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Intercalary Femur and Tibia Segmental Allografts Provide an Acceptable Alternative in Reconstructing Tumor Resections

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Intercalary femur and tibia segmental allografts were implanted in 59 consecutive patients after segmental resection—52 for malignant and seven for benign aggressive bone tumors. The patients were followed up for an average of 5 years. Allograft survival was determined with the Kaplan–Meier method. Infection, fracture, and nonunion rates were determined. The overall 5-year survivorship for the 59 intercalary allografts was 79%, and we found no significant differences between allograft survival in patients receiving or not receiving adjuvant chemotherapy. Infection and fracture rates were 5% and 7% respectively. From 118 host-donor junctions, 11 did not initially heal (9%). The nonunion rate (10 of 69 osteotomies) for diaphyseal junctions was higher than the rate (one of 49 osteotomies) for metaphyseal junctions. Although some patients required reoperations because of allograft complications, it seems that the use of intercalary allograft clearly has a place in the reconstruction of a segmental defect created by the resection of a tumor in the diaphyseal and /or metaphyseal portion of the femur or tibia.

Currently, most patients with malignant bone tumors are treated with limb salvage surgery. Early diagnosis, accurate preoperative staging, and advanced chemotherapy have greatly improved patients‘ survival and indications for limb preservation.

Because of more accurate imaging techniques, many tumors compromising the metadiaphyseal region of long bones currently may be treated with epiphyseal preservation. These tumor resections originate segmental bone defects that can be reconstructed using massive bone allografts. Intercalary segmental allografts provide initial biomechanical stability of the limb, allowing immediate adjacent joints function. Different allograft sizes and lengths are available, and after healing of host–donor junctions, they may be incorporated progressively by the host. However, an adverse effect of chemotherapy in bone healing has been reported,[9,15] and clinical studies have shown a variable incidence of infection (range, 6–30%) fracture (range 9–19%) and nonunion (range, 17–63%).[5,7,8,12–14,23]

The purpose of this study was to analyze survivorship of intercalary femur and tibia segmental allografts in patients with and without chemotherapy and to determine the incidence of deep infection, fracture, and nonunion compared to the internal fixation.

MATERIALS AND METHODS

Between February 1980 and May 2001, 131 intercalary allografts were done at our institution. Those intercalary allografts including a joint arthrodesis, reconstructions of the upper extremity, or only a portion of the circumference of the cortex (hemicylindrical grafts) were excluded from the analysis. The study group included 59 consecutive patients who had a whole cylindrical intercalary femur or tibia segmental allograft reconstruction, and who were followed up for an average of 5 years, with a range between 2 and 22 years. The mean age of the 35 female and 24 male patients was 28 years (range, 4–66 years). The original diagnoses included 52 malignant tumors (26 osteosarcomas, seven chondrosarcomas, seven Ewing‘s sarcomas, six malignant fibrous histiocytomas, four metastatic carcinomas, one adamantinoma, and one liposarcoma) and seven benign tumors (four giant cell tumors, one aneurysmal bone cyst, one osteoblastoma, and one chondromyxoid fibroma). Forty transplants were at the femur and 19 were at the tibia (Figs. 1–5), with a total of 118 host-donor junctions. Sixty-nine of these were diaphyseal and 49 were metaphyseal junctions.

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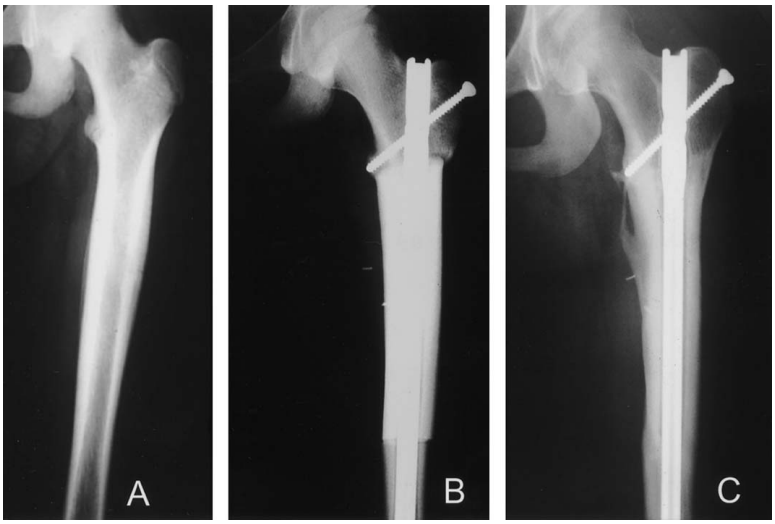

Fig 1A–C. The 9-year radiographic followup shows a 13-year-old girl who had resection of a metaphyseal Ewing's sarcoma of the proximal femur and insertion of an intercalary segmental allograft. (A) The anteroposterior radiograph shows an Ewing's sarcoma of the femur. (B) An anteroposterior radiograph shows the intercalary allograft localized at the proximal femur stabilized with a locked intramedullary nail 2 months after surgery. (C) An anteroposterior radiograph taken 9 years after allograft reconstruction shows incorporation of the graft and healing of both osteotomies.

The surgical procedure began with resection of the lesion, including biopsy scars with appropriate bone and soft tissue margins, and insertion of a fresh deep-frozen allograft segment, sized to fit the bone defect. These nonirradiated allografts were harvested and stored according to a technique that has been described previously.[19] Allografts were selected on the basis of a comparison of radiographs of the patient with those of the donor, to achieve the closest anatomic match. After being thawed in a warm solution, the donor bone was cut to the proper length. All allograft–host junctions were made with a transverse osteotomy. Plates and screws were used for internal fixation in 39 junctions located at the diaphysis, and in 22 in the metaphysis. Intramedullary locked nails were used in 30 diaphyseal and in eight metaphyseal osteotomies. In 19 host-donor junctions, in whom a thin epiphyseal segment was saved, only cancellous screws were used for fixation.

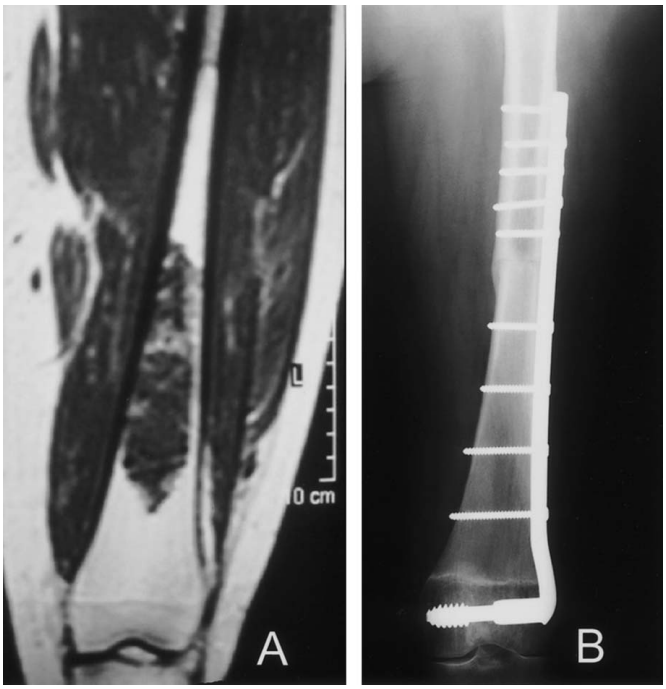

Fig 2A–B. Imaging studies show a metaphyseal intercalary segmental allograft of the distal femur fixed with plate and screws, in a 48-year-old woman who had a resection of a chondrosarcoma. (A) A coronal T1-weighted MRI scan shows the femoral lesion extension. (B) An anteroposterior radiograph of the distal femur intercalary segmental allograft reconstruction fixed with a dynamic condylar screw, obtained at 3 years followup, shows healing of diaphyseal and metaphyseal host-graft junctions.

Antibiotics were given intravenously according to a usual prophylactic protocol, and no routine anticoagulation therapy was used. External splinting was used until the wound had healed. Recently, progressive passive ROM exercises were started 1 week after the operation. Most patients were seen postoperatively at 1 week, 2 weeks, 1 month, 2 months, and 3 months; every 3 months thereafter until 2 years, and then annually. Plain radiographs were taken at every visit, beginning 1 month after the operation.

The clinical records, the postoperative radiographs, and all followup radiographs were reviewed for each patient. Comparable AP and lateral radiographs were chosen for analysis. The method of fixation, the use of adjuvant chemotherapy, the radiographic appearance of the junction, and complications were recorded. The allograft–host junction was considered to be radiographically healed when the junction line no longer was visible or the junction was bridged with periosteal bone on the anteroposterior (AP) and the lateral radiographs.

The allograft survival rate was estimated using the method of Kaplan–Meier.[11] The log-rank test was used to compare the survivorship curves between patients with and without chemotherapy. A p value less than 0.05 was considered significant. The procedure was considered a failure when the allograft was removed either as a revision procedure or amputation. Infection, fracture, and nonunion rates were compared according to the type of internal fixation that was used.

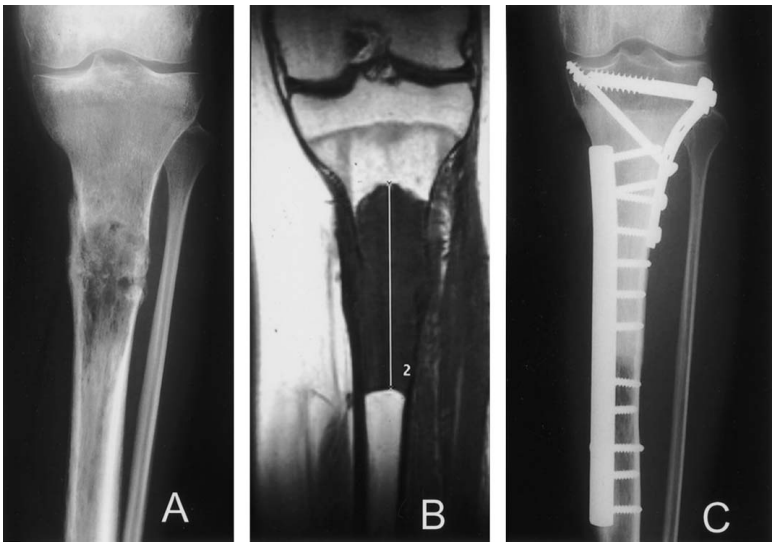

Fig 3A–C. Two-plate fixation in a proximal tibia metaphyseal intercalary segmental allograft in a 14-year-old girl after resection of an osteosarcoma is shown. (A) An anteroposterior radiograph shows the osteosarcoma located at the proximal tibia. (B) A coronal T1-weighted MRI scan taken at the time of surgery shows the tibial lesion with no extension to the epiphysis. (C) An AP radiograph taken 3 years after reconstruction with an intercalary allograft fixed with two plates is shown. The entire length of the allograft is protected with the internal fixation.

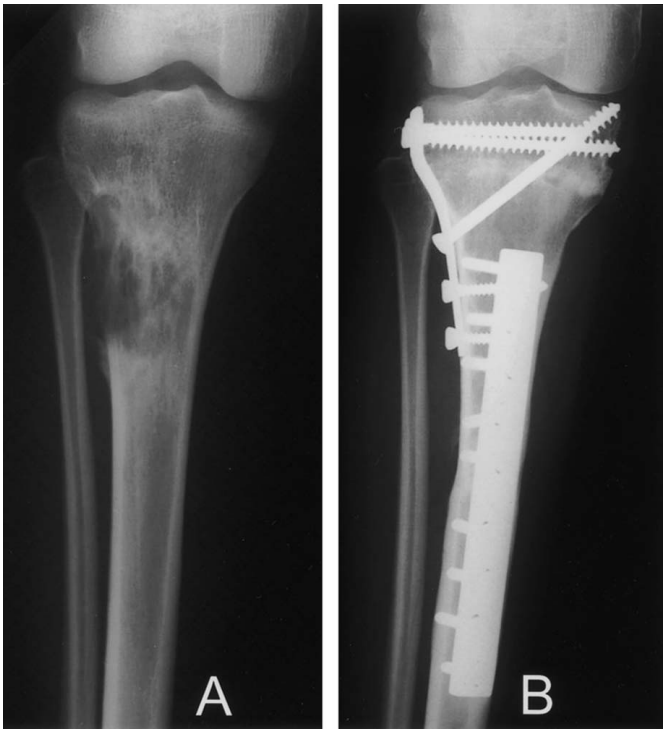

Fig 4A–B. Imaging studies at the 6-year radiographic followup show a 25-year-old woman who was treated with an intercalary segmental allograft after the resection of a fibrosarcoma at the proximal tibia. (A) An AP radiograph shows the affected tibia with a metaphyseal lytic lesion with lateral cortical destruction and soft tissue extension. (B) An AP radiograph shows the allograft reconstruction that was obtained by the 6-year followup. A mature callus can be seen and osteotomy lines are not visible.

RESULTS

The overall survival rate of the 59 intercalary allografts, as calculated with the Kaplan–Meier method, was 79% ± 13% (±2 SE) at 5 years, and there was no significant difference between allograft survivorship in 35 patients treated with chemotherapy [67% ± 21% (±2 SE)] and in 24 patients without adjuvant therapy [91% ± 12% (±2 SE)] ($p = 0.15$). Of the 52 patients who had malignant tumors, five died of pulmonary metastases, 41 patients were continuously disease free, and six patients had no evidence of disease after resection of a local recurrence.

Complications that required a second surgical procedure were recorded for 22 patients including six local recurrences, three deep infections, four fractures, and nine nonunions. In nine of these 22 patients, the allograft needed to be removed, and the patients were considered to have failed results.

Of the six local recurrences, three were localized in the soft tissue and were resected with wide margins (three patients), one was resected with the allograft and reconstructed with an osteoarticular allograft (one patient), and the remaining two patients had an amputation.

Three patients had an acute deep infection develop (5%), one graft was saved with antibiotic treatment and several debridements, and the remaining two were removed and a temporary cement spacer with antibiotics was implanted in each patient. After 6 weeks of intravenous antibiotics and another 6 weeks of oral antibiotics, an intercalary allograft was reimplanted in one patient. The other patient with a cement spacer died of pulmonary metastases without a second reconstruction.

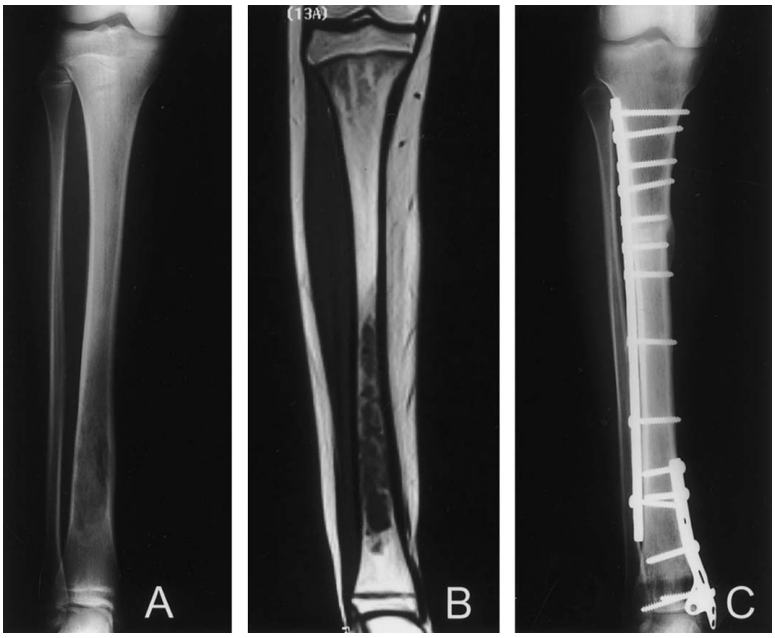

Fig 5A–C. Two-plate fixation in a metadiaphyseal distal tibia intercalary allograft is shown in a 13-year-old-girl who had resection of an osteosarcoma. (A) An AP radiograph shows a lytic lesion without cortical disruption. (B) A T1-weighted coronal MRI scan shows the bone lesion extension in the distal tibia without soft tissue extension. (C) An AP radiograph taken 3 years after reconstruction shows the host-graft unions with mature callus, and preservation of the distal epiphysis.

The fracture rate was 7% (four of 59). All fractures occurred at the distal femur metaphysis and were related with areas of the allograft not covered by the internal fixation. Two of these fractured allografts initially were fixed with plates and two with an intramedullary nail. In all of these patients, the allograft needed to be removed and the patients were considered to have failed results. Three patients had reconstruction with a retransplant, two had another intercalary graft, and one had conversion to an osteoarticular allograft. The remaining patient with a fracture had salvage with an endoprostheses.

Nine patients had a nonunion develop, two at both osteotomies and seven at one osteotomy. These nine patients received preoperative chemotherapy and four received adjuvant radiotherapy. Although they required a second surgical procedure such as replating, autograft addition, or nail dynamization, none was associated with failure of the allograft. Eleven of 118 host–donor junctions did not initially heal (9%). For diaphyseal junctions, the nonunion rate (10 of 69) was higher ($p = 0.04$) than the rate (one of 49) for metaphyseal junctions (15% vs 2%). The nonunion rate for diaphyseal junctions fixed with nails was 22% (seven of 30), and for those fixed with plates and screws, was 8% (three of 39). With the size of the samples, differences were not statistically significant ($p = 0.1$) (Table 1).

DISCUSSION

Segmental femur or tibia bone loses caused by tumor resection can be reconstructed with different techniques. These methods include insertion of metal implants, autogenous bone grafts, distraction osteogenesis, or massive bone allografts.[1,4,6,10–13,18,21] Intercalary segmental allografts can be fixed to small epiphyseal host fragments, obtaining immediate limb stability and allowing active adjacent joint motion (Figs 3–5). After healing of both osteotomies, allografts may be incorporated progressively by the host.[16,17] However, an adverse effect of chemotherapy on bone healing has been reported,[9,15] and clinical studies have shown a variable incidence of infection, fracture, and nonunion.[5,7,8,12–14,23]

We did this study to determine the survivorship of intercalary segmental allograft in patients receiving or not receiving adjuvant chemotherapy and the incidence of deep infections, fractures, and nonunions that occurred with the internal fixation that was used. To evaluate a more homogenous population, we included only segmen-

TABLE 1. Analysis of Nonunion Rates in 118 Host–Donor Junctions in Relation with the Type of Internal Fixation That Was Used

Host–Donor Junction Site and Type of Internal Fixation	Number of Nonunions
Diaphysis (n = 69)	10 (15%)
Plate and screws (n = 39)	3 (8%)
Intramedullary nail (n = 30)	7 (22%)
Metaphysis (n = 49)	1 (2%)
Plate and screws (n = 22)	0
Intramedullary nail (n = 8)	1 (12%)
Cancellous screws (n = 19)	0

tal allografts located at the femur or tibia, excluding joint intercalary allograft arthrodesis and grafts located at the upper extremity. Some potential uncontrolled variables of this study are the amount of soft tissue resection, extension of internal fixation, amount of compression at the host–donor junction, and anatomic allograft fitting.

Previous clinical studies have shown that allografts can survive for decades.[13,16] A long-term followup study had five femur allografts followed in patients for 22 to 36 years.[16] Another study from the same institution had a 5-year survival rate of 73% in 118 knee osteoarticular allografts.[17] Mankin et al[13] reported a survival rate of 76% among 718 patients who had allograft reconstruction. This last study included 163 intercalary allografts that had better results (84%) than osteoarticular allografts (73%) or allograft prostheses (77%). The current study results are consistent with others, showing an overall survival rate of 79% at 5 years.

Some investigators suggest that allografts failures mostly are related to local recurrences, allograft infections, fractures, and nonunions.[2,3,5,7–9,12–15,22,23] The frequency of infection in the overall series of massive allografts reported in the literature ranged from 6–30%.[7,8] There are two extensive series analyzing infections in intercalary allograft reconstructions. One, from one institution with extensive experience in massive bone allografts, had a 12% incidence of infection in 104 allografts.[18] The other, a multicenter study done by the European Musculoskeletal Oncology Society, had a 14% incidence of infection in 113 patients who had reconstruction with an allograft, as intercalary diaphyseal arthrodesis.[5] In the current study, the incidence of infection for segmental tibia or femur intercalary allografts was 5%. This lower rate of infection may be related to a limited amount of surgical exposure done in segmental resections that did not involve the joint, capsule, or ligaments.

There is evidence that one of the major complications that causes bone allograft failure is fracture of the graft.[2,13,18,19,22] The reported prevalence of such fractures has ranged from 9–19%.[2,3,5,15,20,22,23] A higher incidence of allograft fracture also was reported in relation to screw holes, suggesting that allografts are very sensitive to stress-concentrating defects.[22,23] Vander Griend,[23] from 183 allograft–host junctions fixed with plates or nails, reported that plate fixation was associated with a higher rate of fracture of the allograft. The incidence of fracture in our series was 7%, and we found no significant association between fracture and the use of a plate. It has been suggested that the risk of fracture may be diminished by spanning the entire allograft with a long plate to provide extracortical support.[22,23] In our study, all four fractures were located at the distal femur metaphysis and were related to areas not covered by the internal fixation (Figs 3,4).

Hornicek et al[9] suggested that in patients who receive chemotherapy, the incidence of allograft–host junction nonunion is considered to be higher than in patients who do not receive adjuvant therapy. In the current study, a significant association between allograft-host junction nonunion and adjuvant therapy was evident. However, survival rates of segmental allografts in patients with or without chemotherapy were compared and differences were not significant, because none of the patients with a nonunion had an allograft failure.

Other studies that analyzed the effect of internal fixation on healing of large allografts, showed a significant association between achieving stable fixation and development of a nonunion, but no significant differences were found between the rate of union after fixation with a plate and after intramedullary fixation.[23] In our study, patients having plate fixation had lower number of nonunions. However, possibly because of the sample size, the differences between the nonunion rates for diaphyseal junctions fixed with nails (22%) compared with those fixed with plates (8%) were not significant (Figs 3–5).

Most benign, benign-aggressive, and malignant tumors located at the metadiaphyseal region of long bones currently are treated with a segmental resection. Reconstruction of these segmental defects should restore a functional and durable limb, because life expectancy for many of these patients is several decades. Results from this series of patients suggest that segmental allograft reconstruction is an alternative. However, future advances to facilitate allograft host bone fixation and incorporation are needed to obtain more predictable results.

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