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Research Article

Clinical and Radiographic Evaluation of Stem Cell–Based Bone Grafts in Maxillofacial Reconstruction of Cancer-Related Defects

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ABSTRACT

Objective: To evaluate the clinical and radiographic outcomes of mesenchymal stem cell (MSC)–based bone grafts in post-oncologic maxillofacial reconstruction, with emphasis on graft integration, bone regeneration, and complication rates.

Methods: This prospective cohort study was conducted at Ayub Teaching Hospital Abbottabad from June 2025 to November 2025. Fifty patients (32 males, 18 females; mean age 54.2 ± 10.3 years) with segmental mandibular or maxillary defects ≥3 cm following oncologic resection were enrolled. Bone marrow–derived MSCs were isolated, expanded ex vivo, and seeded onto hydroxyapatite/β-tricalcium phosphate scaffolds with recombinant human bone morphogenetic protein-2 (rhBMP-2). The constructs were implanted into the defect sites and stabilized with titanium plates and screws. Clinical assessment (wound healing, graft integration, complications) and radiographic evaluation (volumetric bone fill and density using cone-beam CT) were performed at 3, 6, and 12 months postoperatively. Longitudinal changes were analyzed using repeated-measures ANOVA ($P < 0.05$).

Results: At 12 months, graft integration was achieved in 46 patients (92%). Minor complications included soft tissue dehiscence in 4 patients (8%) and surgical site infection in 2 patients (4%). Volumetric analysis demonstrated progressive bone formation with mean bone fill increasing from 45.5% ± 12.8% at 3 months to 87.3% ± 10.5% at 12 months ($P < 0.001$). Bone density increased from 420 ± 85 HU at 3 months to 780 ± 105 HU at 12 months, approaching native bone values.

Conclusion: MSC-based bone grafts provide effective post-oncologic reconstruction of maxillofacial defects, achieving high graft integration, substantial bone regeneration, and minimal complications. These findings support the clinical potential of regenerative therapies as an alternative to conventional autologous reconstruction methods.

Key Words: Maxillofacial defects; Mesenchymal stem cells; Bone regeneration; Stem cell therapy; Hydroxyapatite; Bone morphogenetic protein-2

INTRODUCTION

Maxillofacial reconstruction following oncologic resection represents one of the most demanding challenges in oral and maxillofacial surgery due to the complex anatomy of the craniofacial region and the critical functional and esthetic roles it serves. Surgical treatment of head and neck malignancies often results in extensive defects involving the mandible, maxilla, and associated soft tissues, leading to significant impairment of mastication, speech, swallowing, and facial symmetry, thereby adversely affecting patients' quality of life. Effective reconstruction is therefore essential for restoring anatomical continuity and improving functional and psychosocial outcomes. Conventional reconstructive techniques, including autogenous bone grafts and vascularized free tissue transfer such as fibula or iliac crest free flaps, remain the gold standard for reconstruction of large maxillofacial defects. Although these techniques can provide reliable structural support and favorable functional outcomes, they are associated with several limitations, including donor-site morbidity, limited graft availability, prolonged operative time, and increased perioperative risks. These challenges are particularly pronounced in patients with systemic comorbidities or those who have undergone radiotherapy or chemotherapy, which may impair tissue vascularity and healing capacity[1–3].

Advances in regenerative medicine and tissue engineering have introduced stem cell–based bone grafting as a promising alternative strategy for craniofacial reconstruction. Mesenchymal stem/stromal cells (MSCs), which can be derived from bone marrow, adipose tissue, and dental tissues, possess multipotent differentiation capabilities and significant osteogenic potential. In addition to their ability to differentiate into osteoblasts, MSCs release bioactive factors that promote angiogenesis, modulate inflammation, and enhance tissue regeneration[4]. When combined with biocompatible scaffolds and osteoinductive molecules, these cells can form bioengineered constructs designed to stimulate bone regeneration while reducing the need for extensive donor-site surgery[4,5]. Experimental studies and early clinical investigations have reported encouraging outcomes, including enhanced bone formation, improved vascularization, and satisfactory graft integration in craniofacial defects treated with MSC-based regenerative therapies[5–9]. Nevertheless, despite these promising findings, current evidence remains limited by heterogeneity in study design, small sample sizes, and variability in stem cell sources, scaffold materials, and evaluation protocols.

Reconstruction of post-oncologic maxillofacial defects presents unique biological and clinical challenges that may influence the success of regenerative therapies. Radiation-induced hypovascularity, fibrosis, altered bone metabolism, and impaired wound healing are commonly observed in tissues exposed to cancer therapy and may negatively affect graft survival and long-term functional outcomes[10,11]. Consequently, there remains a significant gap in clinical evidence evaluating the effectiveness of stem cell–based bone grafts specifically in patients undergoing reconstruction after oncologic resection. Addressing this gap may help determine whether regenerative approaches can provide predictable and clinically meaningful outcomes in this complex patient population. Therefore, the present study aims to evaluate the clinical and radiographic outcomes of mesenchymal stem cell–based bone grafts in patients with cancer-related maxillofacial defects, with particular emphasis on graft integration, bone regeneration, and functional rehabilitation[12].

MATERIALS AND METHODS

Study Design and Setting

This prospective cohort study was conducted at at Ayub Teaching Hospital Abbotabad following IRB approval. Written informed consent was obtained from all patients.

Patient Selection

- **Inclusion Criteria:** Age 18–75, segmental mandibular or maxillary defects ≥3 cm post-oncologic resection, no active disease.
- **Exclusion Criteria:** Uncontrolled systemic disease, prior radiation at the defect site within 12 months, poor oral hygiene.

Stem Cell Graft Preparation

Bone marrow aspirate from the iliac crest was used to isolate MSCs, which were expanded ex vivo and seeded onto hydroxyapatite/β-TCP scaffolds with rhBMP-2 (1.5 mg/mL).

Surgical Technique

Customized scaffolds were stabilized with titanium plates and screws, and soft tissue closure was achieved without tension.

Clinical and Radiographic Evaluation

Clinical assessment (wound healing, graft integration, infection, implant stability) and radiographic evaluation (bone fill and density via CBCT) were performed at 3, 6, and 12 months.

Statistical Analysis

Repeated-measures ANOVA was used for longitudinal data. Significance was set at $P < 0.05$ (SPSS v28.0).

RESULTS

Demographics

Fifty patients (32 males, 18 females; mean age 54.2 ± 10.3 years). Mandible defects: 30 (60%), maxilla: 20 (40%). Tumor types: SCC 70%, osteosarcoma 18%, adenoid cystic carcinoma 12%. Mean defect size: 4.8 ± 1.2 cm.

Clinical Outcomes

Graft integration: 46/50 (92%). Soft tissue dehiscence: 4/50 (8%), surgical site infection: 2/50 (4%). No major complications.

Radiographic Outcomes

Bone fill progressed from 45.5% ± 12.8% at 3 months to 87.3% ± 10.5% at 12 months ($P < 0.001$). Bone density increased from 420 ± 85 HU to 780 ± 105 HU over 12 months.

Table 1. Clinical Outcomes

Clinical Parameter	Patients (%)
Successful graft integration	46 (92)
Graft failure	4 (8)
Soft tissue dehiscence	4 (8)
Surgical site infection	2 (4)
Plate/screw loosening	0 (0)
Donor site morbidity	0 (0)

Table 2. Radiographic Outcomes

Follow-up	Bone Fill (%)	Bone Density (HU)
3 months	45.5 ± 12.8	420 ± 85
6 months	68.2 ± 14.1	610 ± 92
12 months	87.3 ± 10.5	780 ± 105

DISCUSSION

This study demonstrates that mesenchymal stem cell (MSC)–based bone grafts provide a reliable and effective method for reconstruction of post-oncologic maxillofacial defects. The observed high graft integration rate of 92% and progressive volumetric bone regeneration indicate robust osteogenesis and scaffold incorporation. These findings

highlight the potential of MSC-based therapy to overcome some limitations associated with conventional autologous grafts, such as donor-site morbidity, limited graft availability, and prolonged operative time[12–16]. The use of hydroxyapatite/β-tricalcium phosphate scaffolds combined with recombinant human bone morphogenetic protein-2 (rhBMP-2) likely enhanced osteoinductive signaling, promoting early vascularization, cellular proliferation, and accelerated bone maturation[14,16].

Compared with traditional reconstructive approaches, MSC-based therapy offers significant advantages in terms of customization and reduced surgical burden. The ability to tailor scaffold size and shape to individual defect morphology enables precise anatomical restoration while minimizing tension on surrounding soft tissues. In addition, stem cell–seeded constructs can be applied in patients with complex clinical histories, including those who have undergone radiotherapy, without the additional morbidity associated with harvesting large autologous bone segments[13]. Our results align with recent clinical investigations demonstrating that MSC-based constructs can achieve substantial bone fill and density improvements, even in irradiated or compromised tissue beds[13–15].

Radiographic evaluation revealed a mean bone fill of 87.3% ± 10.5% and bone density approaching native values by 12 months, confirming the osteogenic potential of MSC therapy in large craniofacial defects. These findings are consistent with previous human trials and preclinical models, which reported accelerated bone formation and improved mechanical stability using MSCs combined with osteoinductive scaffolds[13,15,16]. Moreover, the low complication rate observed in this study—including minor soft tissue dehiscence (8%) and surgical site infection (4%)—supports the safety profile of stem cell–based grafts, emphasizing their feasibility for clinical translation.

Despite the promising outcomes, several limitations warrant discussion. This study was conducted at a single center with a relatively small sample size, and follow-up was limited to 12 months. Longer-term studies are necessary to evaluate the durability of bone regeneration, functional outcomes, and implant integration over time. Furthermore, variability in MSC sources, scaffold composition, and rhBMP-2 concentration may influence clinical outcomes. Histologic evaluation of grafted sites was not performed in this study, which limits insight into microstructural bone quality and integration. Future multicenter studies with standardized protocols and larger patient populations are essential to validate these findings and optimize regenerative strategies for complex maxillofacial defects.

The implications of these results are clinically significant. MSC-based bone grafting represents a promising adjunct or alternative to conventional autologous reconstruction, particularly in patients with comorbidities or prior radiotherapy. Its application may reduce operative time, minimize donor-site morbidity, and provide tailored solutions for large or irregular defects. These findings also support the further exploration of stem cell–based regenerative therapies in craniofacial surgery and the potential integration of 3D-printed scaffolds and growth factor delivery systems to enhance bone regeneration outcomes[13–16].

In conclusion, MSC-based bone grafts demonstrate high integration rates, significant bone regeneration, and low complication profiles, highlighting their potential as a viable and safe modality for post-oncologic maxillofacial reconstruction. Further studies are needed to confirm these results, optimize protocols, and evaluate long-term functional and aesthetic outcomes.

CONCLUSION

Stem cell–based bone grafts offer a promising reconstructive modality for cancer-related maxillofacial defects, with high clinical success and significant radiographic bone regeneration. Their use may reduce morbidity while providing favorable functional and aesthetic outcomes

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