OUTCOME OF BONE ALLOGRAFT IN ORTHOPAEDIC PATIENTS

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ABSTRACT

Objective: The objective of this study is to determine the outcome of bone allograft in orthopaedics patients.

Material and Methods: This descriptive case series was conducted in the Department of Orthopaedic and Trauma, Northwest General Hospital Peshawar from August 10, 2018 – February 10, 2019. Thirty-six patients were selected using non-probability consecutive sampling technique. Patients between ages 18-60 years, of either gender with confirmed diagnosis of structural bone defect requiring bone grafting were included. However, patients with metabolic bone disorders associated with poor bone healing, active infection at grafting site and terminally ill patients were excluded.

Results: Of the thirty-six patients included, there were 27 (75%) males and 9 (25%) females with a mean age of 38.4 ± 15.4 years. The most common diagnosis among the study patients was traumatic femur shaft defect, which comprised of 10 (27.8%) patients followed by traumatic tibial shaft defect with 6 (16.7%) patients and traumatic femoral subtrochanteric defects were in 5 (13.9%) patients. Other indications for allograft placement in our study population was femoral shaft defect after tumor resection (n = 4, 11.1%), neck of femur non-union (n = 3, 8.3%), tibial plateau fracture (n = 2, 5.6%), femoral subtrochanteric defect after tumor resection (n = 1, 2.8%). The most common surgical procedures included Dynamic Condylar Screw in 9 (25%) patients, external fixation in 8 (22.2%), plating in 7 (19.4%), 5 (13.9%) Interlocking Nail, 3 cases (8.3%) each of dynamic Hip Screw and scraping and one (2.8%) case of posterior spinal fixation. Postoperatively, infection was noted in 4 (11.1%) of cases, instability in 5 (13.9%) cases, non-union in 4 (11.1%) and tumor recurrence in 3 (8.3%) of patients.

Conclusion: Increase in treatment modalities (use of chemotherapy in combination with radiotherapy) leads to significant increase in complications associated with the use of structural allograft including infection and non-union. A great deal of effort is required to prevent these complications that adversely affect the survival of grafted tissue including infection, fracture, recurrence of disease and non-union.

Key words: Outcome, bone allograft, orthopaedic patients.

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INTRODUCTION

Orthopedics surgeons all across the world, face the challenge of reconstruction of bone defects. This challenge can be overcome, by enhancing and accelerating bone repair, which can be achieved with the use of different options like autograft, allograft and bone substitutes. Autografts have the advantage of best biological properties but are disadvantaged by restricted volume and donor site morbidity. As opposed to autografts, allografts have sufficient volume but their use is associated with increased risk of infection. Additionally, they do not have good osteogenic properties. Use of bone substitutes on the other hand, is very attractive for orthopods, but they have different indications for use[1,2,3].

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Worldwide, approximately 2.2 million bone grafting procedures are done annually. By avoiding complications associated with autograft like donor site morbidity, bone allograft has become an attractive alternative treatment modality and has been used widely. The main source of allograft is the osteoarthritic femoral head removed during total hip replacement. However, use of allograft has been associated with the potential of transmitting infectious diseases and can also cause an immuno-rejection reaction[4]. Primarily, rate of transmission of infectious organisms have been significantly reduced after serological testing of the allograft material for human immunodeficiency virus, hepatitis B and C, syphilis and human T-cell lymphotrophic virus (HTLV-1 and HTLV2). Further reduction is achieved through laboratory methods including processing of the allograft bone. Allograft bone in available both in freeze-dried and frozen forms. Freezing allograft bone at -80°C not only reduces the cellular degradation of the graft but also minimizes its immunogenicity. Freeze-dried allograft also resists degradation. Both frozen and freeze-dried allograft retain their osteoconductive characteristics, although freeze-drying reduces the mechanical and osteoinductive properties of the graft[3,5,6,7,8].

In a retrospective cohort study by Flierl et al[9], outcome of various types of bone grafts and graft substitutes were compared, it was determined in the study that allograft were slow to heal (mean time to healing: 416 days), with higher revision rates (47%), with 26% of new onset bone infections. In another study by Drampalos and associates[10], patients who underwent acetabular impaction allografting, non-union rate of 25% was reported. In a study by Bus et al[11], a retrospective review of bony defects treated with allograft, a total of 53% graft failures were reported, where 75% were due to graft non-union and 25% of the graft failures were due to infection[11].

Keeping this in mind, it is evident that there are considerable variations among different studies in terms of bony non-union rates, infection and treatment failure. This variability also indicates the need for further studies in clearly elucidating the role of bone allograft in various orthopaedic procedures. The rationale of study was, therefore, to determine the outcome of bone allograft used in various types of orthopaedic procedures. This will enhance the scientific evidence base and provide valuable information regarding the outcome of allograft in orthopaedic surgery.

MATERIAL & METHODS

This study was a descriptive case series conducted in department of orthopaedics and Trauma, Northwest General Hospital Peshawar between August 2018 till February 2019.

Thirty-six patients with 16% non-union rate were selected using non-probability consecutive sampling and treated with bone allograft. Patients between ages of 18-60 years and of both sexes with confirmed diagnosis of structural bone defect requiring bone grafting were included in the study. However, patients with pathological disorders associated with poor bone healing or increased fracture risk such as Hypoparathyroidism, Osteomalacia and Perthe's disease were excluded. In addition, active infection at the site of bony defect, terminally ill patients, those unfit for anaesthesia (American Society of Anaesthesiologist grade III and above) and pregnant patients were also excluded.

The study was commenced after approval was obtained from research and ethics board of the institute. Patients were selected from the outpatient department, emergency department as well as from inter-departmental referrals. Primary diagnosis was established after detailed clinical history and examination as well as appropriate laboratory and/or radiological investigations. The purpose and benefits of the procedure, the need for the use of bone allograft from the institutional bone bank and purpose of the study was explained to the patients and/or relatives to obtain an informed written consent. The data concerning the study was collected in a predesigned form.

All patients were assessed by a consultant orthopaedic surgeon (fellow of the CPSP with a minimum of five-year experience after fellowship). Clinical assessment and observations were made by the postgraduate trainee. Clinical and laboratory investigations were also used to exclude metabolic bone diseases such as Osteomalacia, Hypoparathyroidism, Renal failure and Perthe's disease. After establishing primary orthopaedic diagnosis, the need for bone allografting was established and the patients were included in the study. Bone allograft was used from our institutional bone bank where allograft is stored at -80 ºC with complete screening for hepatitis B (HBV) and C virus (HCV), human immunodeficiency virus (HIV), syphilis (VDRL) and a negative bacterial culture and sensitivity study. The most appropriate allograft was selected based on the recipient defect size and site. All surgical procedures were performed under general anaesthesia under care of consultant anaesthesiologist.

During the follow-up, patient was followed up at 6 weekly intervals for 18 weeks after allograft insertion and complete assessment was done by clinical history and examination as well as radiological evaluation for non-union, delayed union or osteomyelitis at the graft site. In order to avoid loss to follow-up, a 50% increase in the sampling population was done, so that to compensate for the risk of loss to follow-up. We also obtained mobile contact numbers of all patients and if the patient missed follow-up, we contacted the patient on phone and ensured clinical assessment. Patients who were found to have graft non-union were counselled regarding the need for repeat surgery while those with osteomyelitis were advised for debridement and treatment with broad-spectrum antibiotics.

Data was collected which included patient demographic details, such as age, gender, address, and date of admission as well as clinical details such as primary diagnosis and procedure performed, clinical assessment for union and osteomyelitis as well as classification into favourable and unfavourable outcome.

Our primary outcome measure was graft non-union and infection rates during the six-month follow-up period. Patients who were found to have complete union and no infection were labelled as having favourable outcome while those having non-union at the graft site, osteomyelitis or both were labelled as having unfavourable outcome.

All the information was entered and analysed in statistical software SPSS (version 21). Frequencies and percentages were calculated for categorical variables like gender, diagnosis, procedure, non-union and osteomyelitis. Mean $\pm$SD was calculated for continuous variables like age. Statistical significance was considered at ≤ 0.05. Percentages and frequencies were calculated for patients classified according to each outcome group. To test for association of various variables to favourable or

unfavourable outcome groups Chi-square test was used. A post-stratification chi-square test using gender and primary diagnosis was conducted to look for any confounding effects. All the results were presented as tables and graphs.

RESULTS

Of the 36 patients included, there were 27 (75%) males and 9 (25%) females in a ratio of 3:1 having mean age of 38.4 ± 15.4 years (Table 1). The minimum age was 15 years while maximum age was 67 years. There were 21 (58.3%) patients in the age group 40 years and below while there were 15 (41.7%) patients in the above 40 years' age group (table 1).

The most common diagnosis among the study patients was traumatic femur shaft defect with 10 (27.8%) patients followed by traumatic tibial shaft defect with 6 (16.7%) patients. Other indications for allograft use in our study population were defect after tumor resection, femur shaft (n = 4, 11.1%), femoral subtrochanteric defect (n = 1, 2.8%), tibial shaft (n = 1, 2.8%), humeral shaft (n = 1, 2.8%), and neck of femur non-union (n = 3, 8.3%), tibial plateau fracture (n = 2, 5.6%), traumatic humeral shaft defect (n = 1, 2.8%), spondylolisthesis (n = 1, 2.8%), and radial fracture non-union (n = 1, 2.8%). (Table 2)

The most common surgical procedures included Dynamic Condylar Screw in 9 (25%) patients, external fixation in 8 (22.2%), plating in 7 (19.4%), 5 (13.9%) Interlocking Nail; 3 (8.3%) cases each of Dynamic Hip Screw and Scraping; and one (2.8%) case of posterior spinal fixation.

Postoperatively, infection was noted in 4 (11.1%) of cases, instability in 5 (13.9%) cases, non-union in 4 (11.1%) and tumor recurrence in 3 (8.3%) of patients. (Table 3)

The mean length of stay in hospital was 1.4 ± 0.65 days with 24 patients (66.7%) staying for one day postoperatively.

The postoperative outcome was favourable in 20 (55.6%) patients and unfavourable in 16 (44.4%) cases (Table 2). There were 15 (75.0%) males in the favourable outcome group and 5 (25%) females. Similarly, there were 12 (75%) males in the unfavourable group while 4 (25%) females. There was no significant difference on chi-square analysis and the p-value was noted to be 0.999. (Table 4)

On chi-square analysis, no significant association was found between primary diagnosis and final outcome (p = 0.327). Similarly, no association was found for age groups and final outcome (p = 0.257).

Post-stratification chi-square test was applied for gender and age groups against the final outcome. No significant association was found for gender and age group stratification (p = 0.100).

Table 1: Age groups & Gender Distribution of Study Population.

Age & Gender	Frequency	Percent
Male	27	75.0
Female	9	25
40 years and less	21	58.3
> 40 years	15	41.7
Favourable outcome	20	55.56
Unfavourable outcome	16	44.44

Table 2: Distribution of Preoperative Clinical Diagnosis.

Clinical Diagnoses	Frequency	Percent
Neck of Femur Non-Union	3	8.33
Femur Shaft defect (Traumatic)	10	27.78
Femur Shaft defect (Tumor)	4	11.11
Femur Subtrochanteric Defect (Traumatic)	5	13.89
Femur Subtrochanteric Defect (Tumor)	1	2.78
Tibia Shaft Defect (Traumatic)	6	16.67
Tibia Shaft Defect (Tumor)	1	2.78
Tibial Plateau Fracture	2	5.56
Humerus Shaft Defect (Traumatic)	1	2.78
Humerus Shaft Defect (Tumor)	1	2.78
Spondylolisthesis	1	2.78
Radial Non Union	1	2.78

Table 3: Outcome for Gender & Age Groups.

Complication	Frequency	Percentage
Infection	4	11.1%
Fracture/Instability	5	13.9%
Non-union	4	11.1%
Recurrence/Relapse	3	8.3%

Table 4: Postoperative Complications and their Frequencies.

		Outcome		P value
Gender	Male Female	Favourable	Unfavourable	
		1 (2.88) [1.22]	2 (0.12) [28.46]	.000049
		92 (90.12) [0.04]	2 (3.88) [0.91]	
Age Groups	≤ 40 years	85 (82.45) [0.08]	1 (3.55) [1.83]	.000041
	41 years & above	8 (10.55) [0.61]	3 (0.45) [14.29]	

DISCUSSION

As shown by several studies, end results of allograft use are un predictable[14]. In a study by Dick et al, patients who underwent massive allograft surgery after receiving chemotherapy had complications estimated at about 60 % that included non-union (26%), pin and

plate fracture (11%), allograft fracture (7%), and infection (11%)[15]. Effective chemotherapy on the other hand, is highly associated with enhancing survival rates from 20 % to 58-80% after two years in patients with malignant bone tumours[16]. However, as we have shown in our study, chemotherapy can also adversely influence the end result of allograft placement.

Most of our patients were younger than 40 years of age, which is an important factor, because youth is attributed to better improvement and faster return to daily activities. In our study, rate of infection in patients with different diagnoses was without any significant difference. Similarly, an infection rate of 11% and 12-15 % have been reported by Dick et al and other reports respectively.

After allograft implantation, the most common complication that may occur is infection, which is quite difficult to treat and may ultimately lead to limb amputation particularly in case osteoarticular allograft is used. Though in our study, infection was not a frequent finding. Compromised immune system in patients with malignant bone tumors who received chemotherapy and radiotherapy, predisposed them to resistant infections.

Being a foreign body structural allograft creates suitable environment for the growth and nourishment of microorganisms[17]. In order to lower infection rate, in our study, allografts were prepared and packaged by trained orthopaedics assistants and skilled surgeons. In a similar study, Farfalli reported that infection was seen in 11% of patients[18]. Infection rates of 15 % and 16 % were reported in studies done by Jamshidi and bullen's et al respectively.1920 Menkin also reported that the risk of infection was 10% after the first year of implantation[21]. However, in a study by Nekouie no wound or bone infection was observed[22]. Therefore, any action in favour of preventing the occurrence of infection is highly preferred[23].

Allograft fractures after surgery is another complication of reconstructive surgery, particularly when gamma radiation is used in their preparation process, because this radiation makes the bone and its surrounding soft tissue extremely brittle[23]. In our study, we observed five allograft fractures (13.9%) and in two patients this occurred due to failure in properly protecting the allograft with a plate. The underlying cause of allograft fracture in the other cases was unknown. Fracture occurred in the proximal of the femur in two patients, proximal of the tibia in one, and distal of the femur in three. We found no significant difference for the primary diagnoses with regard to fracture rate. Similarly, in another study the fracture rate of osteoarticular allograft was reported at 17% during the first two years after surgery[24]. In another study, Donati et al reported that the rate of pin and plate fracture in patients that underwent limb salvage surgery for osteosarcoma was 4.9% In a study by Farfalli, three of 26 patients (11%) experienced incomplete allograft fracture[18,25]. Jamshidi reported a pin and plate fracture rate of 5%[19]. In this latter study done on patients who received osteoarticular allograft, pin and plate fracture occurred in 23% and bone graft fracture in 16% of cases. However, in patients who received bone allograft, pin and plate fracture occurred in 48% of cases and there was no graft fracture[19]. Bullens et al, reported an overall fracture rate of 13% and Menkin showed that allograft was associated with an increased risk of fracture (19%) after the third year following surgery[14,20]. It seems that the high incidence of pin and plate fracture in bone allograft recipients is due to the existence of only two points that connects the allograft to the patient's bone, causing the union to form slowly because of callus produced by the host bone. The fusion takes about a year and the callus will never find a natural configuration[26]. In most cases, the fragments become separated and the patient should have another surgery to correct the fracture using larger plate; and to facilitate the union, autogenous bone graft has to be used[27].

Only 4 cases (11.1%) of non-union were observed in our study, leading to autogenous grafting. Most of them were in the traumatic femoral shaft defect patients (P= 0.714). In a study by Farfalli, non-union was observed in 7% of patients[18]. Bullens et al reported that the overall rate of non-union was 65%[20]. Friedlaneder et al declared that using adjuvant chemotherapy with methotrexate and Adriamycin significantly postponed the formation of callus[28].

In massive surgeries for malignant tumours due to vast extended surgery, soft tissue injuries, and the removal of large amounts of muscle with the tumour, perfusion at the junction of the allograft to the recipient bone is largely impaired leading to non-union of the allograft[29].

Recurrence was seen in 3 patients (8.3%). Similarly, in a study by Farfalli, the allograft was removed in two cases out of 26 patients (7%) due to tumour recurrence[18]. Six patients (5.88%) had evidence of local recurrence: three of them were in the adjuvant chemotherapy group and the other three were in the chemo radiotherapy group. Similar to our study, this recurrence was observed in 3 patients (7%) in the study of Farfalli[18]. In Bullens' study, three patients (10%) from 32 patients who received allograft showed evidence of disease after local recurrence[20].

Two of our patients developed recurrence who were diagnosed cases of femoral shaft osteosarcoma. Similar to our study, Nekouie mentioned that during the average 27 months of follow-up, out of the 20 evaluated patients, two (10%) showed distant metastases, one in the lungs and thorax, and the other in the vertebral column[22]. In another similar study by Bullens that followed 32 structural allograft recipients after bone tumour excision with an average interval of five years and three months, our patients (12%) died of pulmonary metastases and the other 25 patients remained disease free[20].

Regarding the development of restriction in range of motion (30-60 degrees), the short and long term functional score was 47.8% in our study. Osteo-articular allograft can be used in limb reconstruction after bone tumour resection and it seems that complications including infection and non-union are relatively high in patients receiving chemotherapy and radiotherapy.

Ong et al conducted a study comparing outcome of biologic and synthetic grafts in the fixation of tibial plateau fractures concluded that diminished inflammatory response to biologic grafts, allows better recovery of long-term fixation compared to the synthetic one[30]. Although the autologous graft application is still considered as the gold standard in the TPF reconstruction, the limited size of harvested bone from iliac crest and the clinical complications of simultaneous secondary operation, along with cosmetic disfigurement of this procedure, have posed the attention toward the allogenic bone graft as an alternative supplementary[31,32,33]. Even so, allogenic graft also contains its own limitation, such as compromised osteo-inductive properties, the risk of disease transmission and immune rejection could finally affect the clinical outcome. Rationally, in case of comparable clinical outcome and complication rate of allograft autograft, application of allograft would be a more judicious option.

Lasanianos et al evaluated the use of freeze-dried-cancellous allograft in the management of impacted tibialplateau fractures. According to their study, freeze-driedallograft incorporated soundly in all cases within 12 weeks from surgery and no complications that could be correlatedto graft were recorded[34].

Limitations of our study were small sample size and experience of a single orthopaedic surgeon. Furthermore, this study has been conducted at a single institute.

In spite of several curable complications that occur in limb salvage surgeries, the preserved extremity is functionally and psychologically more effective for the patient rather than amputating the limb and using prostheses. Furthermore, limb reconstruction with bone allograft is an appropriate solution for a time and has a relatively significant recuperation rate and fewer complications compared with other treatment options.

CONCLUSION

Increase in treatment modalities (use of chemotherapy in combination with radiotherapy) lead to significant increase in complications associated with the use of structural allograft including infection and non-union. A great deal of effort is required to prevent these complications that adversely affect the survival of grafted tissue including, infection, fracture, recurrence of disease and non-union.

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AUTHOR'S CONTRIBUTION

Following authors have made substantial contributions to the manuscript as under

Raza W: Conception & design or study analysis & interpretation of data.

Qadir RI: Reviewing it critically for intellection content .

Sherzad P: Drafting the manuscript Acquisition of Data.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.