Long Term Behavior of Pedicled Vascularized Fibular Grafts in Reconstruction of Middle and Distal Tibia after Resection of Malignant Bone Tumors

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ABSTRACT

Objectives: The aim of this study was to evaluate the long term behavior of pedicled vascularized fibula graft in reconstruction of middle and distal tibia defects following malignant tumor resection with particular emphasis on success in limb salvage and the specific late related complications.

Patients and Methods: Between 1997 and 2006, 16 patients having malignant bone tumors of the middle tibia (10 cases) and distal tibia (6 cases) were candidates for wide resection of their tumors and reconstruction of the bony defect by ipsilateral vascularized pedicled fibular graft based on the peroneal vessels. There were 9 males and 7 females with a mean age of 13 years at time of surgery (range 11-23 years). Mean follow up period was 52 months (range 32-110 months). Fixation was done by cast in 14 cases and by plate and screws in 2 patients. According to the Enneking staging system (1), 9 patients had stage IIB and 7 had stage IIA. Bony union and hypertrophy were assessed radiographically on regular basis. Hypertrophy was estimated in a percentage. Functional limb results were also reported according to MSTS functional scores [2].

Results: The mean length of bony gap bridged was 14 cm (range of 11.0-16.0 cm) and the mean length of fibula harvested was 15.5 cm (range 12-17 cm). Ninety seven percent of patients (15 cases) healed primarily at a mean time of 4.8 months (range 3.5-6 months). Hypertrophy was evident in all patients and ranged from 60 to 210% (mean 91%). Increase in size of the hypertrophied fibula beyond the recipient bone was noticed in three cases (18.7%) and we relate this to weight-bearing forces and not to the size of the recipient bone. The mean time of the fibula to double its size (10 cases) was 21 months (range 18-31 months). Young patients developed full hypertrophy earlier than older patients. Complication rate was low. One patient had non union at the proximal end of the fibulotibial junction and two patients had stress fracture of the fibula.

Conclusion: Long term follow-up of pedicled vascularized fibula in reconstruction of bony defects of the middle or distal tibia after bone tumor resection showed that it is a useful tool in the limb salvage procedure. It is a short procedure, inexpensive, with low rate of late complications. It has a good outcome regarding the union, hypertrophy and the functional outcome.

Key Words: Lower-limb reconstruction – Vascularized fibula graft – Bone tumors.

INTRODUCTION

Large bony defects in the middle or distal of tibia resulting from surgical resection of malignant bone tumors present a difficult reconstructive challenge. Various methods are available to the reconstructive surgeons as allografts, vascularized fibular graft either free or pedicled grafts or endoprosthesis replacement for the distal defects. Drawbacks of allografts include expense, irregular supply especially in developing countries, high rate of complications such as infection, fracture, delayed union and potential for late failure [3,4]. Complications of endoprothetic reconstruction of the distal tibia include infection, inadequate soft tissue coverage, and talar collapse [5,6]. Nonvascularized autogenous bone grafts may go on to nonunion, repeated fractures and do not demonstrate compensatory hypertrophy and so they are not suitable for large defects following malignant bone tumor resection [7].

The pedicled vascularized fibular graft based on the peroneal vessels has been recognized as a useful technique for reconstruction of large tibial bone defects following tumor resection of its middle or distal part [8,9]. It is a straight long bone and consists of dense cortical bone along its length. It provides rapid union in a short time between the graft and the recipient bone similar
to fracture healing. This, coupled with its triangular cross-section allows it to resist angular and rotational stresses. After bone healing has been established, the vascularized fibular graft can be seen to hypertrophy to a varying degree in response to mechanical forces [10].

There are few sizeable series of the outcome of this procedure after bone tumor resection of the middle and distal tibia [8,9,11-14] and fewer which address long-term behavior of the transferred fibula [15-19].

The purpose of this study is to discuss the long term behavior of 16 consecutive patients treated with pedicled ipsilateral transposition of fibula after resection of malignant bone tumors of the middle and distal tibia with particular emphasis on success in limb salvage and functional outcome. We particularly wished to look at the amount of hypertrophy to have occurred in the fibula and the specific related late complications.

**PATIENTS AND METHODS**

This study was conducted in National Cancer Institute, Cairo University, during the period from 1997 to the end of 2006. The study included 16 patients having malignant bone tumors of the middle tibia (10 cases) and distal tibia (6 cases). They were candidate for wide resection of their tumors and reconstruction of the bony defect by ipsilateral vascularized pedicled fibular graft based on the peroneal vessels.

Preoperative staging studies were done for every patient before doing biopsy and included plain radiography, local MRI with contrast, isotopic bone scan and CT chest. Slide revision of the histopathology was done for patients referred to us. MR angiography or angiography was done when vascular invasion is questionable. According to the Enneking staging system (1), 9 patients had stage IIB and 7 had stage IIA.

The diagnosis of osteosarcoma represents most of the cases (13 cases). The other three cases included recurrent Ewing sarcoma after chemo and radiotherapy (2 cases) and soft tissue malignant fibrous histiocytoma infiltrating the mid tibia (1 case). Neoadjuvant chemotherapy was routinely given to all patients having osteosarcoma and Ewing sarcoma.

Patients were selected only if preoperative imaging had shown that satisfactory surgical margins could be achieved without resection of the ipsilateral fibula or compromising its pedicle. Patients had posterior tibial neurovascular bundle involvement, pathological fracture or proximal tibial tumors and extensive pulmonary metastasis were excluded from the study. Patients required en bloc resection of part of the fibula were also excluded from this study.

**Approach to the tibia**

Approach to the tibia was through anterior approach (Fig. 1). Resection with free safety bony and soft tissue margins could be achieved in all cases on intra-operative frozen sections and final analysis.

Approach to pedicled fibular graft was done through the same incision for resection of the tibia. The fibular osteotomies are often possible from this incision without having to take an additional lateral incision to expose the fibula. However, a small incision opposite the head of the fibula was done in some cases having more proximal tumors to expose the lateral popliteal nerve to avoid its injury during the process of fibular transposition. Also, we occasionally use a small lateral incision at the distal end overlying the tip of the lateral malleolus in order to detach the distal fibular ligaments which otherwise prevent adequate centralization of the fibula. Proximal and distal subperiosteal incisions of the fibula were done 1 cm longer than the resected tibia then the fibula is osteomized and mobilized medially. The transferred fibula was inlayed in the medullary canal of the tibia proximally and distally after partial stripping of the periostium. Trascortical screw or, Kirschner (K)-wire at graft host junction was added in some cases because the fibula was not properly fitted. In cases of the distal tibia tumors, the fibula was fitted in the talus after being denuded
from its cartilage with a screw creating ankle arthodesis. Position of the fibula in relation to the tibia or ankle was adjusted under image in a neutral position to avoid marked angulations.

Fourteen patients were put in above knee cast. Two patients refused to put her leg in a cast for a long time, so, internal fixation was done by a plate and screws (Fig. 1). When radiograph showed signs of union proximal and distal, the cast is then changed by a below knee cast in distal tibial tumor cases or at the level of the knee in middle tibial tumor cases to allow for some knee mobility. Gradual weigh bearing was allowed after radiological evidence of union. Full weight bearing without a bracer or cast was allowed when graft hypertrophy matched the size of the shaft of the tibia.

Patients were examined regularly with plain radiograph to determine evidence of bony union, degree of hypertrophy of the transferred fibula and late complications as stress fracture. Regular local MRI or CT, chest CT and isotopic bone scan were also performed to detect any local or distant failure.

Bony union was said to have occurred when radiological bone union between the ends of the fibula and the recipient bone in two planes. Union of the graft proximally and distally was assessed according to Huso et al. [20], with graft union defined as uninterrupted external bony borders between the fibular graft and recipient bone in addition to obscured or absent osteotomy line at both junctions (Fig. 2).

The amount of hypertrophy to have developed in the fibula at the time of final follow-up was calculated as follows, the maximum and minimum widths of the transferred fibula at its thinnest point on the immediate post-operative X-ray films (AP and lateral views) were measured with caliper in millimeters. The value of this measurement was recorded as 'original fibular width'. This procedure was repeated on the final films to obtain the measurement 'final fibula width'. The amount of hypertrophy to have occurred during the follow-up period was therefore the difference between 'original fibula width' and 'final fibula width' and this was expressed as a percentage [19].

The fibula is triangular in cross-section and De Boer [21], has shown that rotation of the fibula by 10° to either side of neutral position, (a reasonable variation between radiographs), can produce an increase in the fibula width of as much as 20%, thus giving a false impression of hypertrophy. Also, Enneking et al. [22] showed that hypertrophy of up to 20% occurs in 32% of nonvascularised grafts, so, we considered the fibula is hypertrophied only when the 'final fibula width' was at least 20% greater than the original fibula length.

A stress fracture was confirmed radiographically, or if a hairline break was seen in the cortex of the graft. An asymptomatic fracture was taken to have occurred if an area of localized callus was noted on later radiographs (Fig. 3 A, B).

![Fig. (2): Union of fibula after 6 months. Note, obscured or absent osteotomy line at both junctions.](image)

![Fig. (3-A): Two stress fractures in a hypertrophied fibula, the proximal one healed by callus formation and the distal one is a recent fracture.](image)

![Fig. (3-B): A stress fractures in early hypertrophied fibula with early healing.](image)
Limb function was estimated according to MSTS functional scores [2]. This scoring system allocates up to five points for each of six different assessments, including pain, functional activity, emotional acceptance, need to external support, walking ability, and gait. Each entity has a score of five points with a total being 30 points. A score of five indicates normality and a score of one indicated significant disability. A middle score of three would suggest problem such as the need for non narcotic analgesics, being unable to play sports, the occasional need for a walking distant stick and a modest limp. A percentage score can be given to each factor.

Post operative chemotherapy or radiotherapy was given according to the nationally agreed protocols.

**RESULTS**

There were 9 males and 7 females with a mean age of 13 years at time of surgery (range 11-23 years). Mean follow-up period was 52 months (range 32-110 months).

**Fibular union and length:**

The mean length of bony gap bridged was 14 cm (range of 11.0-16.0 cm) and the mean length of fibula harvested was 15.5 cm (range 12-17 cm). Bony union at the proximal and distal ends of the fibula was uncomplicated in 15 patients (94%) and was achieved primarily at both ends of the fibula at a mean time of 4.8 months (range 3.5-6 months).

**Graft hypertrophy:**

Measurement of hypertrophy was possible in all patients. All patients developed hypertrophy with different range of percentage. The mean percentage of hypertrophy was 91% (Ranged from 60 % to 210%). Increase in size of the hypertrophied fibula beyond the recipient bone, the tibia, was noticed in three cases (18.7%) (Fig. 4 A,B,C). Measurement of percentage of endoosteal and periosteal hypertrophy separately was impossible due to dense appearance of hypertrophied bone in some cases (Fig. 4 B). The mean time of the fibula to double its size (10 cases) was 21 months (range 18-31 months). Failure of hypertrophy was not seen in our cases, however it was relatively delayed in two cases, one case had nonunion at the proximal junction and required grafting of the nonunited end and the other case had internal fixation with plate and screws (Fig. 4 D).

**Functional limb results:**

Residual limb function was estimated at the 32th month, the minimal follow-up period at which local recurrence occurred in 2 patients. The maximal functional score according to MSTS functional scores were 94% where the minimal functional score was 81% with an average score of 87%.

**Complications:**

*Nonunion:* One patient had nonunion at the proximal end. He required secondary surgery after 13 months to achieve healing in the form of iliac crest grafting of the nonunited end. Time to healing after grafting was five months.

*Stress fractures:* Stress fracture of the transferred fibula was seen in 3 cases (12.5%). One case had asymptomatic stress fracture early after union and before development of hypertrophy. It was detected on follow-up radiographic examination and healed within three months without intervention. The other two cases had stress fracture two months and four months respectively after removal of the cast in hypertrophied fibulae with no history of trauma. Both were treated with a long period of fixation in a plaster cast; however one of them went onto nonunion and was subsequently treated by plating and bone graft (Fig. 5 A,B).

*Angulation:* A slight angulation at the junction of the proximal or distal end of the transferred fibula was seen in 5 cases. The degrees of angulation were minor and did not require surgical intervention. On follow-up radiologically, it was noted that there was more periosteal reaction and thickening of the cortex at the affected angle and side than the other side (Fig. 6).

*Nerve palsy:* Despite careful protection of the lateral popliteal nerve, two patients having middle tibial tumors exhibited signs of palsy in the immediate postoperative period. One of them experienced complete recovery within 5 months and the other had persistent palsy.

*Leg length:* Discrepancy of 1-2 cm was reported in 2 cases having distal tibial tumors. This was managed by a shoe lift.

*Fracture of screws:* Was seen in one patient after achievement of union. The plate was removed and the patient was fixed in a plaster of cast.
Oncologic outcome:

Thirty two months disease free survival (the minimal follow-up period) was 75%. Two cases developed local recurrence at 32 and 33 months respectively after primary resection and two patients develop pulmonary metastasis after 22 and 25 months respectively. Those developed local recurrence, one patient was salvaged by resection of the recurrence including the transferred fibula and the defect was replaced by intercalary prosthesis with coverage by pedicled gastrocnemius muscle flap, however, this was followed by second local recurrence and subsequently amputation was done. The other patient had above knee amputation. Those developed pulmonary metastasis were subjected to metastatectomy and died of disease progression.

Fig. (4-A): Pedicled fibula for the middle third of tibia after 8 years. The percentage of hypertrophy is 210%. Note dense sclerosis of the transferred fibula, the proximal shadow around the fibula is extensive periosteal reaction proved by biopsy.

Fig. (4-B): Pedicled fibula for the middle third of tibia after 6 years (lateral view). The percentage of hypertrophy is 220%. Note dense sclerosis of the transferred fibula, the distal end completely remodeled with tibia.

Fig. (4-C): Pedicled fibula for the distal third of tibia with ankle arthodesis after 13 years. The percentage of hypertrophy is 210%. Note, marked hypertrophy of anterior cortex in relation to the posterior one.

Fig. (4-D): 33% hypertrophy of the fibula after 24 ms, here internal fixation was done by a plate and screws which is the cause of delay in hypertrophy.

Fig. (5): (a) Stress fracture near the distal end in a hypertrophied fibula that showed no evidence of union after conservative management. (b) The same patient showed healing after internal fixation and grafting. Note, hypertrophied fibula can withstand screws.

Fig. (6): Hypertrophied pedicled fibula for the middle third of tibia after 2.5 years. Note, angualtion at the distal end is compensated by marked periosteal reaction and cortical thickening at the affected side.
DISCUSSION

Various reconstructive techniques have been used to reconstruct long bone defects of the middle and distal tibia after malignant bone tumor resection. These included the use of fibular bone grafts, allografts, endoprosthesis and vascularized fibular grafts either pedicled or free [3-6,8,22,23].

Since the fibula was first described [24] as a free flap, it has become the most frequently used source of vascularized bone for limb reconstruction of long diaphyseal defects. However, most published reports using contralateral free vascularized fibula to reconstruct tibial bone defects were dealing mostly with traumatic cases [25,26]. Free flap is not without disadvantages. Those include the necessity for two surgical teams, experience with microvascular technique, lengthy surgery and the occasional need for revision procedures. A direct comparison of pedicled fibula with free flap transfer while leaving the ipsilateral fibula for tibial bone defects is not possible without a double-blind randomized trial. In our study, we practiced the technique of pedicled fibular transfer to reconstruct middle and distal tibia defects after tumor resection and limited the indications for free fibula transfer to cases required en bloc resection of the fibula aiming at limiting the morbidity to the affected limb.

Overall bony union in our series was achieved primarily in 94% of patients at a median time of 4.8 months. This compares favorably with results demonstrated by other series [8,11,18]. Early union allows early weight bearing, the fundamental factor that enhances the development of hypertrophy. The Nonunion at the proximal junction in the reported case may be due to early removal of the upper part of the cast by the patient himself. Healing occurred completely after grafting the nonunited end with iliac bone graft. Most of our patients received postoperative chemotherapy and one received postoperative radiotherapy. Conversely; it appears to have no detrimental effect on union.

Vascularised fibular graft has the ability to develop hypertrophy when subjected to mechanical loading [27,28,29]. Although, hypertrophy has been noted by many authors, it has not often been quantified. In those studies that have addressed measurement of hypertrophy, the variation in methods used precludes direct comparisons. For example, some authors merely measure the amount in mm or cm [15,26,30] whereas others only comment on its presence or absence or give no method of calculation [8,16,28] and few have adopted a scientific approach [11,25].

De Boer et al. [11] introduced a graft hypertrophy index which equals $\frac{G2}{R2} - \frac{G1}{R1}$ divided by $G1R1$. $G1$ is the graft diameter at the proximal junction at operation. $R1$ is the host bone diameter at the proximal junction. $G2$ is the graft diameter at the proximal junction at the most recent follow-up and $R2$ is the host bone diameter at the proximal junction at the most recent follow-up. A positive index value confirms hypertrophy. However, Amr et al. [31] stated that this hypertrophy index is unreliable because this index is a measure of fibular hypertrophy in relation to recipient bone. False results are obtained when callus formation at the recipient bone is more abundant at the proximal end of the fibula. In addition; hypertrophy of the fibula is not homogenous at both upper and lower ends of the graft. Falder et al. [19] measured hypertrophy and expressed it as a percentage of the difference between ‘original fibula width’ and ‘final fibula width’. Following the same calculation of Falder et al. [19] in the present study, median percentage of hypertrophy was 91%. However, direct comparison with the present study was impossible because their study included only free fibular transfer and included upper and lower limb cases and tumor and non tumor cases. Also; there are variations in follow-up period.

De Boer and associates proposed three different entities of hypertrophy: periosteal (bone formation around the graft), endosteal (the cortex and medullary canal have increased in diameter) and a mixture of the two [11]. However, their studies to calculate hypertrophy did not look at measurement of these separate entities. While it would be possible to expect the new bone formed during hypertrophy to originate both from the periostem and endostem, it was impossible in the present study to measure the endosteal diameter of the fibulae consistently with any accuracy, particularly in cases which had been followed up for longer than 4 years, due to the dense appearance of the hypertrophied bone.
It is well known that hypertrophy occurs more common when the limb is mechanically loaded. On the other hand, stress deprivation may result in failure of hypertrophy [32]. We have no cases of failure of hypertrophy, however, delayed hypertrophy (>18 ms) was seen in one case who had internal fixation due to stress shielding. We found that external fixation by plaster cast allows for direct and continuous load-bearing and it is well tolerated at the same time by most patients.

The amount of hypertrophy has been found to increase with time since surgery in the present study and exceeded the diameter of the recipient bone for the whole length of the fibula bone in 18.7% of cases. Fujimaki and Suda [28] found in their experimental study that hypertrophy does not exceed the size of the recipient bone and they believed that the size of the recipient bone was an influential factor in the amount of hypertrophy. However, we believe and agree with Falder et al. [19], that the load bearing is the main factor to the amount of hypertrophy and not the size of the recipient bone.

Falder et al. [19] found that there is no correlation between age and degree of hypertrophy. In the present study, hypertrophy was evident in all our age groups but, the time of development of significant hypertrophy was noted to be shorter in younger patients. This may be related to continuous walking of younger patients. This exposes the fibula to continuous mechanical stresses which is the main factor of development of hypertrophy.

The achievement of rapid union between the vascularized graft and the recipient bone and the development of hypertrophy, which is not the case with the use of allografts and non-vascularized bone grafts, contributes to the stability of the limb and the achievement of good functional results. The average functional result in the present study was 87%. This is nearly comparable to other studies [11,16,17,26]. We had one case of stress fracture in early hypertrophied bone. The mechanical properties of the hypertrophied bone are not known [33]. However, care should be taken during walking and adequate support of the fibula is required until sufficient hypertrophy occurs to allow safe full weight bearing.

The main disadvantage of distal tibia reconstruction in the present study is ankle arthodesis and little shortening of the affected limb; however this was well tolerated by all patients without major disabilities. Endoprosthetic replacement of the distal tibia has the potential advantage of immediate stability and rapid restoration of ankle function; however, there have been few publications for endoprosthetic replacement of the distal tibia after tumor resection with a few numbers of patients. The reported complications are infection, inadequate soft tissue coverage, and talar collapse [5,6].

Achieving stability after fibular transposition is the key to facilitating union. Zaki et al. [34] state that fixation with a long plate and several screws is better than minimal osteosynthesis, however Ebied et al. [8] in their series recommended fixation with screws, K-wires or circulage wires and externally fix the limb in a plaster cast. This method of fixation was also used in nearly most of the cases in the present study (87.5%). The main disadvantage of this method is the resulting slight angulation at the flap junctions either proximally or distally, however, this was compensated by excessive periosteal reaction opposite the affected angle. Two patients (12.5%) in the present study were fixed with plate and screws upon their request. Despite stress shielding, their fibulae developed hypertrophy however this was delayed in comparison with the rest of cases. Still, we recommend simple fixation with screw or wires and plaster cast as internal plate fixation causes delays the onset of hypertrophy.

The reported late donor site morbidity [35-37], associated with free fibular flap transfer as motor weakness and flexion contracture of the toes have a low prevalence in the present study. This may be due to leaving the muscles originating from the transferred fibula unreleased. Early in the study; we had one case of lateral popliteal nerve palsy. The possibility of over
traction to the nerve may be the cause. That is why we preferred later in the study to expose and protect the lateral popliteal nerve through a separate lateral small incision over the head of the fibula.

**Conclusion:**

Long term follow-up of pedicled vascularized fibula in reconstruction of bony defects of the middle or distal tibia after bone tumor resection showed that it is a useful tool in the limb salvage procedure. It is a short procedure, inexpensive, with low rate of late complications. It has a good outcome regarding the union, hypertrophy and the functional outcome.

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