INSIGHTS-JOURNAL OF
HEALTH AND REHABILITATION

COMPARISON OF AUTOGENOUS-BONE-GRAFT VS BONE-SUBSTITUTE IN NONUNION OF LONG BONES IN TERMS OF EARLY UNION

Original Research

Shuja Uddin[1]*, Asif Khan[1], Shafqat Waseem[1], Aqeel Dhillon[1], Shoaib Saleem[1], Mubashir Farhan[1]
[1]Department of Orthopedic Surgery, Lahore General Hospital, Lahore, Pakistan.
Corresponding Author: Shuja Uddin, Department of Orthopedic Surgery, Lahore General Hospital, Lahore, Pakistan. drshujauddin111@gmail.com

Conflict of Interest: None | Grant Support & Financial Support: None

ABSTRACT

Background: Nonunion of long bones remains a challenge in orthopedic surgery, often resulting in pain, disability, and impaired function. While autogenous bone grafts (ABG) are traditionally preferred for their osteogenic properties, their use is limited by donor site morbidity. Bone substitutes like hydroxyapatite (HA) have emerged as alternatives due to their osteoconductive capabilities. Comparative studies are necessary to evaluate the effectiveness of ABG versus HA in achieving early union in nonunion cases.

Objective: To compare the effectiveness of autogenous bone grafts and hydroxyapatite bone substitute in promoting early union in long bone nonunion.

Methods: A randomized controlled trial was conducted at General Hospital, Lahore, Pakistan, from January 2021 to January 2023. Eighty patients with nonunion of long bones, aged 15 to 70 years, were enrolled via probability randomized sampling. Patients were randomly assigned to two groups: Group A received autogenous bone grafts, while Group B was treated with hydroxyapatite bone substitute. Clinical and radiological evaluations were conducted at regular intervals to assess bone union. Statistical analyses were performed using an independent t-test, with significance set at $p < 0.05$.

Results: The mean age of patients in Group A was 27.32 ± 12.17 years, while in Group B it was 31.10 ± 10.12 years. Group A comprised 37 males (92.5%) and 3 females (7.5%), whereas Group B included 34 males (85%) and 6 females (15%). Union rates were 90% in Group A and 85% in Group B, with no statistically significant difference ($p = 0.499$).

Conclusion: This study indicates that both autogenous bone grafts and hydroxyapatite bone substitutes are effective in treating long bone nonunion, with slightly higher union rates observed in the ABG group. Both modalities provide viable options for promoting bone healing in nonunion cases.

Keywords: Autogenous bone graft, bone substitute, hydroxyapatite, long bone, nonunion, orthopedic surgery, union rate.

INTRODUCTION

Bone grafting is a commonly employed surgical technique in orthopedics, with an estimated 2.2 million procedures performed annually worldwide (1). Despite advancements in fracture management, nonunion—characterized by the absence of healing progression for three months and persisting unhealed for nine months—remains a significant challenge, affecting 5 to 10 percent of all fractures (1,2). Nonunion, often associated with pain, joint stiffness, and functional impairment, can lead to considerable disability and job loss (3). A range of factors, including fracture type, location, soft tissue involvement, underlying bony pathologies, and the treatment approach used, influence the incidence of nonunion (1,2). Given its impact on patient quality of life and economic burden, restoring bone integrity in nonunion cases through effective grafting techniques is crucial to promote timely bone healing (4). Autogenous bone grafting (ABG), which involves relocating a segment of bone from one site to another within the same individual, is traditionally considered ideal for filling bone defects due to its osteogenic, osteoinductive, and osteoconductive properties. It avoids immunological reactions and disease transmission, given its natural histocompatibility. However, ABG has limitations, including a limited donor-site volume (50-55 cm), potential complications at the donor site such as chronic pain, infection, neurovascular injury, and additional blood loss, as well as the need for an additional surgical procedure (5,6). Consequently, bone substitutes have garnered interest as alternatives to ABG, offering a larger quantity of graft material and circumventing donor-site morbidity while maintaining favorable physical properties (7).

Superior synthetic bone graft substitutes, including calcium sulfate ($CaSO_4$), bioactive glass, and ceramics like coralline hydroxyapatite and tricalcium phosphate ($3CaPO_4$), have been developed with properties that promote bone formation and remodeling. They exhibit biocompatibility, osteoconductivity, and osteointegration, along with minimal fibrotic response. Specifically, coralline hydroxyapatite, approved by the Food and Drug Administration in 1992, has demonstrated effectiveness in treating metaphyseal defects, providing mechanical support comparable to cancellous bone, albeit with a need for protection against excessive loading until bony ingrowth is complete (8,9). Despite the growing body of research on bone substitutes, comparative data between hydroxyapatite bone grafts and autogenous bone grafts in terms of early union in long bones remains limited. Hydroxyapatite has primarily been studied in femoral fractures and within Western populations (10,11). This study aims to address this gap by comparing autogenous bone grafts with hydroxyapatite bone substitutes in promoting early union across various long bones in a diverse population, with the objective of elucidating the most effective approach for enhancing bone healing in nonunion cases.

METHODS

The study was conducted as a randomized controlled trial at a single center, the Orthopedic Unit of Lahore General Hospital, Lahore, over a period of two years, from January 2021 to January 2023. A total of 80 patients, aged between 15 to 70 years, were selected using a probability randomized sampling technique from the orthopedic outpatient department, all of whom were diagnosed with nonunion in one or more long bones. Exclusion criteria included patients with active infections, those who had undergone more than one surgery at the nonunion site, individuals with pathological fractures (based on medical records), and those on immunosuppressive or chemotherapy drugs. All eligible participants were randomly assigned to one of two treatment groups: Group A (n=40) received autogenous bone grafts (ABG), while Group B (n=40) was treated with hydroxyapatite (HA) as a bone substitute. Ethical clearance was obtained from the Institutional Review Board, and informed consent was secured from all participants prior to inclusion in the study. In Group A, the autogenous bone grafts were harvested from the iliac crest on the ipsilateral side of the fracture site. For Group B, hydroxyapatite crystals were used as the bone substitute. Stabilization of the fracture nonunion was achieved through secure instrumentation, ensuring stable fixation at both the proximal and distal ends of the affected bone.

Patients were scheduled for routine postoperative follow-up at 2, 4, 6, 8, 10, and 12 weeks to monitor bone union progress. Radiological union was determined by the presence of callus formation and the disappearance of the fracture line in both anteroposterior and lateral radiographic views. Clinical union was assessed by the absence of pain or tenderness at the fracture site and the patient's ability to bear weight without discomfort. Data were entered into SPSS version 20 for statistical analysis. Age, a quantitative variable, was expressed as mean ± standard deviation (SD), while gender, a qualitative variable, was represented as frequency and percentage. The effectiveness of ABG and HA in promoting bone union was analyzed using the independent t-test to determine any statistically significant differences between the two groups. The independent t-test, an inferential statistical test, was employed to evaluate mean differences between the groups, with a p-value of < 0.05 considered statistically significant.

To strengthen the study's rigor, specific fixation techniques were carefully selected based on the location and severity of each fracture, ensuring stability at both the proximal and distal sites of the nonunion. Standardized fixation procedures were followed to minimize potential variability in healing outcomes. Additionally, potential confounding variables, such as fracture type and associated soft-tissue injuries, were recorded and monitored to allow for more precise comparative analysis between the two groups. This approach aimed to control for differences in fracture characteristics that could influence healing rates, thereby enhancing the validity of the findings regarding early bone union outcomes between autogenous bone grafts and hydroxyapatite substitutes.

RESULTS

The mean ages of participants in Group A and Group B were 27.32 ± 12.17 years and 31.10 ± 10.12 years, respectively. In terms of gender distribution, Group A consisted of 37 males (92.5%) and 3 females (7.5%), while Group B included 34 males (85%) and 6 females (15%). The analysis revealed that both treatment groups achieved similar bone union rates, with no statistically significant difference between them. Specifically, the union rate was observed to be 90% in Group A and 85% in Group B, with a chi-square value of 0.4571 and a p-value of 0.499.

Table 1: Union Achieved in Treatment Groups

	Group-A	**Group-B**
Yes	36(90%)	34(85%)
No	4(10%)	6(6%)
Total	40	40

Chi-Square Test= 0.4571

p-value= 0.499

During follow-up evaluations, no union was observed in either group by the 2nd or 4th week, clinically or radiologically. By the 6th week, clinical union was achieved in 25% of Group A and 5% of Group B. Radiological union remained absent in both groups at this stage. At the 8th week, clinical union rates had markedly increased to 90% in Group A and 85% in Group B, while radiological union rates reached 55% and 50% in Group A and Group B, respectively. By the 10th and 12th weeks, clinical and radiological union rates in both groups reached their highest values, with 90% in Group A and 85% in Group B for both parameters.

Table 2: Clinical and Radiological Union Rates by Follow-up Week in Group A and Group B

Follow-ups	**Clinical Union (%)**		**Radiological union (%)**	
2nd week	Group-A	0	Group-A	0
	Group-B	0	Group-B	0
4th week	Group-A	0	Group-A	0
	Group-B	0	Group-B	0
6th week	Group-A	25	Group-A	0
	Group-B	5	Group-B	0
8th week	Group-A	90	Group-A	55

Follow-ups	Clinical Union (%)		Radiological union (%)	
	Group-B	85	Group-B	50
10th week	Group-A	90	Group-A	90
	Group-B	85	Group-B	85
12th week	Group-A	90	Group-A	90
	Group-B	85	Group-B	85

Although Group A displayed a slightly higher overall union rate compared to Group B (90% versus 85%), the difference was not statistically significant, indicating comparable efficacy of autogenous bone grafts and hydroxyapatite in promoting bone healing in long bone nonunion cases.

DISCUSSION

In the past, autologous bone grafting was often associated with notable postoperative complications stemming from both the harvesting and grafting processes (13). With the advent of advanced bone substitutes and osteoinductive agents, the role of autologous bone grafting as the gold standard for nonunion management has been challenged. Innovations over recent decades have seen a shift toward ceramic materials, including hydroxyapatite and calcium-phosphate-based pastes, while contemporary advancements continue to explore tissue-engineered products integrating growth factors and stem cells, pushing the boundaries of traditional grafting techniques. While the literature lacks direct comparisons of autologous bone grafts and bone substitutes specifically for long bone nonunion, this study aimed to address that gap. Findings from Michael A. Flierl's research indicate an 8.6% nonunion rate in patients treated with autografts (10). The current study observed a similar rate for autografts, with a 10% nonunion rate, closely aligning with Flierl's findings and supporting the efficacy of autologous grafts. Similarly, Takanobu Nakase's study on hydroxyapatite ceramics demonstrated a 91.66% healing rate over an extended follow-up, with only one patient requiring a secondary procedure for supplemental autografting (11). Although Nakase's research corroborates the effectiveness of hydroxyapatite, it did not employ a comparative framework, limiting its relevance in evaluating relative efficacy between treatments.

The findings of this study align closely with results from Ramprasad R's work, which reported a 98% union rate using autogenous bone grafts and rigid fixation, with minor, manageable complications that did not affect functional outcomes (12). While the union rate in this study for autogenous bone grafts was slightly lower at 90%, the consistency across studies underscores the reliability of autologous grafting for nonunion management. However, unlike previous studies, the randomized controlled design used here offers a more robust comparative perspective on the use of bone substitutes. Further evidence for the potential of bone substitutes is demonstrated by a 2016 study investigating a combination of bone marrow-derived mesenchymal stem cells (BM-MSCs) and hydroxyapatite granules for treating long bone nonunion. This study revealed that patients treated with BM-MSCs achieved faster functional and radiographic recovery than those treated with autografts, with comparable outcomes between groups at the one-year follow-up, highlighting the emerging viability of stem-cell-based bone substitutes in expediting union (15). Moreover, Ding et al. demonstrated the enhanced osteogenic capability of hydroxyapatite-nanoparticle and silk fibroin composites infused with bone morphogenetic protein-2 (BMP-2), which suggests that controlled BMP-2 release could further augment bone healing properties (16).

The strengths of this study lie in its randomized controlled design and systematic follow-up approach, allowing for a balanced assessment of bone union rates across two distinct grafting methods. However, certain limitations remain. The relatively short follow-up period, restricted to 12 weeks, may not fully capture long-term outcomes or delayed union cases, and the sample size, while sufficient for primary comparisons, limits the generalizability of the findings. Furthermore, the study did not incorporate advanced biological adjuncts, such as growth factors or stem cells, which have shown potential in augmenting the effects of bone substitutes in other research. Future studies could expand on this work by examining longer-term outcomes and integrating these adjunct therapies to enhance the evidence base for optimizing nonunion treatment strategies.

INSIGHTS-JHR
INSIGHTS-JOURNAL OF HEALTH AND REHABILITATION

CONCLUSION

This study demonstrated that both autogenous bone grafting (ABG) and hydroxyapatite bone substitute are effective options for treating nonunion of long bones. While autogenous bone grafting showed a slightly higher rate of union, both treatments provided comparable outcomes in promoting bone healing. These findings suggest that hydroxyapatite can serve as a viable alternative to ABG, offering similar efficacy without the need for a donor site, thus broadening the options available for managing nonunion cases effectively.

REFERENCES

1. Lewandrowski KU, Gresser JD, Wise DL, Trantolo DJ. Bioresorbable bone graft substitutes of different osteoconductivities: a histologic evaluation of osteointegration of poly(propylene glycol-co-fumaric acid)-based cement implants in rats. Biomaterials. 2000;21(8):757-64.

2. Calori GM, Albisetti W, Agus A, Iori S, Tagliabue L. Risk factors contributing to fracture non-unions. Injury. 2007;38 Suppl 2

3. Borrelli J, Prickett WD, Ricci WM. Treatment of nonunions and osseous defects with bone graft and calcium sulfate. Clin Orthop Relat Res. 2003;(411):245-54.

4. Beaman FD, Bancroft LW, Peterson JJ, Kransdorf MJ. Bone graft materials and synthetic substitutes. Radiol Clin North Am. 2006;44(3):451-61.

5. Samartzis D, Shen FH, Goldberg EJ, An HS. Is autograft the gold standard in achieving radiographic fusion in one-level anterior cervical discectomy and fusion with rigid anterior plate fixation? Spine (Phila Pa 1976). 2005;30(15):1756-61.

6. Giannoudis PV, Dinopoulos H, Tsiridis E. Bone substitutes: an update. Injury. 2005;36 Suppl 3

7. Trenholm A, Landry S, McLaughlin K, Deluzio KJ, Leighton J, Trask K, et al. Comparative fixation of tibial plateau fractures using α-BSM™, a calcium phosphate cement, versus cancellous bone graft. J Orthop Trauma. 2005;19(10):698-702.

8. Betz RR. Limitations of autograft and allograft: new synthetic solutions. Orthopedics. 2002;25(5 Suppl)

9. Jacobsen KA, Al-Aql ZS, Wan C, Fitch JL, Stapleton SN, Mason ZD, et al. Bone formation during distraction osteogenesis is dependent on both VEGFR1 and VEGFR2 signaling. J Bone Miner Res. 2008;23(5):596-609.

10. Flierl MA, Smith WR, Mauffrey C, Irgit K, Williams AE, Ross E, et al. Outcomes and complication rates of different bone grafting modalities in long bone fracture nonunions: a retrospective cohort study in 182 patients. J Orthop Surg Res. 2013;8(1):33.

11. Nakase T, Fujii M, Myoui A, Tamai N, Hayaishi Y, Ueda T, et al. Use of hydroxyapatite ceramics for treatment of nonunited osseous defect after open fracture of lower limbs. Arch Orthop Trauma Surg. 2009;129(11):1539-47.

12. Ramprasad R, Mittal A, Biju R, Prasad YS, Santosh S. Non-union long bones treated with rigid fixation and autogenous bone grafting: A series of 50 cases. Int J Biomed Res. 2015;6(12):982-7.

13. Oakley MJ, Smith WR, Morgan SJ, Ziran NM, Ziran BH. Repetitive posterior iliac crest autograft harvest resulting in an unstable pelvic fracture and infected non-union: case report and review of the literature. Patient Saf Surg. 2007;1:6.

14. Kanakaris NK, Paliobeis C, Manidakis N, Giannoudis PV. Biological enhancement of tibial diaphyseal aseptic non-unions: the efficacy of autologous bone grafting, BMPs and reaming by-products. Injury. 2007;38 Suppl 2

15. Ismail H, Phedy P, Kholinne E, Djaja Y, Kusnadi Y, Merlina M, et al. Mesenchymal stem cell implantation in atrophic nonunion of the long bones: A translational study. Bone Joint Res. 2016;5(7):287-93.

16. Ding Z, Fan Z, Huang X, Lu Q, Xu W, Kaplan DL. Silk–hydroxyapatite nanoscale scaffolds with programmable growth factor delivery for bone repair. ACS Appl Mater Interfaces. 2016;8(37):24463-70.

