Retrospective Outcome Analysis of Allogenic Bone Graft

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Abstract
Bone bank has become an essential requirement for centers that perform tumor and reconstructive surgeries. It provides allogenic bone procured from cadavers as well as live donors in the form of surgical residues. Thus, we conducted a retrospective observational study on recipients who underwent various reconstructive procedures using fresh frozen allograft obtained from the live donors through surgical residues in a newly established bone bank. The outcomes of cases operated where allogenic bone grafts were used between January 2018 and November 2020 were analyzed in terms of infection and time taken for the grafts to incorporate, allowing weight-bearing in the lower limbs. A total of 223 grafts were obtained as surgical residues from replacement surgeries and traumatic amputations performed on non-salvageable limbs. Out of these, 70 grafts were transplanted into eligible recipients, who were followed up for at least one year. Among the 70 recipients, 15 were lost to follow-up. The outcome data of the remaining 55 recipients was tabulated, including infections (early, delayed and late) and the achievement of weight-bearing milestones when transplanted in lower limbs. Out of the 55 cases, allografts were used alone in 20 cases, while in 35 cases, they were augmented by implants or cement. Two cases (3.6%) experienced acute infections, and another two cases (3.6%) had chronic infection. The mean time for weight-bearing was found to be 7 months when used alone and 3.5 months when augmented with cement or an implant. Additionally, five patients did not show complete integration of the graft. The results of using allogenic bone graft are quite encouraging, suggesting their potential as biological adjuvants in reconstructive surgeries.

Keywords
- allograft
- bone bank
- outcome analysis
- infection
- graft incorporation

Introduction
Bone forms the strength of the skeletal system. Losing a part of it can disable a person not only physically but also mentally and economically. There have been advances in the replacement of lost bone by metal implants but the option of biological reconstruction if available is always considered superior in a developing country like ours where cost is a major issue. Autologous grafts though are the best biological adjuvants because of the ideal property of osteoconduction, osteoinduction, and osteogenesis, but have its

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limitation of donor site morbidity and limited availability. Allogenic bone due to its osteoconductive property, when transplanted into the recipient, acts as a scaffold for the formation of new bone and provides immediate stability to the void created. It is seen that the bone is not guided by rhesus factor (Rh) or human leukocyte antigen (HLA) compatibility; hence, bone from a healthy human can be transplanted into another human without the risk of rejection that is seen in transplantation of other tissues. The risk and disadvantage of using bone allografts are transmission of potential infection and lack of osteoinductive property but still the advantages far outweigh the disadvantages.

The use of allograft from the bone bank is finding importance in surgeries such as bone tumors, spinal arthrodesis, and pediatric skeletal reconstructions where the amount of bone required outweighs the limited bone available as autografts.

In India, the transplantation of bone as allograft is guided by “The transplantation of human organ and tissue act of 1994,” which was amended in 2014 to “The transplantation of human organs and tissues act 2014.” We had established a bone bank in January 2018 and started procuring surgical residual grafts from the arthroplasty surgeries on no profit basis. Here we audited those recipients who received fresh frozen crushed allograft in terms of incidence of infection and duration of graft incorporation to allow weight bearing when transplanted in lower limbs. Our primary objective was to identify incidence of infection among the cases after reconstruction with allograft. Our secondary objectives were to isolate the organism causing infection in such cases and to note the average weight bearing time after the surgery that would correspond to the graft incorporation time and the functional status of patient after the surgery.

Materials and Methods

We performed a retrospective analysis of the cases who received bone allograft from the period between January 2018 and November 2020. The graft that was procured after taking informed consent was from the surgical residues of arthroplasty and traumatic amputated limbs surgeries. No charges were incurred on the donor as well as recipient for the procured and used graft. Of the total 223 grafts procured till November 2020, 70 were used in the recipients for various indications like tumors, limb and joint reconstructions, and pediatric surgeries. For samples procured from traumatic amputation limbs, a total of six samples were sent from various sites around the procured bone.

The allograft that was removed underwent standard procedure of saline and a small tissue sample was sent for culture, followed by antibiotic wash followed by dipping the sample in absolute alcohol. The donor also underwent preoperative nucleic acid amplification test (NAAT) for various transmittable diseases like human immunodeficiency virus, hepatitis C virus, hepatitis B surface antigen, malarial parasite, and tests for syphilis. The allograft thus procured was kept in deep freezer at −80°C. Once the result of NAAT and cultures were reported to be negative, the tissues were then ready for use in the recipients.

At the time of transplantation, the graft was thawed at room temperature. It was then washed in a standard fashion with saline and antibiotic solution. The cartilage over the graft was removed and the bone was used. All the patients of transplantation were followed for one year and the outcome was recorded as infections (acute and chronic) and mean time of weight bearing when done in lower limbs.

The diagnosis of infection was made on the basis of Centers for Disease Control and Prevention criterion for organ surgical site infection. The infections were further classified into early, delayed, and late. Early infection was considered when culture positive discharge was found within 2 weeks of surgery, delayed infection when there was culture positive discharge after 2 weeks, and late infections were culture positive discharge after 10 weeks of surgery. But for our understanding we classified early and delayed infections as acute and late infection as chronic infections.

The duration at which the patient was allowed to bear weight on the lower limb was also documented based on clinical and radiological healing of the graft in the lower limb. Clinical grading into excellent, good, fair, and poor was made at 6 months and one year.

Results

Of the 70 recipients, 40 were males (57.14%) and 30 were females (42.86%). All the donors were NAAT negative and there was no growth reported on culture from the sample taken from the donor tissue. Out of 70 recipients, 31(44.28%) were of various musculoskeletal tumors, 35(50%) were of the limb and joint reconstructive surgeries, and four (5.71%) patients were of pediatric indications (Table 1). Of them 15 were lost to follow-up. Of the 55 cases, in 20 cases the allograft was used alone and in 35 cases allograft was supplemented with cement and/or implant. Allograft was used in 52 lower limbs and three in upper limb cases. Out of 55 cases, two (3.6%) patients had acute infection, both of which were medically treated. Two (3.6%) patients had chronic infection, both of which were surgically debrided (Table 2). The organism isolated was Staphylococcus aureus (in 3 cases) and Klebsiella (in 1 case) (Table 3). Weight bearing in the transplanted lower limb ranged from 3 month where the allograft was used along with bone cement ± implant to 15 months where the allograft was used alone (Table 4) (Table 5). Five patients did not show complete integration of allograft into the parent bone till the last follow-up and so were not allowed to bear weight on the lower limb (Table 6).

Discussion

Use of bone allograft is a salvageable procedure for various oncological and reconstructive surgeries. Earlier in the past all these bones removed as surgical residues were discarded. But now with the advent of NAAT testing and modern storage devices, we are able to store these bones and use it in the recipients without the risk of rejection due to Rh compatibility. The transplantation performed is in accordance with
Here, in our newly established bone bank a total of 223 graft were procured as surgical residue, of which 70 allografts were used from a period of January 2018 to November 2020. The patients were followed up for one year after surgery. Of the 70 patients, 15 patients were lost to follow-up.

Table 1 Various indications where allograft was used

<table>
<thead>
<tr>
<th>Indication</th>
<th>Number (n = 70)</th>
<th>Number (n = 55) included in study</th>
</tr>
</thead>
<tbody>
<tr>
<td>Musculoskeletal tumors</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Benign</td>
<td>15</td>
<td>10</td>
</tr>
<tr>
<td>Locally aggressive</td>
<td>16</td>
<td>14</td>
</tr>
<tr>
<td>Limb and joint reconstructive surgeries</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nonunion</td>
<td>17</td>
<td>14</td>
</tr>
<tr>
<td>Arthroplasty (hip and knee)</td>
<td>12</td>
<td>10</td>
</tr>
<tr>
<td>Arthrodesis</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Pediatric surgeries</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Musculoskeletal tumor</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>Deformity correction</td>
<td>3</td>
<td>2</td>
</tr>
</tbody>
</table>

Table 2 Incidence of infection in various indications

<table>
<thead>
<tr>
<th>Indications</th>
<th>Number of patients (n = 55)</th>
<th>Acute infection</th>
<th>Chronic infection</th>
</tr>
</thead>
<tbody>
<tr>
<td>Musculoskeletal tumors</td>
<td>24</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Limb and joint reconstructive surgeries</td>
<td>27</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Pediatric surgeries</td>
<td>4</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Table 3 Type of organism growth for various indications and the treatment given

<table>
<thead>
<tr>
<th>Indication</th>
<th>Type of infection</th>
<th>Organism identified</th>
<th>Treatment given</th>
</tr>
</thead>
<tbody>
<tr>
<td>Musculoskeletal tumors</td>
<td>Acute 1 Chronic 0</td>
<td>Staph. aureus 1</td>
<td>IV antibiotics 1 Debridement 0</td>
</tr>
<tr>
<td>Limb and joint reconstruction</td>
<td>Acute 1 Chronic 2</td>
<td>Staph. aureus 2</td>
<td>IV antibiotics 1 Debridement 2</td>
</tr>
<tr>
<td>Pediatric surgeries</td>
<td>Acute 0 Chronic 0</td>
<td>Staph. aureus 0</td>
<td>IV antibiotics 0 Debridement 0</td>
</tr>
</tbody>
</table>

Table 4 Number of lower limb surgeries where allograft was used alone and with augmentation with cement or implant

<table>
<thead>
<tr>
<th>Lower limb surgeries (n = 52)</th>
<th>Allograft used alone in lower limb (n = 20)</th>
<th>Allograft used along with bone cement/implant in lower limb (n = 32)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Musculoskeletal tumors</td>
<td>22</td>
<td>9</td>
</tr>
<tr>
<td>Limb and joint reconstructive surgery</td>
<td>29</td>
<td>10</td>
</tr>
<tr>
<td>Pediatric surgery</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

Table 5 Average time to bear weight (in months) in lower limbs for various indications

<table>
<thead>
<tr>
<th>Indication (n = 52)</th>
<th>Average time to bear weight (months)</th>
<th>Overall average (in months) SD</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Musculoskeletal tumors</td>
<td>Limb and joint reconstruction</td>
</tr>
<tr>
<td>Allograft used alone in lower limbs (n = 20)</td>
<td>6</td>
<td>8</td>
</tr>
<tr>
<td>Allograft supplemented with cement and/or implant in lower limbs (n = 32)</td>
<td>3</td>
<td>4</td>
</tr>
</tbody>
</table>

Abbreviation: SD, standard deviation.
Based on graft recipients, majority were used for the limb and joint reconstructive surgeries followed by various musculoskeletal tumors, pediatric indications. In the study done by Stepanovic and Ristic, the grafting was done for lower limb fracture (36.08%), reconstructive surgery after failed fixation in trauma patients (25.78%), and revision total hip arthroplasty (18.56%). In another series by Man et al, 80% of the allograft were used in arthroplasty procedure, 11% in spinal surgery, and 4% in rest of the surgeries. In another series by Neilson et al, they had used allograft in hip revision (34%), fracture (24%), and nonunion (13%). In another series by Kappe et al, out of 188 cases, 43 cases were of revision cup, 35 cases of one stage revision stem and cup, and 31 cases of anterior lumbar body fusion. In our series, the number of patients underwent allograft surgery was mostly of tumor group, and 18.18% of the patients were from the arthroplasty group. The indication seen in various studies shows usage of allograft in variety of surgeries.

The overall incidence of infection in our series is reported to be 7.2% of which 50% of them were treated by medical management and rest 50% required surgical debridement. In the series of Kappe et al, the overall rate of infection was 6.9%. In the series of Man et al the overall infection rate was 4.6%. In another series by Winter et al the postoperative infection was reported to be 4.9%. In another series by Stepanovic et al, only 2.2% of the cases developed postoperative infection. The overall incidence of higher infection can be attributed to the smaller sample size and long follow-up in comparison to the other series.

The most common organism that was isolated was Staphylococcus which was in three cases out of four. In the series of Kappe et al, the most common organism was Enterococcus faecalis in 4 out of 11 cases and Staphylococcus was found in one of the cases. In the series of Man et al, out of 11 cases had Staphylococcus as main organism. In other series of Neilson et al, out of 7 cases of infection only 2 cases were of gram-positive cocci. In another large series by Stepanovic et al, out of 37 cases of infection, Staphylococcus (coagulase negative, aureus, and epidermidis) was found in 20 cases. In another series that was reported to be as review of 10 years of bone banking in Australia by Winter et al, 50% of the organism isolated were from Staphylococcus series. The infection due to Staphylococcus is mainly due to contamination of the sample handling during procurement or implantation.

In our series, the lower limb surgeries were 52, of which 29 (55.8%) were of limb reconstructive surgeries and 22 were of musculoskeletal tumors. Out of these cases, the graft was used alone in 10 and 9 cases, respectively, and in rest of the cases it was augmented either with implant or bone cement. The average time to bear weight where allograft was used alone was 6 months for musculoskeletal tumors and 8 months for limb reconstructive surgeries. The cases where the allograft was used along with bone cement or metallic implants the average time to bear weight was 3 and 4 months respectively for tumour and limb reconstructive surgeries. In the study by Jajoria and Sural, the average time of consolidation was 5.3 months. In another study by Roudbari et al, 96.6% of the patients had incorporation of graft within 6 months of surgery. The time to bear weight corresponds to the incorporation of allograft with the parent bone to give clinical and radiological opinion for bearing weight on the limb.

In our series, out of 55 cases 6 patients had poor outcome at 6 months that decreased to 4 cases at 12 months. In another series by Jajoria and Sural, there were none with poor results and 50% of the cases did excellent according to Enneking criterion for functional evaluation after allograft surgery. In the study done by Mankin et al, they had 71% results to be satisfactory. Hence, we present a series with large number of cases with a smaller number of failures. The limitation of this study was that 15 cases (21%) of the cases were lost to follow-up.

**Conclusion**

From our study, we conclude that allograft is a viable option for the tumor and reconstructive surgeries in a developing country like ours with the economic constraints of using bone graft substitute. The excellent-to-fair functional outcome in our series is quite encouraging to be used in lower limb surgeries as well. Long-term functional results of these surgeries are encouraging for carrying out further studies.

**Availability of Data and Materials**

All included studies used in this retrospective study are available online. The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request. Data regarding this study is not available in any electronic databases.

**Ethics Approval Statement**

Approval from the institutional ethics committee was obtained. (Letter No- AIIMS/IEC/22/02).
All authors have read the final prepared draft of the manuscript and approved this version, in its current format if considered further for publication.

Authors’ Contribution
V.M. helped in planning of report, literature search, and writing of the manuscript. M.D. contributed to literature search, manuscript preparation, and correspondence. D.S. was involved in quality assessment of the included studies, writing, and revising of the manuscript. A.G. and S.D. wrote and revised the manuscript. A.K. helped in data management, outcome assessment, and revision of the manuscript.

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Conflict of Interest
None declared.

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Consent to Publish

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