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The outcome of fresh frozen allografts in bone healing: a prospective study, in a tertiary care centre, India

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ABSTRACT

Background: Massive bone loss is a major problem in modern orthopaedics. Allograft use in clinical practice has become a desirable option. Allografts are used to reconstruct bony defects in different disorders in orthopaedic surgeries. Fresh frozen allograft is a reconstructive biologic option for osseous defects. This article evaluates the outcome of fresh frozen allografts in bone healing in different orthopaedic procedures.
Methods: Prospective non-randomized trial was conducted in 136 patients of any age presenting to orthopaedic OPD with bone defects/disorders requiring bone grafting in a tertiary care centre. Ann et al radiological criteria for new bone formation, was used for grading outcome.
Results: The age of the patients varied between 12-76 years. About 8.1% patients belonged to 10-25 years age group, 39% to 26-40 years, 25% to 41-50 years, 15.4% to 51-60 years, 6.6% to 61-70 years and 5.9% to above 70 years age group. Mean age was 39.7 years. There were 61% male and 39% female patients. Minimum follow-up period was 1 month and maximum 4 years. Allografting was performed for 46 fractures with bone loss, 33 fractures with non-union/delayed union, 25 arthroplasties, 13 arthrodeses and 19 tumours. Follow-up results at two months showed that 84.6% had good, 12.5% had fair and 2.9% had bad results.
Conclusions: Allografting is one of the best options available for bone defects, especially in younger patients with a high life expectancy because of its potential durability.

Keywords: Fresh frozen allografts, Bone healing, Outcome, Prospective study

INTRODUCTION

After Bauer described the transplantation of bones stored by refrigeration in 1910, for the first time, there have since been significant advances in fresh frozen allografts.

Massive bone loss is a significant problem in modern Orthopaedics and the reasons for massive bone loss may be multiple, including resection of the tumour, high energy trauma, uncontrolled infections, or prosthetic revisions. Although endoprosthetic reconstruction has improved in recent years, biologic reconstruction is an available alternative option for large-extremity osseous defects. Fresh frozen allograft reconstruction has a long history in orthopaedics and has been used for a long time in such conditions with massive bone loss. A fresh-frozen allograft is a reconstructive biologic option for large-extremity osseous defects that, if there is not a significant complication, are durable for many decades.[1]

Apart from being an acceptable means of disease treatment, allograft tissue use in clinical practice has become a desirable option in many cases. The use of tissue allografts reduces patient morbidity and suffering and spares limbs and lives in many cases.

Fresh frozen allografts reconstruction has many advantages like the possibility of attaching the host

ligaments and muscles to the graft, progressive incorporation by the host and availability for all anatomic sites. Many surgeons have identified various advantages of allografting over autografting.[1] Because it is theoretically unlimited supply, ensures reduction of morbidity associated with harvesting an autograft, proper size and shape of the graft desired for a specific surgery can be possible with an allograft, we can preserve the patient's bone stock for later use if at all, the allograft fails.

Like any other procedures, Fresh frozen allografts reconstruction is also not free of disadvantages, including complications of host-donor junction, joint deterioration and transmission of diseases from donor to host. Techniques used for processing the graft, such as radiation, may affect the graft strength and elastic modulus. Adequate anatomic matching, infection prevention, modern internal fixation, stable soft tissue reconstructions, and accelerated rehabilitation protocols are the methods by which we could improve the outcome of massive allografts reconstruction with.[1]

Allograft bone can be used successfully in a wide array of orthopaedic procedures. Transplantation of fresh frozen bone allografts have been used as a salvage procedure for various bone disorders including elbow fractures, failed knees following total knee arthroplasty, massive osteolytic bone loss in revision total knee arthroplasty, spinal fusion surgeries and lumbar spinal surgeries.[2-9]

Massive deep-frozen bone allografts have been used in patients with bone tumours, fibrous dysplasia of the femur's neck, and revision arthroplasty. Freeze-dried bone allografts, such as cancellous chips and cortico-cancellous chips, have been used in conditions like tumours and fibrous dysplasia, arthroplasty, treatment of pseudarthrosis, fractures, spinal fusion, and in maxillofacial defects. Cancellous blocks have been explicitly used for spinal fusion and demineralised cortical dust mainly in maxillofacial surgery.[10]

The best uses of bone allografts are filling bone cavities, buttressing, and augmenting autograft bone quantity. In revision reconstructive surgery, the bone allograft is used to replace the bone stock in protrusio, acetabular dysplasia, and proximal femoral deficiency. The best and most common indication for bone allograft use in tumour surgery is after curettage or excision of benign lesions. Allografts may be used to reconstruct bony defects after excision of malignant tumours and in the surgical treatment of metastatic disease.[11]

One of the studies on elbow allograft reconstruction has shown that, during the past 20 years, 23 patients had undergone elbow allograft reconstruction and showed variable results and a high complication rate. Ten of 14 patients with elbow allografts observed for an average of 7.5 years reported satisfactory results. Allograft removal was required in six patients: infection in two patients, instability in three patients and resorption in one patient. Three patients with instability had since undergone successful total elbow arthroplasty. Two patients had been observed for less than one year, and another patient died during the study period. Complications occurred in 16 out of 23 patients. They concluded that this operation is not recommended for routine use and is viewed as a salvage procedure. The use of allografts in elbow reconstruction does not preclude subsequent reconstruction with another allograft or fusion. In patients with insufficient bone stock, the allograft re-establishes bone mass to permit an arthrodesis or reconstructive arthroplasty.[2]

Pathophysiological aspects of fresh frozen allografts: Fresh frozen allografts induce bone formation by both osteoinduction and osteoconduction. Osteoinduction is by a protein called BMP which gets inactive with other forms of preservation unlike in freezing. On the other hand, osteoconduction needs a healthy and robust bone matrix that is not provided with preservation methods like irradiation or autoclaving. Freezing of allografts also reduces the immunogenicity significantly.

The present study was attempted to evaluate the outcomes of fresh frozen allografts in bone healing in different orthopaedic procedures.

METHODS

A prospective non-randomised trial was conducted among 136 patients who attended the orthopaedic OPD of Apollo hospital, Jubilee Hills, Hyderabad from January 2001-December 2003 with various bone disorders and requiring allografts.

Selection and exclusion criteria

It included patients of any age presenting to orthopaedic OPD with bone defects/disorders requiring bone graft transplantation (benign tumours, non-union, and revision arthroplasty) and giving consent to undergo bone allograft transplantation were included in the study. Those patients who had a history of immunosuppression, immunodeficiency, steroid therapy, and chronic disorders like malignant tumours were excluded from the study.

Procedure for procurement of bone allograft

Allografts were procured from patients who underwent total joint replacements in total knee and hip replacements and Hemi-replacement arthroplasty for fracture neck of the femur.

All patients are tested for HIV, HBsAg, and HCV preoperatively. Only those patients who are tested negative for these are selected for procurement of allograft from them. Per operatively, a specimen of the bone/ capsule is sent for culture, and only those specimens which were negative for any culture are stored for use. The grafts are used only after three months from the date of procurement

(THE WINDOW PERIOD). Prior consent from the recipient is necessary for the usage of allograft in him/her. Once the bone is procured per-operatively, it is soaked in betadine solution for a minimum of ten minutes and then thoroughly washed with normal saline using a pulse lavage. Then, the cartilage was removed entirely using a nibbler/electric saw, and only bone was finally washed and double packed in a sterile poly-ethylene cover. The double packed cover was placed in a sterile metal container which was sealed and labelled with the date of procurement and placed in a freezer at -30^0 C. When the allograft was to be used, the metal container with the date which was the earliest to be put in the freezer was retrieved and opened in the sterile OT conditions and placed in a bowl of normal saline at room temperature for the bone to be thawed. Then the bone was shaped or made into smaller pieces according to the site where it was placed.

Procedure during surgery

Preoperatively, all the patients were subjected to necessary investigations, including routine blood investigations, radiographs and MRI in tumour patients. The pre-anaesthetic check-up was done to obtain clearance for surgery. Bone allograft transplantation was done in all the included study participants. Postoperatively, the outcome was assessed clinically and radiologically immediately after surgery, at monthly intervals till one year, then once in every six months till four years.

The criterion for grading the results included

Patients were followed up at monthly intervals. Based on Ann et.al radiological criteria for new bone formation, the outcome was graded as good, fair and bad. Good callus formation on radiographs in cases of fractures and non-unions, ability to bear weight without pain, intact prostheses in cases of joint replacements, no recurrence of tumours in cases of tumour resection, and there should be a clinical and radiological joint fusion in cases of arthrodesis.

Ethical clearance

The study protocol was submitted, and ethical clearance was obtained from the institutional ethics committee (IEC). Written informed consent was obtained from all the study participants after explaining the research in their vernacular language. Confidentiality was assured and maintained throughout the research. The participants participated in the study, out of their voluntary will and were free to withdraw from the study if confidentiality was breached.

Statistical analysis

Data collected were entered in Microsoft excel spreadsheet and analysed using excel or epi-info. Descriptive data were expressed as numbers and percentages (Table 1).

RESULTS

Allografting was performed on a total of 136 patients. Age of the patients ranged from a minimum of 12 years to a maximum of 76 years. Out of 136 patients, 11 (8.1%) patients belonged to 10-25 years age group, 53 (39%) to 26-40 years, 34 (25%) to 41-50 years, 21 (15.4%) to 51-60 years, 9 (6.6%) to 61-70 years and 8 (5.9%) to above 70 years age group. Mean age of study participants was 39.7 years. There were 83 (61%) male patients and 53 (39%) female patients (Table 1). Minimum follow up period was one month, and the maximum was four years. Allografting was performed for various surgeries including 46 (33.8%) fractures with bone loss, 33 (24.3%) fractures with non-union or delayed union, 25 (18.4%) total joint replacements, 13 (9.6%) arthrodeses and 19 (13.9%) tumours including aneurysmal bone cyst. Follow-up results at two months after the procedure showed that 115 (84.6%) had good results, 17 (12.5%) had fair and 4 (2.9%) had bad results (Table 1 and Figure 1). A few examples of surgeries involving allografting from our series are shown in the Figures 2-5.

Table 1:Characteristics of study participants, (n=136).

Characteristics	Number	Percentage (%)
Age (years)		
10-25	11	08.1
26-40	53	39.0
41-50	34	25.0
51-60	21	15.4
61-70	09	06.6
>70	08	05.9
Sex		
Male	83	61
Female	53	39
Follow up period (months)		
<6	09	06.6
7-12	38	28.0
13-24	46	33.8
25-36	29	21.3
36-48	14	10.3
Surgeries for which allograft was used		
Fracture with bone loss	46	33.8
Fractures with non/delayed unions	33	24.3
Total joint replacements	25	18.4
Arthrodesis	13	09.6
Tumours	19	13.9
Outcome		
Good	115	84.6
Fair	17	12.5
Bad	04	02.9

Among the four patients with bad results, two patients had compound injuries with bone loss and so, managed by primary allografting. The other two were female patients in whom there was a recurrence of giant cell tumour (GCT)

after allografting. Rest of the cases did not have any complications like infection, rejection or fracture of the graft. All the patients who had good to fair results (132, 97.1% patients), at the end of a two month, follow up, none of them showed any deterioration in subsequent follow-ups. Of these 132 patients, 86 (63.2%) patients had more than six months follow up, eight (5.9%) patients whose good results had a follow-up period of more than one year.

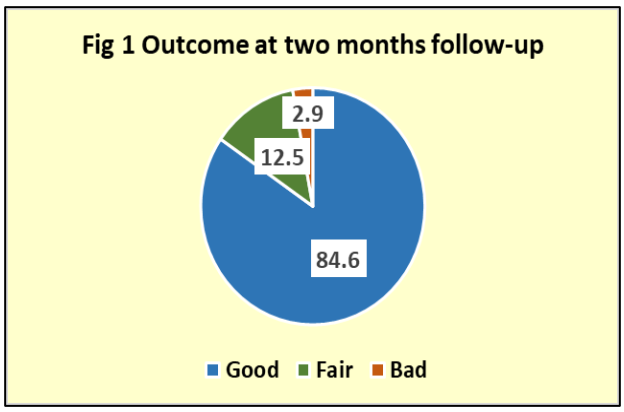

Figure 1: Outcome at two months follow-up.

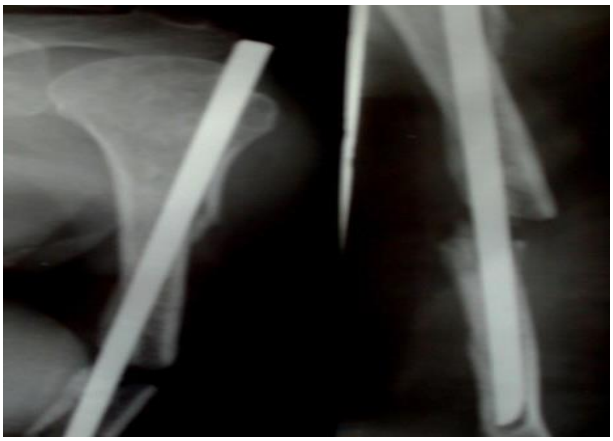

Figure 2: A X-ray of non-union fracture of humeral shaft.

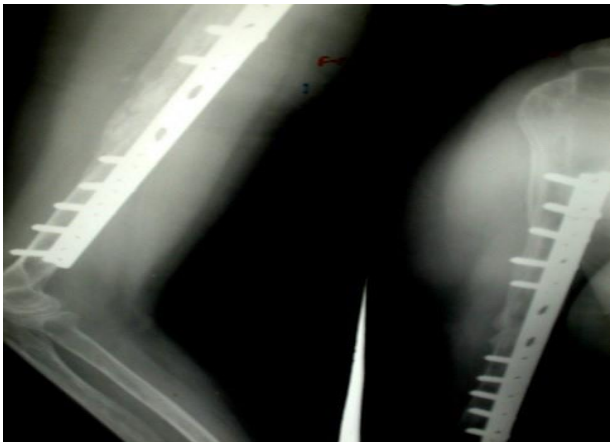

Figure 3: X-ray of good union 2 years after plating and allografting.

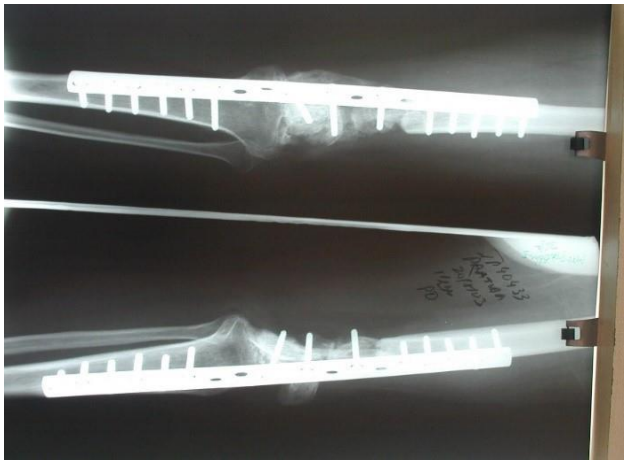

Figure 4: A 18 months post op X-ray of arthrodesis of the knee joint using a long plate and allograft.

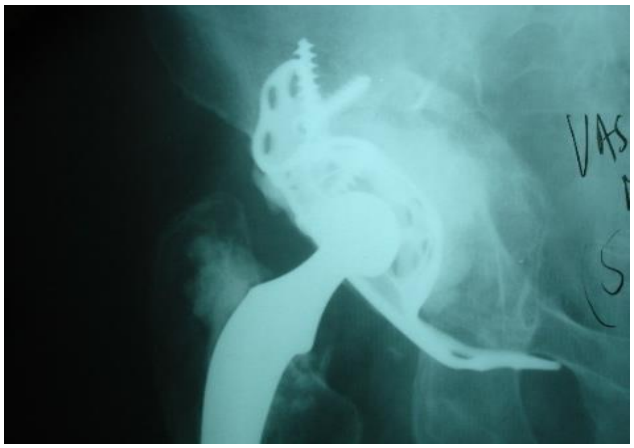

Figure 5: Five months post op X-ray of a revision THR of allograft used to fill in the acetabular defect.

DISCUSSION

Many studies have been conducted on the use of bone allografts in bone disorders or defects. A study conducted by An et al allografts was used for spinal fusion.[8] It was a prospective study in which comparison was made between allograft and autograft in the same individual. The authors compared autografts, frozen allografts, freeze-dried allografts, and a mixture of allograft and autograft in the same patient undergoing an instrumented postero-lateral lumbar spine fusion. The study sample included 20 patients with nine men and 11 women. The minimum age was 29 years, and maximum was 72 years (Range 29-72 years). The mean age was 43.5 years which is consistent with the present study (39.7 years). All the twenty patients were subjected to postero-lateral fusions of the lumbar spine with pedicle screw instrumentation. During the procedure, an autogenous posterior iliac crest bone graft was placed on one side, and an allograft was placed on the other side in each patient. Bone fusion quality was assessed and graded from grades 1 to 4. Grade 1 solid fusion was observed in 16 of 20 cases (80%) on the autograft side while on the other hand, grade 4 resorption

was seen in all seven cases on the freeze-dried grafting side. Resorption of frozen allografts occurred in three of five cases, while partial fusions were achieved in the remaining cases. When a mixture of autograft and freeze-dried allograft was used, grade 1 solid fusion was achieved in four of eight cases, and partial fusions were achieved in the others. On bone densitometry, significantly greater bone density was observed on autograft sites, followed by a mixture of autograft and freeze-dried allograft, frozen allografts, and only freeze-dried allografts in sequential order.[8]

In the present study, follow-up results at two months after the procedure showed that 115 (84.6%) had good results, 17 (12.5%) had fair, and 4 (2.9%) had unsatisfactory results. A study was conducted by van Loon et al to evaluate the clinical and radiographic results of TKA's with morselised and stable femoral bone grafting.[6] From April 1989 to February 1996, 6 primary and 18 revision TKA's with femoral bone grafting was performed in 22 patients. Mean age of patients was 62 years. The diagnosis of 24 knees among 22 patients showed rheumatoid arthritis in 11 knees, osteoarthritis in 10 knees, osteonecrosis in 2 knees and haemophiliac arthropathy in one knee. Twelve had large femoral defects, 9 had medium, 3 had small femoral defects. The femoral bone defects were contained in 10 and uncontained in 14 cases.

For reconstruction impacted morselised fresh frozen trabecular bone grafts were used in 13 knees, stable bone grafts in 7 knees and combined grafts in 4 knees. Twenty-one cases were clinically evaluated at an average of 38 months (range: 9-89 months) using the knee society knee score and average functional score. It was observed that the average Knee society knee score increased by 39 points to 85 points at follow-up. The average functional score increased by 22 points to 48 points. Two cases with stable femoral bone grafts failed due to aseptic loosening. There were no infections. Osteopenia around the femoral component was found in 10 knees on radiographic follow-up. Circumferential radiolucency around the femoral stem was observed in two knees, and minor radiolucency at the anterior part of the femoral component could be detected in 5 knees. Radiographic incorporation was observed in 5 of the 6 cases that could be evaluated. Histologic analysis of two biopsies revealed incorporation of the morselised bone graft. The authors conclude that impacted morselised bone grafting may be used for contained and small-to-medium uncontained femoral bone defects in combination with cemented TKA.[6]

A literature review conducted about allograft bone use in lumbar spine surgery revealed that allograft incorporation is comparatively slower and lesser than autografts. Compared with freeze-dried grafts, fresh-frozen grafts are more potent, more immunogenic and more wholly incorporated. Decreased fusion rates have been observed when allografts are used alone or combined with autografts for posterior lumbar spinal procedures. However, reasonable fusion rates have been observed when allografts are used anteriorly and well-suited for reconstructive procedures, especially if combined with posterior fusions. Thus, allograft bone can be used to produce successful outcomes in lumbar spine surgeries if used appropriately.[9]

Dean et al conducted a studied the long-term results of allograft transplantation for elbow reconstruction.[2] They found that during the past 20 years, 23 patients had undergone elbow allograft reconstruction with variable results and a high complication rate. Satisfactory results were obtained in 10 out of 14 patients treated with elbow allografts and followed up for an average of 7.5 years. Allograft removal was required in six patients: for infection (two), instability (three), and non-union and resorption (one). Three patients with instability had since undergone successful total elbow arthroplasty. Two patients had been observed in less than one year, and another patient died during the study period. Complications occurred in 16 of 23 patients. They concluded that this operation is not recommended for routine use and is viewed as a salvage procedure. Subsequent reconstruction with another allograft or fusion may still be considered or performed despite allografts' usage in elbow reconstruction. The allograft serves to re-establish bone mass for arthrodesis or reconstructive arthroplasty surgeries in those patients who have had a deficiency of bone stock.[2] Thus, similar to the present study, many studies have shown the effectiveness of bone allografts in different bone reconstruction surgeries in orthopaedics.

Limitations

The main limitation of this study was that a uniform review period was not possible in all patients as a few of them were lost to follow up. And, comparison between the sub sects of procedures was not possible.

CONCLUSION

For any kind of surgery that involves bone from minor defects to significant bone loss after tumour resection, the bone allografts can be used. Bone allografts act as a natural substitute to repair skeletal defects. Because there is a significantly less or limited supply of bone autograft, the allografts offer a practical alternative. They also allow structural restoration of the skeleton and their surfaces support bone formation. The fresh-frozen allografts seem to be a better alternative to autografts as the demand for bone grafts increases clinically with improved orthopaedics surgery techniques. Much expertise is not required for preparing the allograft, and it is not a tedious procedure. It can be done regularly in institutions where the joint replacements are done. Strict adherence to aseptic conditions is needed for processing fresh-frozen allografts, which can be practiced even in minimal resource settings. The long-term results are encouraging and could pave the way for broader usage of allografts, bulk allografts and probably cadaveric retrieval of large bony sections to be

used as allografts. Allograft reconstruction is one of the best options available for bone defects, especially in younger patients with high life expectancy because of its potential durability.

Recommendations

More such studies may be conducted in varied population groups to provide better evidence. Multicentric studies in large samples may provide sufficient evidence about the effectiveness of allografting in orthopaedic surgeries. Finally, we conclude with a statement, "With promising results using allografts, "Bone banking at an institutional level is not a far-fetched idea".

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