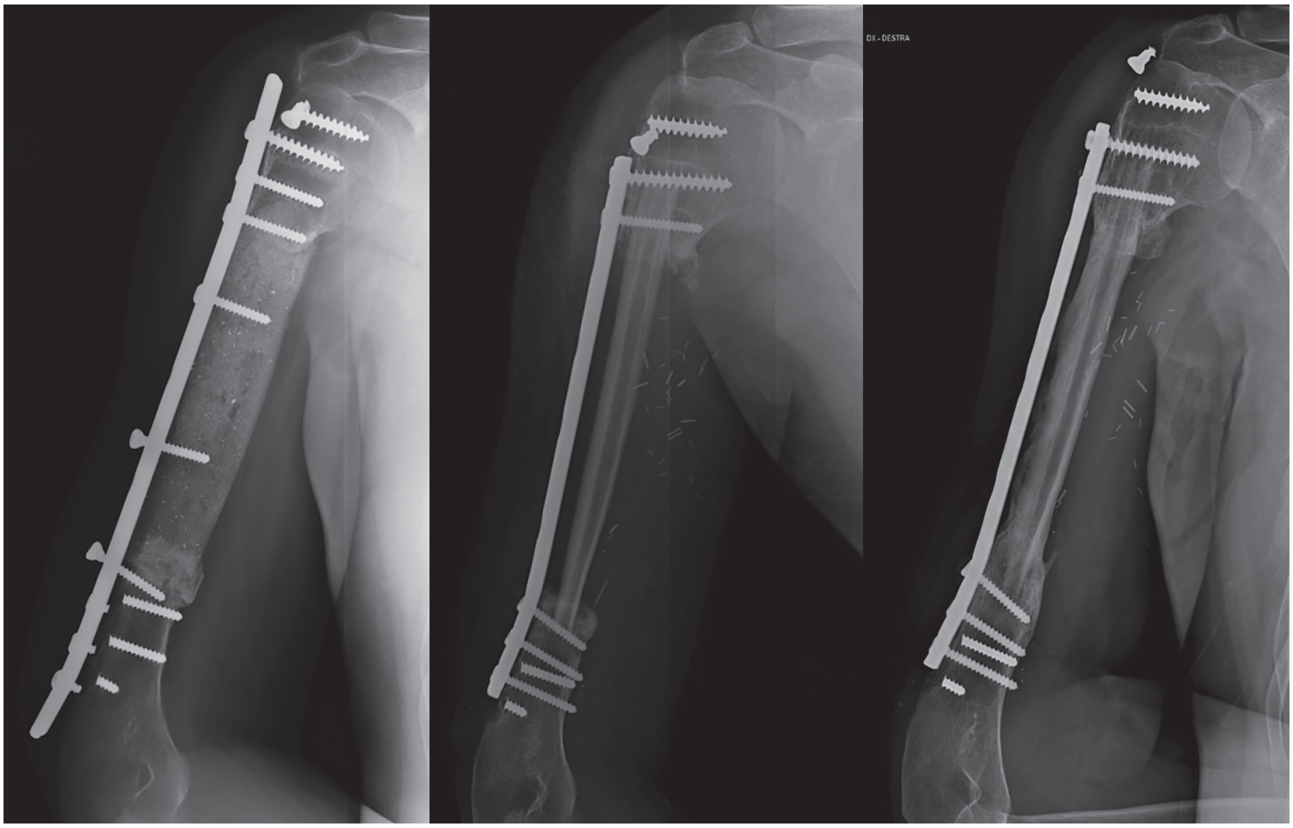

Fig. 5-6-7. — Case 16. A 44 year-old man reported Ewing sarcoma of the humeral diaphysis. He underwent neoadjuvant chemotherapy and intercalary resection. Reconstruction was performed with cement spacer and plate. Hardware breakage and plate loosening were the causes of failure. VFA was used as inlay graft. At last follow-up x-rays showed hypertrophy and excellent osteo-integration of the autograft.

knee varus deformity. We treated non-unions with autografts (autogenous cancellous bone) plus new synthesis with titanium plate (case 8), with stainless steel plate and autografts (case 9), new synthesis and cortical bone graft (case 15) and synthesis with stainless steel screws and cortical bone graft (case 19). We had 2 allograft fractures : case 11, treated with endomedullary nail and massive allograft and case 1, treated with new VFA, plate and massive allograft (this was the only case in which we removed the previous allograft). We performed corrective osteotomy for varus knee deformity in case 18. Case 25 experienced infection, treated with 2 surgical debridements. Case 23 had important limb shortening (4,5 centimeters), treated with expandable nail. A new synthesis with plate and autografts was performed in case 14, due to plate breakage. Case 26 had non-union at the distal osteotomy, treated with new synthesis. VFA was never removed. Average VFA follow-up was 92 months (46-240 months).

DISCUSSION

Our study has two important limitations. First, the group is heterogeneous, in terms of patient age, site of reconstructions and length of bone defect. However, this is one of the largest series for this type of reconstruction. Second, we have no control group with alternative approaches.

Due to early diagnosis, advanced chemotherapy and accurate preoperative imaging techniques, many tumors involving the diaphyseal and metadiaphyseal region of the long bones can be treated with epiphyseal preservation (*26*). Surgical options for reconstructing diaphyseal and metadiaphyseal defects include intercalary endoprosthesis, distraction osteogenesis, autogenous extracorporeally irradiated bone, massive allograft, VFA and the combination of massive allograft with VFA (*1,3,7,9-11,14,19-21,23,28,32*).

Nowadays intercalary bone allografts have been shown to have better functional results compared with prosthesis, allograft-prosthetic composites and osteoarticular allografts because they preserve native joints (*15,18,26*). They represent the best solution in the treatment of intercalary bone resections. However, during the past 20 years, several studies have analyzed long-term intercalary allograft results, underlying main problems, such as non-unions, fractures and infections, which are higher in patients receiving chemotherapy. Hornicek et al. reported the results of 945 massive bone allografts (intercalary, osteoarticular and alloprosthesis) confirming that patients who received chemotherapy had a higher risk of non-union (27% compared to 11%), infections (7,9%) and fractures (18%) compared to those who did not receive chemotherapy (*22*). Farfalli et al. (*15*) in 2012 presented 26 tibial intercalary allograft reconstructions, reporting infections (11,5%) and incomplete fractures (11,5%) as the main complications, followed by non-union (7,6%). Brunet et al. reported 13 intercalary allograft reconstructions of femur and tibia following bone tumor resections. They found 8% rate of non-union/allograft fracture and 43% of infection (*5*). Aponte-Tinao et al. in 2012 reported 83 cases of intercalary allograft of the femur observing a 24% non-union rate and a 17% fracture rate. Non-union was more common at diaphyseal junctions than at metadiaphyseal ones and nail fixation was considered as risk factor for non-union compared to plate fixation (*3*). A higher non-union risk using intramedullary nails was confirmed by Frisoni et al., who analyzed the results of 114 intercalary femoral resections for bone tumors : they found 31,5% rate of failures, due to non-unions, fractures and failures of fixation. They found poor results using intramedullary nails and titanium plates as fixation, so they suggested use of stainless steel plates, eventually supported by VFA in defects longer than 17 centimeters, especially in patients who require post-operative chemotherapy (*18*).

Allograft fracture in massive intercalary bone allografts of the lower limb represent a dramatic complication and can be treated with new allograft and synthesis or only with a new synthesis. Aponte-Tinao et al. recently reported their series of 135 patients who underwent intercalary resection of the lower limbs for bone tumors. They described 19 fractures (16 in the femur and only 3 in the tibia), reporting no statistically significant differences with age and gender. All femoral fractures were managed with resection of the previous allograft and reconstruction with a second intercalary allograft. However, the fracture rate for this second intercalary reconstruction was higher than the primary group. So they concluded that in femoral fracture of pediatric and young adults, a second attempt at salvage of an intercalary allograft should be performed, eventually associated with a VFA, whereas in older patients, it might be preferable to proceed to endoprosthesis or osteoarticular allograft (*2*). The lower rate for tibia fractures is already mentioned in other reports (*3,15*) and may be explained by the presence of the fibula that may diminish the overloads in the allograft.

Allograft non-unions have been treated with several methods, such as autogenous cancellous bone apposition with eventual successful healing in 66% of cases (*22*). But when non-union is associated with allograft resorption and/or hardware failure in the femur, a VFA is recommended as salvage technique (*16-18*).

The use of free vascularized fibula was first described by Taylor et al. (*29*) in 1975. Then, this technique has been widespread in both orthopaedic and plastic surgery. Several authors described its use to restore long bone defect after bone tumor resection (*4,5,10,14,25,27*). Its use as salvage method was first reported in 2000 by Duffy in a series of patients with radiation-induced long bone fractures (*12*). Then, only 2 authors reported on the use of VFA as salvage technique in failed long bone reconstructions after tumor resection confirming its validity as rescue technique (*6,17*).

The VFA can be used as an onlay strut to span the allograft-host non-union, allograft fracture or pathologic fracture non-union. The surgical technique involves harvest of a proper length of fibula to span the defect in question. This can involve the use of a long piece of bone, especially if both the proximal and distal allograft-host junctions have non-unions. The fibula is usually placed medially, anastomosed with a branch of the femoral artery and vein and fixed to the long bone with two lag screws with washers (*16*). In the setting of tibial pathological fracture non-unions or allograft complications, it is possible to use the fibula as pedicle transfer, eliminating the need for microsurgical anastomoses (*16*). However, the fibula can be used also as an inlay (intramedullar) graft, as described by Capanna et al. in 1993. This technique combines a massive allograft and a VFA with the aim of improving allograft incorporation and decreasing the risk of mechanical complications (*8*).

One of the major advantages of using VFA is its ability to hypertrophy, as described by Manfrini et al., who analyzed the imaging at long-term of the combined inlay VFA, showing the progressive hypertrophy of the fibula and the eventual union between the fibular periosteal surface and the endosteal cortex of the allograft (*24*). Although the causes of hypertrophy are not completely understood, Muramatsu et al. suggested that this can be induced by the mechanical stimulation provided by weight-bearing. In their paper, they reported higher hypertrophy in the inlay graft compared to the non-weight-bearing of the onlay fibula (*25*). Donor site complications have been described after VFA harvesting and the most common are flexor allucis longus retraction and ankle valgus deformity in children (*9*).

Our results are similar to the other studies. Campanacci et al. reported on the results of 12 failed femoral reconstructions after bone tumor resections. They used 7 VFA as biologic augmentation in intercalary allograft non-unions and a combination of new allograft and VFA in the other 5 patients. They had 2 major complications (1 allograft fracture with associated deep infection and 1 VFA fracture with hardware failure) that required surgical revisions but no failures of the VFA. At final follow-up the average MSTS functional score was 90%. No donor site complications were described (*6*). Friedrich et al. reported on the functional results of 33 VFA as salvage technique in failed long bone reconstructions after bone tumor resections. They had 7 major complications, of which 2 non-unions which healed after non-vascularized iliac crest bone grafts and 5 infections that they attribute to the allograft and not to the VFA. They had 23 good or excellent functional results but 5 patients ended up with limb loss (*17*).

Intercalary massive bone grafts represent the gold standard after resection of bone tumor of the long bones but are encumbered by several complications such as non-unions, fractures and infections, especially in patients receiving chemotherapy and/or radiotherapy. VFA has proven to be a valid and effective tool for treating secondary mechanical failures in oncological limb reconstructions, with a low complication rate and a high percentage of success. The rationale for this approach is to combine the mechanical strength of an allograft with the biologic activity of VFA. The allograft provides bone stock and early stability, while the addition of the VFA substantially facilitates the host-allograft union.

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