American Cleft Palate–Craniofacial Association

Original Article

The Cleft Palate-Craniofacial Journal
1-8

DOI: 10.1177/10556656211025197
journals.sagepub.com/home/cpc
SAGE

Comparative Assessment of Autogenous Cancellous Bone Graft and Bovine-Derived Demineralized Bone Matrix for Secondary Alveolar Bone Grafting in Patients With Unilateral Cleft Lip and Palate

Vijay Kumar, MDS[1], Vidya Rattan, MDS[1], Sachin Rai, MDS[1], Satinder Pal Singh, MDS, DIBO[1], and Jai Kumar Mahajan, MS, MCH[2]

Abstract

Objective: Comparison between bovine-derived demineralized bone matrix (DMBM) and iliac crest graft over long term for secondary alveolar bone grafting (SABG) in patients with unilateral cleft lip and palate (UCLP) in terms of radiological and clinical outcomes.

Design: Prospective, randomized, parallel groups, double-blind, controlled trial.

Setting: Unit of Oral and Maxillofacial Surgery, Oral Health Science Centre, Postgraduate Institute of Medical Education & Research, Chandigarh.

Participants: Twenty patients with UCLP.

Interventions: Patients were allocated into group I (Iliac crest bone graft) and group II (DMBM) for SABG. Outcomes were assessed at 2 weeks, 6 months, and then after mean follow-up period of 63 months.

Outcomes Measures: Volumetric analysis of the grafted bone in the alveolar cleft site was done through cone beam computed tomography using Cavalieri principle and modified assessment tool. Clinical assessment was performed in terms of pain, swelling, duration of hospital stay, cost of surgery, alar base symmetry, and donor site morbidity associated with iliac crest harvesting.

Results: Volumetric analysis through Cavalieri principle revealed comparable bone uptake at follow-up of 6 months between group I (70%) and group II (69%). Modified assessment tool showed no significant difference between horizontal and vertical bone scores over short- and long-term follow-up. In group II, there was higher cost of surgery, but no donor site morbidity unlike group I.

Conclusions: Demineralized bone matrix proved analogous to iliac crest bone graft as per volumetric analysis over shorter period. However, although statistically insignificant, net bone volume achieved was lower than the iliac crest graft at longer follow-up.

Keywords

secondary alveolar bone grafting, demineralized bone matrix, cancellous iliac bone graft, cleft lip and palate

Introduction

Secondary alveolar bone grafting (SABG) of the residual alveolar cleft in patients with cleft lip and palate (CLP) is a well-established procedure. It provides bone tissue at the site of alveolar cleft site, which helps in stabilization of the maxillary alveolar arch and periodontium, facilitates the closure of oro-nasal fistulas, permits the eruption of teeth augments nasal alar base, and allows the orthodontic movement (Amanat & Langdon, 1991). Several sources of autogenous bone have been

[1] Unit of Oral and Maxillofacial Surgery, Oral Health Sciences Centre, Postgraduate Institute of Medical Education & Research, Chandigarh, India
[2] Department of Paediatric Surgery, Postgraduate Institute of Medical Education & Research, Chandigarh, India

Corresponding Author:
Vidya Rattan, Unit of Oral & Maxillofacial Surgery, Oral Health Sciences Centre, Postgraduate Institute of Medical Education & Research, Chandigarh 160012, India.
Email: drvidyarattan@gmail.com

used, but anterior iliac crest is regarded as the gold standard for grafting because it has strong osteogenic potential that provides immunocompatible bone cells. Apart from rapid integration, a superior success of iliac cancellous bone in closing the cleft defect has been largely documented (Bertz, 1981; Yilmaz et al., 2000).

However, there are various disadvantages of harvesting an autologous iliac bone graft including donor site morbidity, gait disturbances, excessive resorption rate, prolonged duration of hospital stay, hematoma formation, and long operating time. This may further culminate to unusual postsurgical complications pertaining to harvest of iliac crest bone such as hypersensitivity, infection, pelvic instability, and paresthesia, affecting 10% to 30% of patients (Arrington et al., 1996).

This has led to a search for an alternative suitable material. Various materials have been used for the alveolar cleft defect such as bioabsorbable hydroxyapatite, β-tricalcium phosphate, demineralized bone matrix (DMBM), and bone morphogenic protein 2 (BMP). Of these, bovine-derived DMBM is an inductive bioresorbable cortical xenograft. It is the type I collagen protein component of bone, which is a safe and biocompatible bone graft with osteoinductive properties. It has been used in periodontal bony defect, postextraction, bone cavity filling, dehiscence and fenestration, and transalveolar sinus lifting procedures.

Comprehensive evaluation of the literature reveals that there are a few studies (Francis et al., 2013) using DMBM for SABG assessing outcomes for a period of 6 months or 1 year; however, there is lacunae of long-term prospective studies to evaluate bone graft outcomes in terms of bone volume (Stasiak et al., 2019). Therefore, the aim of this study was to compare bovine-derived DMBM with iliac crest graft over long term for SABG in patients with unilateral cleft lip and palate (UCLP) in terms of radiological and clinical outcomes.

Materials and Methods

Study Design and Participants

This prospective, randomized, parallel group controlled trial was conducted among the patients with CLP presenting to the Unit of Oral and Maxillofacial Surgery, Oral Health Science Centre, Postgraduate Institute of Medical Education & Research, Chandigarh. Ethical clearance was taken from the ethical committee of the institute (NK/1151/MDS/14162-63). The patients were recruited between the period of June 2013 and December 2014 and followed up to February 2020. Included participants had unilateral cleft lip, alveolus and palate, and were between the age group of 7 and 16 years, while those with previous alveolar surgery (failed bone graft or gingivaperiosteoplasty), bilateral cleft, and with any other systemic disease or syndrome were excluded. Twenty patients were randomly allocated into 2 groups through a computer-generated randomized sequence. Opaque envelopes containing random numbers were preprepared and were kept aside by a nurse. Patients were asked to pick 1 envelope. They were then allocated to 2 groups accordingly (Figure 1). Group I included iliac crest bone graft, whereas group II included bovine-derived DMBM. Preoperative intraoral periapical and occlusal radiographs were obtained for all the patients. The patients received orthodontic treatment, and the plan of SABG was decided by orthodontist after suitable preparation in from of presurgical expansion of arches with fixed orthodontic appliances or quad helix appliance, dental extractions, and professional oral prophylaxis. Patients were explained the surgical procedure and the risk involved through patient information sheet. Patients and their primary caregiver were then asked to sign the written informed consent form. It was a double-blind study as the primary investigator and the analyzer during radiological and photographic evaluation were unaware of the patient's allocated group.

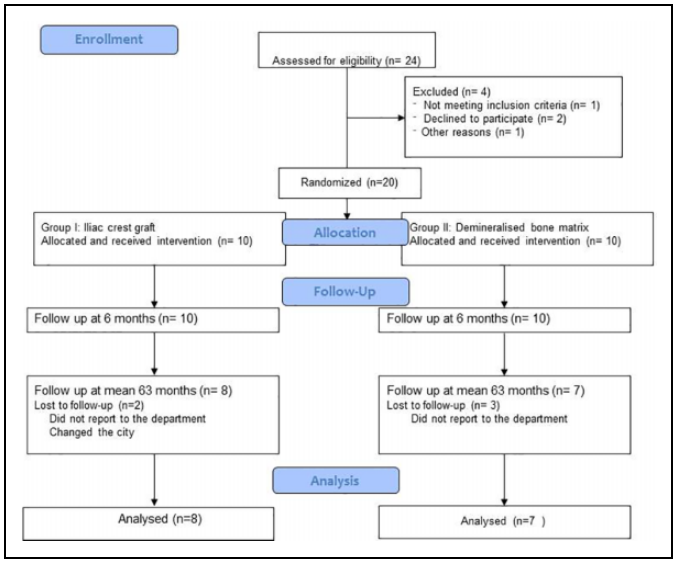

Figure 1. CONSORT flowchart.

Intervention

Surgical procedure. Secondary alveolar bone grafting was performed by the same surgeon using same surgical technique. An incision was made around the labial component of the fistula and extended along the margin of the alveolar cleft vertically toward the alveolus on each side. On reaching alveolar crest, the incisions were carried within the gingival sulci of the teeth on their labial aspect. In the lesser segment, the incision was extended to the molar region, while that in larger segment was extended till premolar region. Next, an oblique and posteriorly directed back cut was made toward the vestibule. The mucoperiosteum was elevated off the bony walls of the cleft from the alveolar crest to the nasal floor, exposing the lateral aspect of the anterior nasal spine and the lower pyriform rim. Palatal mucoperiosteum was mobilized and retracted, the soft tissue within the fistula on the palatal side was dissected superiorly to the nasal floor. This tissue was turned over toward and used to reconstruct the nasal floor. Closure of the nasal layer proceeds from posterior to anterior using a 4-0 resorbable Vicryl suture.

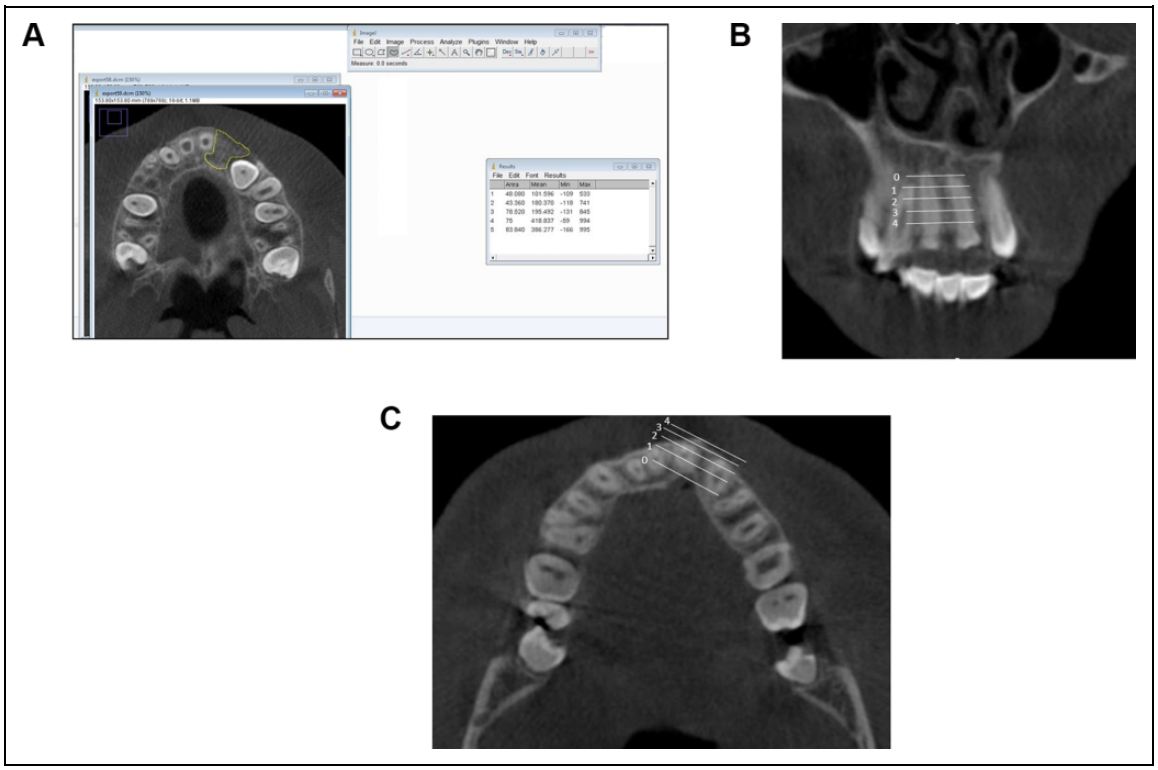

Figure 2. A, Volumetric evaluation by Cavalieri principle and planimetry technique using image J software in 1-mm axial sections. B, Vertical score 0 to 4 (white lines). C, Horizontal score 0 to 4 (white lines) using tooth mesial to cleft by modified assessment tool (Anver et al., 2020).

The palatal flaps were then advanced medially and secured together with interrupted 4-0 resorbable sutures. At this time, before placement of the bone graft, adequate labial soft-tissue mobility was confirmed that provided a tension-free closure over the bone graft. Alveolar cleft sites were filled with cancellous bone harvested from anterior iliac crest using conventional trapdoor technique in group I patient. In group II patients, bovine-derived DMBM—Osseograft (Advanced Biotech Private Limited; size $\sim$250 µm) mixed with autologous blood was placed followed by covering it with absorbable type I collagen membrane (Healguide; Advanced Biotech Private Limited). Analgesics, antibiotics, and chlorhexidine mouthwash were prescribed according to standard protocol.

Outcomes

Outcomes were assessed at 2 weeks, 6 months, and then after mean follow-up period of 5.25 years (63 months). Since the patients were recruited at different ages and the treatment of CLP has patient individualized approach, the follow-up period varied from 48 to 75 months.

Radiological evaluation. Graft volume was assessed with cone beam computed tomography (CBCT; Kodak 9500 cone beam 3-D system; Carestream Health). Small field of view (9 × 15) with a minimum of 0.2 mm voxel size was used, and volumetric data were reconstructed and sectioned into 1 mm isotropic volume in axial section. Short-term radiological evaluation was performed at 2 weeks postoperatively and at 6-month follow-up. The volume of harvested bone was calculated using the Cavalieri principle and the planimetry technique.

Cavalieri principle is a steoreological method of volume estimation of various biological tissues/organs (Emirzeoglu et al., 2005; Bayram et al., 2012). It gives numerical values, thereby providing accurate quantitative measurements (Gundersen & Jensen, 1987) by multiplying total area of the parallel section with the slice thickness. The surface area of every section was measured by means of the planimetry technique, using Image J software (Figure 2A). The sum of the areas was used to estimate the volume using the following formula: $V = t \times \Sigma A$; where t refers to the section thickness of consecutive sections and ΣA is the total sectional area of the consecutive sections. This method though gave very authentic results but could only be used as long as new bone could be delineated. Therefore, long-term assessment was conducted at mean follow-up period of 5.25 year (63 months) on the basis of method adopted from a previous study conducted by Anver et al. (2020) in which bone was evaluated both horizontally (horizontal score) and vertically (vertical score). This modified scale has been derived from other 2 scales documented by Suomalainen et al. (2014) and Wangsrimongkol et al. (2013). It was again done using CBCT images sections. For vertical height measurement of newly formed bone, the tooth mesial to the cleft was selected and a line along the long axis of tooth was drawn. It was then divided into 4 equal sections from apex to

Table 1. Comparison of Volume (in mm^3) Between 2 Groups at 14th Day and 6 Months.[a]

Grafted bone volume (mm^3)	Group	Mean ± SD	Range	*P* value
Volume of graft at 14th day	I	1564.74 ± 527.22	899.12-2379.68	.975 (NS)
	II	1557.98 ± 412.09	257.82-1835.26	
Volume of bone at 6 months	I	1095.46 ± 402.59	758.64-2100.99	.907 (NS)
	II	1073.82 ± 415.13	128.60-1775.36	

Abbreviation: , NS, nonsignificant.
[a]Student *t* test.

1 mm below the cementoenamel junction. Taking these sections as reference, bone height was measured and scored from 0 to 4. "Score 0 denotes 0% to 24% of expected bone height, 1 = 25% to 49% of expected bone height, 2 = 50% to 74% of expected bone height, 3 = 75% to 99% of expected bone height, and 4 = 100% of expected bone height" (Figure 2B). Horizontal dimension of bone was estimated on the distal aspect of tooth mesial to the cleft. At mid root level, taking labiolingual width of the tooth as reference value, scoring for new bone formation was done from 0 to 4. "Score 0 means no bone present, 1 = 0% to 49% of root width covered by bone, 2 = 50% to 99% of the root width covered by bone, 3 = 100% of the root width covered by bone, and 4 means bone extends beyond width of root in both dimensions" (Figure 2C). The CBCT images were evaluated by 2 independent examiners for which κ value was calculated to test for inter-rater reliability. This method was also implied at 6 months to ensure a common method of bone evaluation at short- and long-term follow-up.

Clinical evaluation. Clinical examination was done preoperatively, 14th day and after 6 months.

Preoperative evaluation. It included clinical history and examination; preoperative facial measurement (cm) done using 3 lines: line 1 from the tip of tragus of the right ear to the midpoint of philtrum of the upper lip; line 2 from the midpoint of philtrum of the upper lip to the tip of tragus of the left ear; and line 3 from lateral canthus of eye on cleft side to soft-tissue pogonion. Nasal alar base symmetry was evaluated preoperatively and postoperative after 6 months using extraoral photographs by 2 blinded observers. Examiners graded patients from 0 to 3 on the basis of criteria used earlier by Dickson et al. Score 0 = minimum or no change from preoperative alar base position. Score 1 = 25% to 50% improvement. Score 2 = 50% to 75% improvement, and score 3 = 75% to 100% improvement.

Intraoperative evaluation. It involved recording of time taken for the surgery (minutes).

Postoperative evaluation. It was done on the first, second, and fourteenth days and later at 6 months. It included pain at grafted site by Visual Analogue Scale (VAS), swelling by comparing with preoperative facial measurement, infection of cleft site, dehiscence, alar base symmetry, length of hospital stay, cost of procedure, and iliac crest site morbidity such as pain, gait disturbance, infection, hematoma, paresthesias, and scarring. Orthodontic treatments began after 6 months and orthodontically/spontaneous tooth movements were recorded at month 6 and then at subsequent orthodontic treatment visits.

Statistical analysis. The continuous data were presented as mean ± SD. First, the normality of the data was assessed by Shapiro-Wilk test. Descriptive and inferential statistics were used. Means of 2 groups were compared using Mann-Whitney *U* test. Time-related variables were compared using paired *t* test and Wilcoxon signed-rank test as applicable. Qualitative or categorical variables were described as frequencies and proportions. Proportions were compared using χ^2 test. A *P* value <.05 suggests statistical significant data. All calculations were done using SPSS version 21.

Results

There were 10 participants in each group, with comparable mean age of 12 ± 3.23 years in group I and 12.20 ± 2.74 years in group II. The sample in group I is composed of 4 males and 6 females, while that in group II consisted of 7 males and 3 females. Group I had 3 patients with cleft lip and alveolus and 7 with CLP. Group II had 2 patients with cleft lip and alveolus and 8 patients with CLP. There was no statistically significant difference between the 2 study groups (*P* value = .370).

All patients underwent surgical procedure without anesthetic complications. Group I and group II had 2 and 3 cases, respectively, which were lost to follow-up after 6 months.

Radiological Outcomes

Volumetric analysis done at 14th day and 6 months showed that the volume of grafted bone in both the groups was similar with no significant difference (Table 1). At 14th day, the volume of grafted bone was 1564.7 mm^3 versus 1557.9 mm^3 in group I and group II. The uptake of the bovine-derived DMBM was 69%, which was found to be similar to the cancellous bone from anterior iliac crest, that is, 70% in terms of volume after 6 months. Bone resorption in both the groups was same, with a follow-up period of 6 months, that is, 30% in group I and 31% in group II (*P* > .05).

Long-term radiological analysis was conducted to evaluate vertical and horizontal bone height formation by 2 independent investigators with substantial agreement (κ = .78). Vertical and horizontal discrete scores for each patient are given in Supplementary material. Mean values of both the parameters

Table 2. Comparison Within and Between 2 Groups at 6 Months and Long-Term Follow-Up (63 Months).[a]

	At 6 months			Mean follow-up (63 months)		
	Group I, N = 10 Mean (SD)	Group II, N = 10 Mean (SD)	Between groups *P* value	Group I Mean (SD)	Group II, N = 7 Mean (SD)	Between groups *P* value
Vertical score	2.90 (0.56)	2.30 (0.82)	.093 (NS)	2.50 (0.53)	2.14 (0.90)	.44 (NS)
Horizontal score	3.50 (0.70)	3.50 (0.97)	.720 (NS)	3.38 (0.51)	3.29 (1.11)	.69 (NS)
Within groups *P* value	.083 (NS)	.157 (NS)		.317 (NS)	.157 (NS)	

Abbreviation: NS, nonsignificant.
[a]Mann-Whitney *U* test and Wilcoxon signed-rank test.

suggested that there was no significant difference between the 2 groups at 6 months. Similar outcomes were observed at final follow-up where difference in the mean values of horizontal and vertical bone growth was statistically insignificant (Table 2). Within-group assessment revealed that though there was bone resorption from 6 months to final follow-up, this difference was not significant ($P < .05$; Table 2). Considering overall changes in bone height and volume over the period of time, it may be suggested that there was substantial bone resorption of around 30% in the first 6 months. Thereafter, this rate was reduced, and a stabilization in the bone dimension was observed over the mean follow-up period of 5 years.

Clinical Outcomes

Clinical parameters such as pain at grafted site, facial swelling on first, second, and fourteenth postoperative days were comparable in both groups. Improvement in alar base symmetry was achieved in both groups, around 50% cases in group I showed 25% to 50% improvement whereas in group II it was as high as 70%. There was no significant difference in the time taken for surgery and duration of hospital stay between the groups. However, the cost of surgery in group II was significantly higher than that in group I, which was due to the additional cost of bone grafted and collagen membrane (Table 3). Surgery using Osseograft along with Healguide collagen membrane cost almost double to that of iliac crest graft. None of the patient showed infection at the grafted site or complete dehiscence. In group I, 3 patients showed partial dehiscence without bone loss, whereas in group II, 1 patient showed partial dehiscence with slight bone loss but uneventful healing while other 3 had partial dehiscence without bone loss. It was seen that the unerupted tooth could erupt through the grafted bone in 3 patients in group I and 1 in group II, whereas orthodontic movement of the adjacent teeth in the grafted bone was achieved in 4 patients in each group (Figure 3A-G).

Morbidities Associated With Iliac Crest Harvesting

Pain due to iliac crest harvesting was moderate to severe in intensity seen on the second day in almost all the patients that ranged from 4 to 10, and 4 patients showed pain even at 14th day that ranged from 1 to 7 on VAS. Gait disturbance was observed in all patients on day 2 and in 5 patients on day 14, which resolved over a period of time. Infection was seen in 1 case. Dehiscence, paresthesias, delayed and healing were seen in 1 case only. Perceptible scar was there in almost all patients, with 1 patient having extensive scarring at 6 months.

Table 3. Demographic and Clinical Parameters Between 2 Groups.

Criteria	Group I	Group II	*P* value
Mean age (year)	12 ± 3.23	12.20 ± 2.74	.88 (NS)
Mean time taken for surgery (minutes)	111.20 ± 42.63	109.10 ± 29.48	.9 (NS)
Median pain score at cleft site (VAS)			
24 hours	2	2.5	.577 (NS)
48 hours	1.5	1.5	.935 (NS)
2 weeks	0.75	0	1.00 (NS)
Swelling (cm), mean ± SD			
1st day			
Horizontal	13.64 ± 0.94	13.50 ± 0.77	.72 (NS)
Vertical	11.26 ± 0.65	11.22 ± 0.76	.90 (NS)
2nd day			
Horizontal	13.50 ± 1.01	13.46 ± 1.02	.93 (NS)
Vertical	11.26 ± 0.98	11.23 ± 0.97	.94 (NS)
14th day			
Horizontal	12.77 ± 1.13	12.83 ± 1.03	.90 (NS)
Vertical	10.81 ± 0.74	10.64 ± 0.99	.67 (NS)
Mean duration of hospital stay (days)	6 ± 1.054	5.10 ± 2.183	.256 (NS)
Mean cost of surgery	6120 ± 3475.88	11242.80 ± 2531	.001 (S)
Alar base symmetry, N (%)			
0	5 (50)	3 (30)	.65 (NS)
1	5 (50)	7 (70)	

Abbreviations: NS, nonsignificant; VAS, Visual Analog Scale.

Discussion

The patients with CLP have a complex skeletal deformity that usually requires surgical intervention at various ages. The SABG procedure is an integral part of the cleft palate treatment with numerous benefits.

Radiographic outcome in the terms of height gained by interalveolar septum postoperatively using Bergland index (1986) on 2-dimensional radiographs has been used as standard method to measure success of the graft. However, a three-

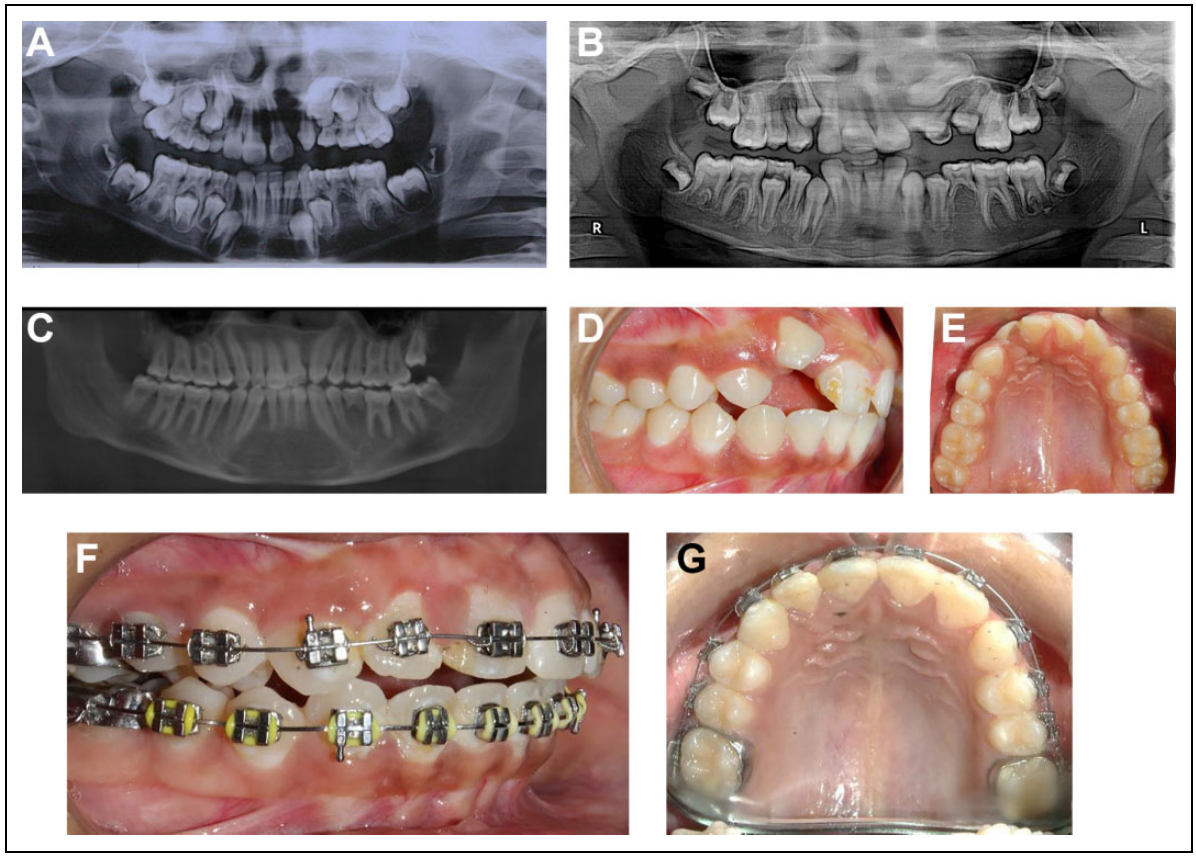

Figure 3. Tooth movement through the grafted bone in both groups: group I (A-C), group II (D-G). A, Preoperative orthopantomogram (OPG). B, OPG at 6- month follow-up. C, OPG at 73-month follow-up showed canine eruption through grafted bone. D, Preoperative lateral view of canine (13). E, Preoperative occlusal view. F, Postoperative lateral view showing eruption of canine (13) through grafted bone. G, Postoperative occlusal view showing alignment of canine (13) within arch.

dimensional CBCT provides a more precise and meticulous analysis and hence was the tool of choice in this study (Waitzmann et al., 1992; Rosenstein et al., 1997). Moreover, Dickinson et al. (2008) had earlier performed volumetric analysis and compared the 2 groups, rhBMP versus Iliac crest, at preoperative and 6-month follow-up using 1-mm axial section using Image J program in CBCT and observed that small field of view was used, which effectively reduces the amount of radiation exposure.

Actual volume of the bone formed was assessed using Cavalieri principle, a stereological method, which has been used earlier for volumetric estimation of mandibular condyle and brain by Bayram et al. (2012) and Rosen et al. (1990), respectively. This technique has been used for the first time in the quantitative volumetric assessment in secondary alveolar bone grafting procedure. The volume of bone graft required to completely fill the alveolus was comparable (1564 mm^3 vs 1557 mm^3) in 2 groups. Therefore, both the groups were similar in all the aspects.

Our outcomes at 6-month follow-up are in agreement with study by Zhang et al. (2012), who reported that the average loss of bone volume after 6 months was 29.3% using iliac crest with CBCT. Similarly, success rate using cancellous bone is usually reported to be greater than 80% (Bergland et al., 1986; Kortebein et al., 1991). In the current study, it was found to be around 70%. Success rate in group II was 69%, which was in agreement with the study by Kim et al. (2010) who reported it to be 61.7%. Thuakaban and Nuntanaranont. (2006) using 2-dimensional occlusal radiographs compared similar groups, that is, iliac crest graft and deproteinized bovine bone with iliac crest graft, and showed 31% and 27% resorption, respectively, after 2 years. This method gave more precise and impeccable results; however, it could not be used for long-term follow-up as over time, it becomes almost impossible to clearly delineate the newly formed bone from the previously existing bone.

Therefore, another scale was incorporated as modified assessment tool for long-term follow-up. At 6 months, our findings depict 75% to 100% vertical bone formation in 8 cases of iliac crest graft, which is in accordance with to that reported by Suomalainen et al. (2014). However, in our study, the number of patients (9) with 75% to 100% horizontal bone growth was higher. Considering long-term follow-up, mean values for both horizontal and vertical bone growth in both the groups were in accordance to those reported by Anver et al. (2020), who conducted retrospective study on patients with CLP treated with iliac bone graft and observed the radiographic

changes in the bone formed over 6 years. Trindade et al. (2012) reported more than 75% growth in height of interdental bone in about 70% to 80% patients with 4-year follow-up using Bergland scale; whereas in our study, only 4 cases had more than 75% vertical growth at the final follow-up. This difference was perhaps due to higher sensitivity and accuracy of CBCT used in our study in contrast to 2-dimensional radiographs used in the aforesaid study. Resorption of the bone formed over the follow-up period was also insignificant within the groups, thereby reaffirming the effectiveness of bovine-derived DMBM—Osseograft, similar to other studies (Kim et al., 2010; Benlidayi et al., 2012). Overall changes in the bone were in accordance to those reported by Feichtinger et al. (2007), who observed bone loss of 49.5% in 1 year followed by stabilization for over the next 2 years. Initial bone resorption followed by stabilization was probably due to stimulation of grafted bone either through orthodontic movement or through canine eruption.

Further considering clinical parameters, pain at iliac crest harvested site was moderate to high within the range of 4 to 10. Pain gradually reduced in intensity in 6 patients, except in 4 patients who experienced pain even at 14th day. Our results were in concordance to Swan et al. (2006) who reported VAS scores in the range of 2 to 10 at iliac crest harvested site. In our study, infection was noted in 1 patient after 10 days, which was managed with local injection of antibiotics, leading to resolution of the symptoms. Gait disturbance was seen in all the patients of group I at day 2, which was subsequently persisted in 5 patients at day 14. Similar findings were reported by Swan et al. (2006) where median time taken until the child could walk "normally" was 7 days (range 0-56). Generally, patients in the group I required slightly longer duration of stay because of pain and difficulty in walking for few days. Five points included in our study were modified from the study by Yuasa and Sugiura. (2004) and Bamgbose et al. (2005) for the facial swelling measurement. The present study showed no difference in the facial swelling between the 2 groups at various time interval. Therefore, there was no additional inflammatory response to bovine-derived DMBM in group II. Factors such as cleft morphology and alveolar cleft width might affect the improvement in alar base symmetry. Dickinson et al. (2008) studied alar base support and showed comparable grades in improvement in patients treated with BMP-2 versus iliac bone graft. Correspondingly, in our study, the alar base augmentation was similar between the 2 groups.

To the best of our knowledge, Cavalieri principle used for the volumetric analysis of the bone formed following SABG in this study is a novel approach. Strong study design diminishes the possible sources of bias, such as reporting bias, detection bias, and Hawthorne effect. As per the recent systematic review by Stasiak et al. (2019), there is dearth of long-term prospective studies in this area. Our study addresses this gap by assessing not only short-term but also long-term (63 months) outcomes. Data collection and evaluation over at all follow-up and further contrasting their radiological outcomes both within groups and between groups is a comprehensive approach to draw any conclusion.

The major limitation of our study was the small sample size owing to limited time frame of recruitment. Therefore, the outcomes cannot be generalized. Five cases were lost to long-term follow-up, thereby skewing the outcomes. Participants included had a broad range of age at the time of recruitment influencing the final aggregate. The preoperative imaging was done with occlusal and periapical radiographs, which cannot exclude the possibility that the DMBM group might had a preoperative alveolar bone defect smaller than the iliac crest bone graft group. Moreover, the novel method of volumetric analysis could not be used for long-term analysis.

Conclusion

Bovine-derived DMBM proved analogous to iliac crest bone graft through volumetric analysis. However, although statistically insignificant, net bone volume achieved was lower than the iliac crest graft at longer follow-up. The DMBM provided similar outcomes in most of the clinical parameters evaluated and prevented the donor site morbidity.

Authors' Note

Unit of Oral and Maxillofacial Surgery, Postgraduate Institute of Medical Education and Research, Chandigarh.

Ethical committee number of the institute (NK/1151/MDS/14162-163).

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

ORCID iD

Vijay Kumar, MDS https://orcid.org/0000-0003-2344-9225

Supplemental Material

Supplemental material for this article is available online.

References

Amanat N, Langdon JD. Secondary alveolar bone grafting in clefts of the lip and palate. *J Craniomaxillofac Surg*. 1991;19(1):7-14.

Anver TD, Mirzai L, Li P, Powell KK, Waite PD. Long-term postoperative cone-beam computed tomography analysis of secondary bone grafting in 79 patients with unrepaired alveolar clefts. *J Oral Maxillofac Surg*. 2020;78(7):1164-1170.

Arrington ED, Smith WJ, Chambers HG, Bucknell AL, Davino NA. Complications of iliac crest bone graft harvesting. *Clin Orthop Relat Res*. 1996;(329):300-309.

Bamgbose BO, Akinwande JA, Adeyemo WL, Ladeinde AL, Arotiba GT, Ogunlewe MO. Effects of co-administered dexamethasone and diclofenac potassium on pain, swelling, and trismus following third molar surgery. *Head Face Med*. 2005;1:11. doi: 10.1186/1746-160X-1-11. PMID: 16274480; PMCID: PMC1291385.

Bayram M, Kayipmaz S, Sezgin OS, Küçük M. Volumetric analysis of the mandibular condyle using cone beam computed tomography. *Eur J Radiol*. 2012;81(8):1812-1816.

Benlidayi ME, Tatli U, Kurkcu M, Uzel A, Oztunc H. Comparison of bovine-derived hydroxyapatite and autogenous bone for secondary alveolar bone grafting in patients with alveolar clefts. *J Oral Maxillofac Surg*. 2012;70(1):e95-e102.

Bergland O, Semb G, Abyholm F, Borchgrevink H, Eskeland G. Secondary bone grafting and orthodontic treatment in patients with bilateral complete clefts of the lip and palate. *Ann Plast Surg*. 1986;17(6):460-474.

Bertz JE. Bone grafting of alveolar clefts. *J Oral Surg*. 1981;39(11): 874-877.

Dickinson BP, Ashley RK, Wasson KL, O'Hara C, Gabbay J, Heller JB, Bradley JP. Reduced morbidity and improved healing with bone morphogenic protein-2 in older patients with alveolar cleft defects. *Plast Reconstr Surg*. 2008;121(1):209-217.

Emirzeoglu M, Sahin B, Selcuk MB, Kaplan S. The effects of section thickness on the estimation of liver volume by the Cavalieri principle using computed tomography images. *Eur J Radio*. 2005; 56(3):391-397.

Feichtinger M, Mossböck R, Kärcher H. Assessment of bone resorption after secondary alveolar bone grafting using three-dimensional computed tomography: a three-year study. *Cleft Palate Craniofac J*. 2007;44(2):142-148.

Francis CS, Mobin SS, Lypka MA, Rommer E, Yen S, Urata MM, Hammoudeh JA. rhBMP-2 with a demineralized bone matrix scaffold versus autologous iliac crest bone graft for alveolar cleft reconstruction. *Plast Reconstr Surg*. 2013;131(5):1107-1115.

Gundersen HJ, Jensen EB. The efficiency of systematic sampling in stereology and its prediction. *J Microsc*. 1987;147(3):229-263.

Kim YK, Kim SG, Lim SC, Lee HJ, Yun PY. A clinical study on bone formation using a demineralized bone matrix and resorbable membrane. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 2010; 109(6):e6-e11.

Kortebein MJ, Nelson CL, Sadove AM. Retrospective analysis of 135 secondary alveolar cleft grafts using iliac or calvarial bone. *J Oral Maxillofac Surg*. 1991;49(5):493-498.

Rosen GD, Harry JD. Brain volume estimation from serial section measurements: a comparison of methodologies. *J Neurosci Methods*. 1990;35(2):115-124.

Rosenstein SW, Long RE, Dado DV, Vinson B, Alder ME. Comparison of 2-D calculations from periapical and occlusal radiographs versus 3-D calculations from CAT scans in determining bone support for cleft-adjacent teeth following early alveolar bone grafts. *Cleft Palate Craniofac J*. 1997;34(3):199-205.

Stasiak M, Wojtaszek-Słomińska A, Racka-Pilszak B. Current methods for secondary alveolar bone grafting assessment in cleft lip and palate patients – a systematic review. *J Craniomaxillofac Surg*. 2019;47(4):578-585.

Suomalainen A, Åberg T, Rautio J, Hurmerinta K. Cone beam computed tomography in the assessment of alveolar bone grafting in children with unilateral cleft lip and palate. *Eur J Orthod*. 2014; 36(5):603-611.

Swan MC, Goodacre TEE. Morbidity at the iliac crest donor site following bone grafting of the cleft alveolus. *Br J Oral Maxillofac Surg*. 2006;44(2):129-133. doi: 10.1016/j.bjoms.2005.04.015.

Thuaksuban N, Nuntanaranont T. Iliac crest bone grafting of the alveolar cleft: clinical and quantitative radiographic assessment. *Asian J Oral Maxillofac Surg*. 2006;18(2):105-112.

Trindade-Suedam IK, da Silva Filho OG, Carvalho RM, de Souza Faco RA, Calvo AM, Ozawa TO, Trindade AS Jr, Trindade IE. Timing of alveolar bone grafting determines different outcomes in patients with unilateral cleft palate. *J Craniofac Surg*. 2012;23(5):1283-1286.

Waitzman AA, Posnick JC, Armstrong DC, Pron GE. Craniofacial skeletal measurements based on computed tomography: part I. accuracy and reproducibility. *Cleft Palate Craniofac J*. 1992;29(2):112-117.

Wangsrimongkol T, Manosudprasit M, Pisek P, Sutthiprapaporn P, Somsuk T. Alveolar bone graft evaluation agreement using cone beam computed tomography in cleft lip and palate patients: a pilot study. *J Med Assoc Thai*. 2013;96(suppl 4):S36-S43.

Yilmaz S, Kiliç AR, Keles A, Efeoğlu E. Reconstruction of an alveolar cleft for orthodontic tooth movement. *Am J Orthod Dentofac Orthop*. 2000;117(2):156-163.

Yuasa H, Sugiura M. Clinical postoperative findings after removal of impacted mandibular third molars: prediction of postoperative facial swelling and pain based on preoperative variables. *Br J Oral Maxillofac Surg*. 2004;42(3):209-214.

Zhang W, Shen G, Wang X, Yu H, Fan L. Evaluation of alveolar bone grafting using limited cone beam computed tomography. *Oral Surg Oral Med Oral Pathol Oral Radiol*. 2012;113(4):542-548.