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Outcomes of Xenograft with Platelet-rich Fibrin versus Autogenous Bone in Alveolar Cleft Grafting

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Background: The use of a suitable graft material helps with sufficient osseointegration. The aim of this study was to compare the clinical and radiographic outcomes of two types of alveolar bone graft materials, xenografts with platelet-rich fibrin (PRF) and autogenous grafts, in patients with alveolar clefts.
Methods: Thirty-six patients with alveolar clefts were enrolled in this study. Those patients were randomly divided into two groups: group A, where the autogenous iliac bone graft was used to fill the alveolar defect, and group B, where the xenograft with PRF was used to fill the alveolar defect. After 6 months of grafting, patients were assessed in terms of pain, duration of hospital stay, and donor site morbidity associated with iliac crest harvesting, while bone formation was evaluated radiographically using cone beam computed tomography.
Results: The results showed no statistical differences as regards baseline and perioperative data. Operative duration was significantly lower among xenograft with PRF patients. Both groups had comparable postoperative success scores, and total failure was reported in a total of three patients (one patient in group A and two patients in group B).
Conclusions: With no potential donor site morbidities, xenograft with PRF is an equivalent bone transplant replacement to the autologous iliac bone graft. Additionally, it is associated with a significant success rate, and a significant decrease in operative time and hospital stay. Many future studies are warranted to draw firm conclusions. *(Plast Reconstr Surg Glob Open 2024; 12:e6106; doi: 10.1097/GOX.0000000000006106; Published online 30 September 2024.)*

INTRODUCTION

Cleft lip and palate (CLP) are the most common congenital anomalies affecting the orofacial region. Successful management requires coordinated care from various disciplines, including plastic surgery, orthodontics, genetics, speech pathology, and others, to achieve functional and aesthetic well-being.[1]

Alveolar cleft is the most common congenital bone defect caused by abnormal primary palate development.[2] Since its introduction in 1972, alveolar bone grafting (ABG) has been widely accepted to correct the alveolar bone defect in most cleft centers.[3] The purpose of ABG is to restore dental arch continuity and maxillary stability, close the oronasal fistulae (ONF), facilitate subsequent orthodontic treatment, enhance nasal symmetry, establish better oral hygiene, limit growth disturbances, etc.[4]

Autogenous and nonautogenous bone grafts have been used for the augmentation of alveolar clefts in recent decades.[5] Autograft is still considered the gold standard because it provides a good scaffolding for osteoconduction and contains growth factors for osteoinduction as well as progenitor cells for osteogenesis. However, autograft procedures have the risk of donor site morbidity and are limited by graft availability. Hence, other types of bone grafts, such as allografts, xenografts, and synthetic bone grafts, are now widely used in reconstructive maxillofacial surgery.[6]

Xenografts are bone tissues harvested from one species and transplanted into another, typically from bovine or equine sources. The properties of xenografts are dependent on their origin, constitution, and processing techniques.[7] The tissues are completely devitalized, and any cellular or immunogenic materials are removed to prevent disease transmission and rejection.[8] Xenografts possess poor osteoinductive properties due to rigorous

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processing but maintain osteoconductive properties due to the preservation of the graft's macrostructure.[8]

Xenograft finds several applications in dentistry; it is a common bone graft biomaterial used in many other indications. Factors such as bone morphogenetic protein, platelet-rich plasma, or platelet-rich fibrin (PRF) are sometimes used to supplement the xenografts.[9] PRF is a second-generation technology consisting of an autologous leukocyte-platelet-rich fibrin matrix, composed of a tetramolecular structure, with leukocytes, platelets, and stem cells within it, which acts as a biodegradable scaffold that favors the development of micro-vascularization and releases cytokines and growth factors, which play a crucial role in the healing process.[10,11]

The aim of this work was to compare the outcomes of xenograft with PRF versus autogenous bone graft in secondary ABG.

Takeaways

Question: Comparison between xenograft with platelet-rich fibrin (PRF) versus autogenous bone in alveolar cleft grafting.

Findings: This study enrolled 36 patients with alveolar clefts, divided into two groups: autogenous iliac bone graft (group A) and xenograft with PRF (group B). After 6 months of grafting, bone formation was evaluated radiographically using CBCT. We found that both groups had comparable postoperative success scores.

Meaning: With no donor site morbidity, xenograft with PRF may play a role as an alternative bone graft material in cases of cleft alveolus. Additionally, it is associated with a significant success rate, and a significant decrease in operative time and hospital stay.

PATIENTS AND METHODS

This prospective noninferiority study was a two-arm parallel-group randomized controlled clinical trial. The study involved 36 patients who were screened at the outpatient clinic of the plastic surgery department, Assiut University Hospitals and Operation Smile Egypt Center, Assiut, Egypt, who were seeking correction of cleft alveolus in the period between March 2020 and November 2022.

The study included patients aged 7–15 years with nonsyndromic cleft lip and alveolus or cleft lip and palate (CLP) as inclusion criteria. Exclusion criteria included patients receiving previous primary or tertiary ABG, active infections, and underlying diseases.

Clefts included 10 bilateral and 16 unilateral cleft alveolus patients, for a total of 36 sites in the sample. Each patient was randomly assigned to his/her group using the QuickCalcs method for randomization.[12] The selected patients were grouped into two categories, with 18 samples in each, as group A for patients who received autogenous ABG and group B for patients who received xenograft with PRF.

The following clinical parameters were evaluated by two blinded observers: alveolar arch continuity, alar base symmetry, the presence of ONF, recipient and donor site complications, and hospital stay. This was coupled with a radiographic examination using cone beam computed tomography (CBCT) by one of our radiologists. The CBCT scan was taken with New-Tom VGi (QR s.r.l., Verona, Italy) at 110 kV, choosing a field of view of 12×8 cm and a boosted dose. Axial slices were reconstructed parallel to the occlusal plane. Measurements were made with the manufacturer's software, NNT Viewer version 13.0 (QR s.r.l., Verona, Italy). The dimensions of the bony bridge were evaluated with a novel success scale.[13]

Bone height, width, and the level of the nasal floor were quantitatively measured in relation to the adjacent teeth. In cases of unerupted canines, measurements were made in relation to the next adjacent erupted tooth. As a result, the scale did not require the completion of the orthodontic movements in the area.

Surgical Procedures

Under general anesthesia, the soft tissue in the superior iliac crest was injected with 0.5% lidocaine and 1:100,000 parts of epinephrine. Incision of the skin and subcutaneous tissue was done until reaching the iliac crest, followed by elevation of the cartilage cap; then the cancellous bone was harvested with an osteotome and cut into small bone granules (Fig. 1). The bone granules were then carefully implanted into the alveolar cleft of group A.

PRF was prepared as described by Choukroun.[14] Ten milliliters of blood was collected in vacuum tubes without anticoagulants, which were then immediately centrifuged at a rate of 3000 rpm for 10 minutes. After centrifugation, the resultant product consisted of three layers. The topmost layer consisted of acellular platelet-poor plasma, a PRF clot in the middle, and RBCs at the bottom of the test tube. The attached red blood cells were scraped off of it and discarded. The collected PRF was then mixed with xenograft (OneXeno Graft, cortico-cancellous bovine powder > 2.0 mm, 1.0 mL, Germany) and placed inside the alveolar defect of group B (Fig. 2).

The soft tissue in the gingiva surrounding the alveolar cleft was injected with 0.5% lidocaine and 1:100,000 parts of epinephrine. At the alveolar cleft site, gingival sulcus incisions were performed on both sides of the cleft. Mucoperiosteal flaps were elevated and reflected. The oral and nasal floor mucosa were surgically dissected (Fig. 3A). The detection and correction of ONF had been performed (Fig. 3B). For group A, the autogenous iliac bone graft was used to fill the alveolar defect (Fig. 3C), and in group B, xenograft and PRF were used to fill the alveolar defect (Fig. 2C). Next, the cleft site was closed without tension by the advancement of the gingival flaps (Fig. 3D).

Patients in both groups received a single postoperative morphine dose based on patient weight (0.1 mg/kg), followed by maintenance doses of injectable nonsteroidal antiinflammatory drugs (NSAIDs) during the hospital stay and oral NSAIDs after discharge for 5–7 days.

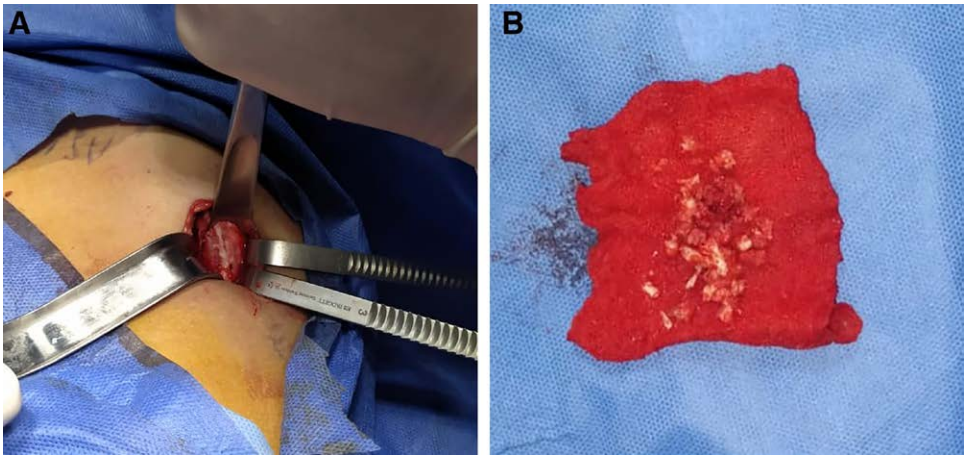

Fig. 1. Autogenous bone graft harvesting. A case from group A showing (A) harvesting of autogenous bone graft; (B) autogenous bone graft granules.

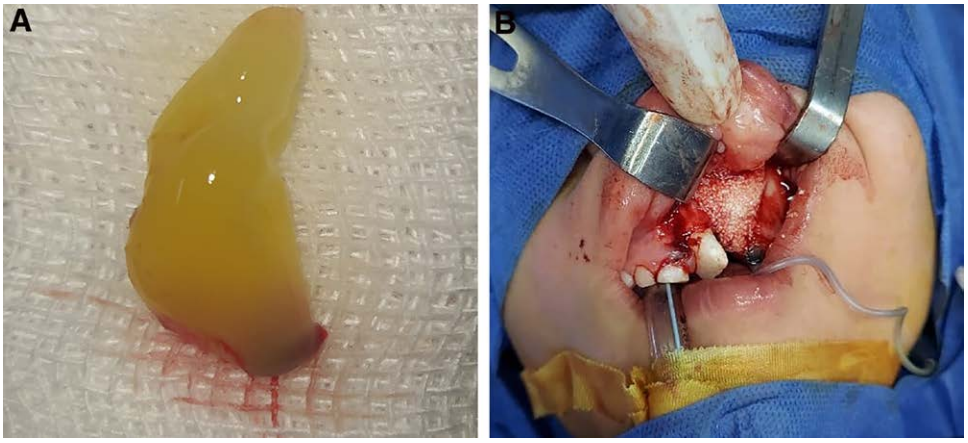

Fig. 2. PRF preparation. A, Platelet-rich fibrin (PRF). B, Bone graft within the defect [xenograft with PRF (group B)].

Evaluation

Clinical Evaluation

The clinical examination was performed preoperatively, on the 14th day, and 6 months postoperatively. Alar base symmetry was evaluated preoperatively and after 6 months using extraoral photographs by two blinded observers. Examiners graded patients from 0 to 3 based on criteria used earlier by Dickson et al (2008): score 0, a minimum or no change from the preoperative alar base position; score 1, 25%–50% improvement; score 2, 50%–75% improvement; and score 3, 75%–100% improvement.[15]

Intraoperative Evaluation Involved the Recording of the Time Taken for the Surgery (Minutes)

Postoperative evaluation assessed cleft site infection; dehiscence; alar base symmetry; length of hospital stay; and iliac crest site morbidity, including pain, infection, hematoma, and scarring.

Radiological Evaluation Using CBCT

Bone height (H). Multiple coronal slices were analyzed, dividing adjacent roots into four equal quarters (Fig. 4; Table 1). Each case was assigned a score of H4 (best) to H1 (worst), according to the deepest notching of the *salveolar* bone, with a score of H0 if no continuous bony bridge was detected.

Bone width (W). An axial slice, which equally divided the bony bridge between the adjacent roots, was analyzed. Bone width was scored as W2 (best) if it was over half the width of the adjacent roots, or W1 (worst) if it was less than half, labiopalatially, with a score of W0 if no continuous bony bridge was detected.

Nasal floor (N). Multiple coronal slices were analyzed, dividing adjacent roots into four equal quarters. Each case was assigned a score of N4 (best) to N1 (worst), according to the greatest extent of the nasal floor, with a score of N0 if no continuous bony bridge was detected.

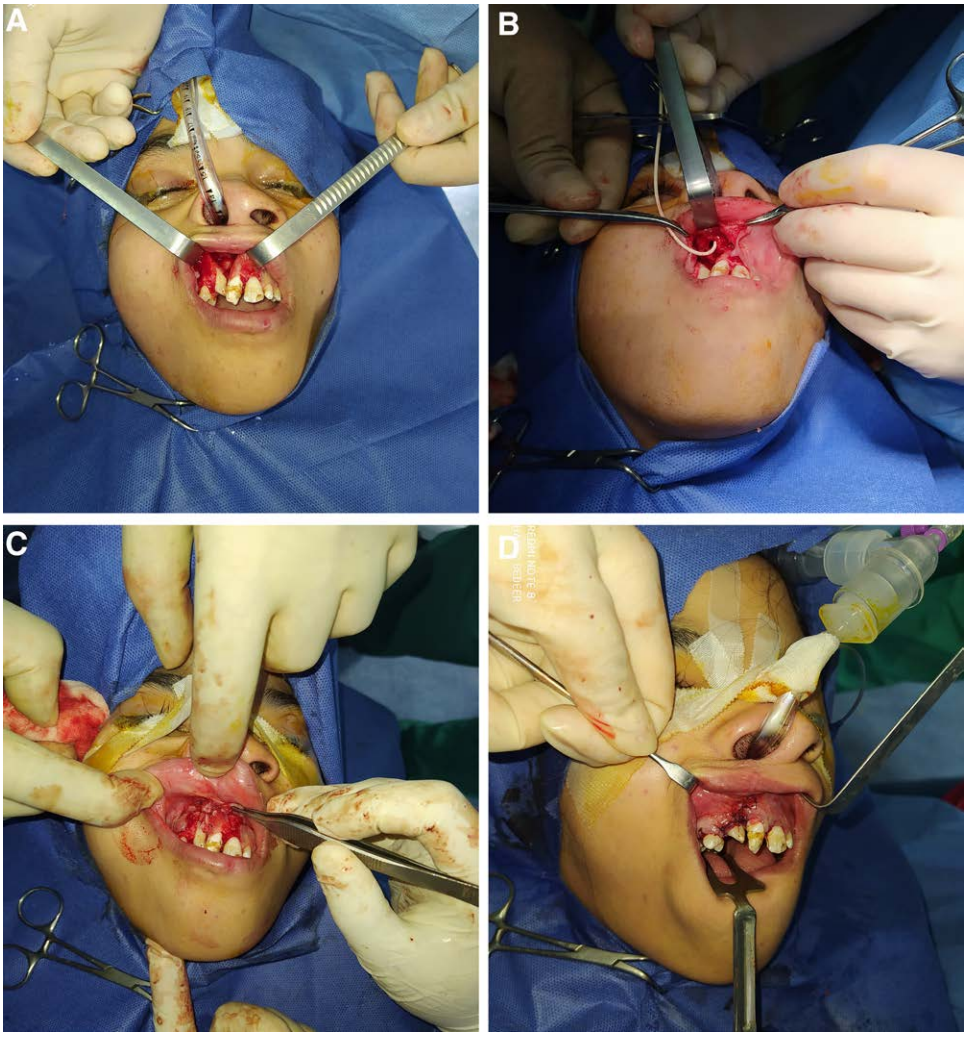

Fig. 3. Surgical technique. A case of a female patient, 11 years old, who presented with a right complete cleft alveolus. A, Gingival sulcus incisions and elevation of the mucoperiosteal flap. B, Detection of oronasal fistula. C, Bone graft within the defect [autogenous iliac bone graft (group A)]. D, Closure of the mucoperiosteal flap.

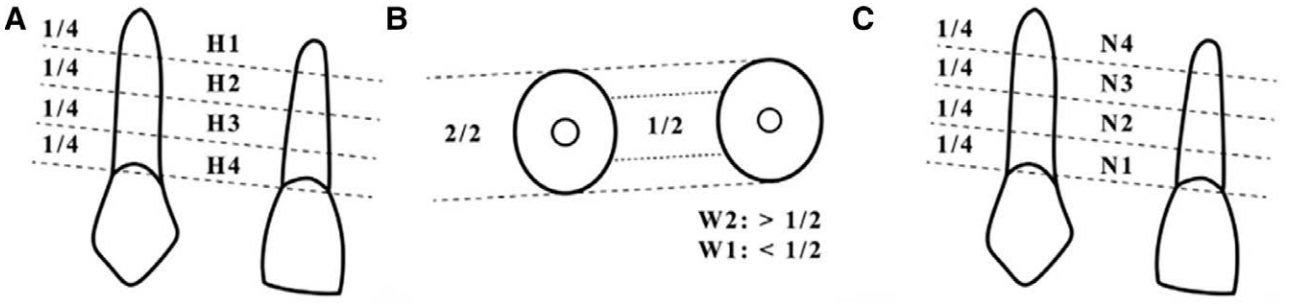

Fig. 4. Schematic illustration of the new success scale for alveolar cleft repair. Bone height—H, coronal slice (A); bone width—W, axial slice (B); nasal floor—N, coronal slice (C).[13] Reproduced from Kamperos G, Theologie-Lygidakis N, Tsiklakis K, et al. A novel success scale for evaluating alveolar cleft repair using cone-beam computed tomography. *J Craniomaxillofac Surg.* 2020;48:391–398. © 2020 Elsevier. Used with permission.

The study assigned each case three scores (H, W, and N) to form a total score of 10 for total success, 9 for acceptable results, 8 for compromised results, 7 for unfavorable results, 6 for extremely unfavorable results, and 0 for total failure. Total scores 9–10 were defined as success and total scores 0–8, as failure. Representative cases are presented in Figures 5 and 6.

Table 1. The New Success Scale for Alveolar Cleft Repair, Based on CBCT[13]

New Success Scale for Alveolar Cleft Repair		
Bone height (H)	H4	>3/4 of normal height
	H3	1/2–3/4 of normal height
	H2	1/4–1/2 of normal height
	H1	<1/4 of normal height
	H0	No continuous bony bridge across the clef
Bone width (W)	W2	>1/2 of the width of the adjacent roots
	W1	<1/2 of the width of the adjacent roots
	W0	No continuous bony bridge across the cleft
Nasal floor (N)	N4	Extent of the nasal floor up to the apical 1/4 of the adjacent root
	N3	Extent of the nasal floor up to 1/2 of the adjacent roots
	N2	Extent of the nasal floor up to 3/4 of the adjacent roots
	N1	Extent of the nasal floor more than 3/4 of the adjacent roots, approaching the cementoenamel junction.
	N0	No continuous bony bridge across the cleft
Expression of total score	Score-10	Total success
	Score-9	Acceptable
	Score-8	Compromised
	Score-7	Unfavorable
	Score-6	Extremely unfavorable
	Score-0	Total failure

CBCT: cone beam computed tomography.

Statistical Analysis

Statistical analysis was performed using IBM SPSS Statistics, version 23, 64 bits. Symmetrically distributed parameters were presented as the mean and SD. Student *t* tests were used to compare continuous variables between both groups, whereas paired *t* tests were compared between baseline and follow-up data in each separate group. The chi-square test was applied to analyze categorical data. In general, the level of confidence was kept at 95%, and a *P* value less than 0.05 was set as the level of significance.

RESULTS

Clinical Outcomes (Table 2)

In group A, there were 10 men and eight women, and in group B, there were eight men and 10 women ($P = 0.505$). Both groups had insignificant differences with regard to the mean age of patients ($P = 0.11$), patients' sex ($P = 0.5$), and detected ONF ($P = 0.07$). Group A had a significantly longer duration of surgery (100 ± 21.21 versus 81.11 ± 21.99 (minutes); $P = 0.013$). One of the patients (#16) had minor ONF, which had been discovered only during surgery, not during preoperative evaluation.

There was a significant difference in the duration of hospital stay between the two groups; it was about 4.33 ± 0.97 versus 1.94 ± 0.54 for patients in groups A and B, respectively. Improvement in alar base symmetry was achieved in both groups; around 72% of cases in group A showed 25%–50% improvement, whereas in group B it was about 66%.

None of the patients showed complete dehiscence at the grafted site. In group A, three (16.7%) patients showed partial dehiscence without bone loss, whereas in group B, four (22.2%) patients showed partial dehiscence (one patient with slight xenograft loss, whereas the three other patients had partial dehiscence without xenograft loss). It was seen that the unerupted tooth had erupted through the grafted bone in seven patients in group A and six in group B (Fig. 5).

All cases in group A experienced pain and gait disruption; however, no other donor site complications such as infection, hypertrophic scarring, or dehiscence were reported.

Radiological Outcomes (Table 3)

All patients had a score of 0 at the baseline evaluation before the correction. Both groups postoperatively had insignificant differences regarding bone height, bone width, nasal floor, and total postoperative success score. Total success was reported in seven (38.9%) and four (22.2%) patients in groups A and B, respectively ($P = 0.278$). Acceptable success was reported in five (27.8%) and seven (38.9%) patients in groups A and B, respectively ($P = 0.4795$). A compromised result was reported in two (11.1%) patients and in one (5.6%) patient in groups A and B, respectively ($P = 0.546$). Unfavorable results were reported in one (5.6%) and two (11.1%) patients in groups A and B, respectively ($P = 0.546$). Extremely unfavorable results were reported in two (11.1%) patients in each group ($P = 1$). Total failure was reported in one (5.6%) and two (11.1%) patients in groups A and B, respectively ($P = 0.546$).

DISCUSSION

Clefting of the alveolar process occurs in 75% of patients with CLP. A perialveolar ONF connects the alveolus, anterior hard palate, and nasal floor and is commonly associated with a bony cleft.[16]

The age for alveolar reconstruction is debated, and the timing of alveolar reconstruction is influenced by maxillary growth and dental age.[17] Maxillary growth is complete around 8 years, whereas maxillary canine eruptions typically occur before 10. Grafting should be completed before the canine eruption for tooth stability.[18,19] In our study, there were 18 cases in each group. In group A, six patients were under 10 years old, whereas 12 were over 10 years old. In group B, 11 patients were under 10 years old, whereas seven were over 10 years old. Despite this wide range of age, there was no significant correlation between the age of the patients and graft failure/success. This result is similar to those of Murthy and Lehman[20] and Mahardawi et al.[21]

Despite the widespread belief that the iliac bone is safe to use as a source for ABGs, there have been instances of problems, such as pain, scarring, prolonged hospitalization, and sensory loss,[22–24] that have prompted researchers to look for less intrusive ways to harvest the bone.[25] Trephination is a preferred technique over curettage for large autologous bone grafts, but cautious harvesting, meticulous consideration of three-dimensional anatomy, and well-controlled trephination depth are essential.[26]

In our study, almost all the patients experienced moderate to severe pain following iliac crest harvesting on the

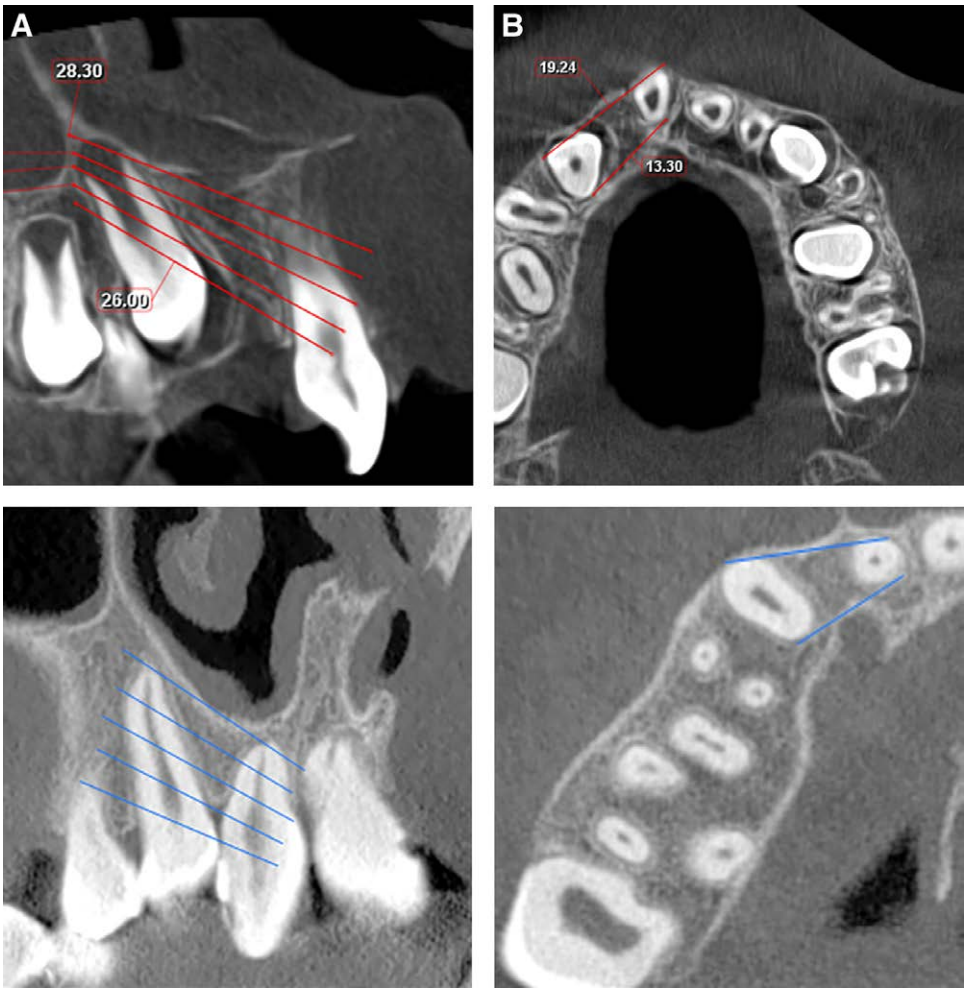

Fig. 5. Reconstructive cases with autogenous bone grafts using the new success scale. Total score (bone height: H, bone width: W, nasal floor: N): (column top to bottom) coronal slice (A); axial slice (B).

second day, with scores ranging from 4 to 10 on the visual analogue scale. Six patients continued to experience pain on the 14th day, with scores ranging from 1 to 6 on the VAS. All patients experienced gait disruption on days 1 and 2, and only two patients on day 14, which resolved over time. Our clinical results regarding pain and gait disturbance corroborated the findings of Swan et al[27] and Kumar and Rattan.[15]

Xenograft is an inexpensive, readily available material, easy to prepare, and easy to apply. These all influenced the procedure's cost, the length of the operation, the hospital stay, and single teamwork.

Recently, a new protocol for outpatient iliac crest bone grafting has been introduced, allowing patients to recover in their familiar home environment.[28] In our study, this was a crucial goal we worked to achieve. In group B, which had xenograft with PRF, the mean duration of hospital stay was 2 days, which is lower than most previous studies. In group A, the mean duration of hospital stay was 4 days, which was similar to that reported by many other investigators.[24,27,29]

The Bergland scale is a widely used tool for evaluating ABGs, categorizing cases based on radiographic measurements of the bony bridge.[30] Other scales, such as the Enemark, Long, Kindelan, Chelsea, and SWAG scales,[31–35] have limitations because they only use plain radiographs for bone height assessment, and traditional x-rays have imaging issues.[13] Few CT studies have established standards for postsurgical outcomes, lacking a unified success scale that considers all aspects of the bony bridge. It is suggested to use two independent measures for assessing the height and width of the bridge, with a total score generated from each dimension.[36,37]

Kamperos et al reported a unique scale that is the first to take into account all dimensions of the bone bridge and establish a single threshold for successful results. The radiographic outcome in terms of bone height, width, and nasal floor gained postoperatively using CBCT radiographs has been used as a standard method to measure the success of the graft.[13]

Our outcomes at the 6-month follow-up are in agreement with the study by Kamperos et al, who reported that the success rate using cancellous bone is about 61%. The success rate in group B was around 61%, which was in agreement with the study by Kumar et al, who reported it to be 69%.[15]

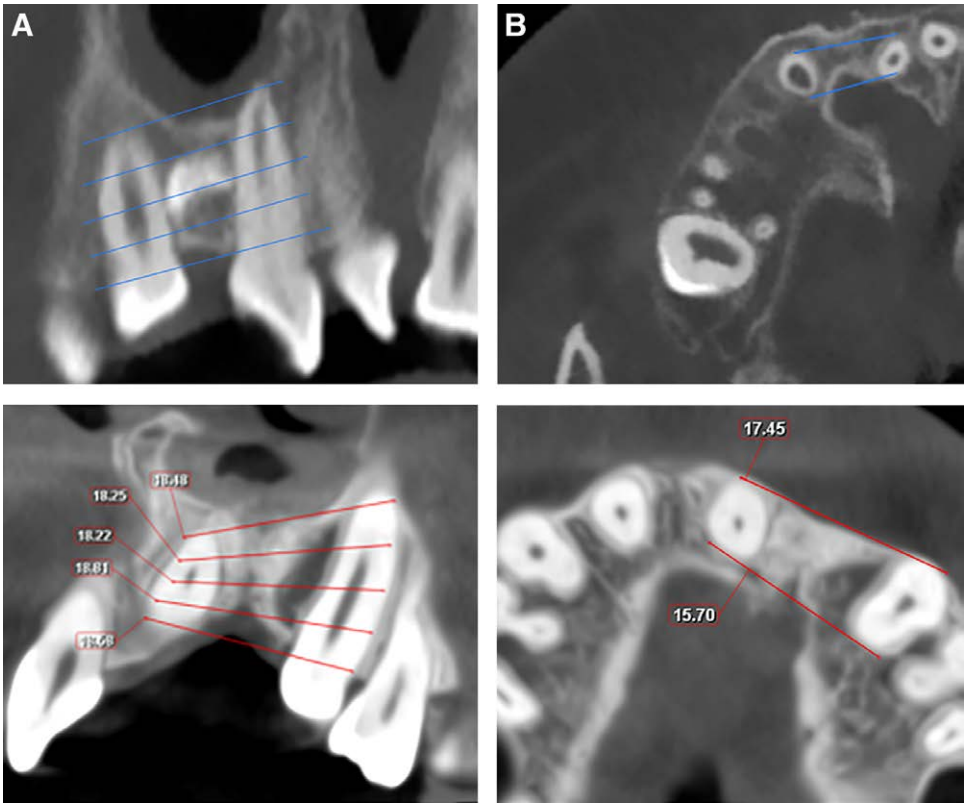

Fig. 6. Reconstructive cases with xenograft and PRF using the new success scale. Total score (bone height: H, bone width: W, nasal floor: N): (column top to bottom) coronal slice (A); axial slice (B).

Table 2. Patient Demographic, Presurgical, Surgical, and Postsurgical Parameters

Criteria	Group A	Group B	*P*
Baseline data			
Age (y)	12.13 ± 3.07	10.56 ± 1.96	0.070
Sex			
Male	10 (55.6%)	8 (44.4%)	0.505
Female	8 (44.4%)	10 (55.6%)	
ONF	18(100%)	15(83.3%)	0.070
Operative data			
Correction of ONF	18 (100%)	16 (88.9%)	0.146
Operative time (min)	100 ± 21.21	81.11 ± 21.99	0.013*
Postoperative evaluation			
Alar base symmetry			
0	5 (27.8%)	6 (33.3%)	0.717
1	13(72.2%)	12 (66.7%)	
Hospital stay (d)	4.33 ± 0.97 4 (3–6)	1.94 ± 0.54 2 (1–3)	0.000*
Dehiscence at cleft site	3 (16.7%)	4 (22.2%)	0.674

ONF: oronasal fistula.

Alnajjar et al filled the alveolar cleft using injectable PRF and xenograft. They then used CBCT to compare the bone density with that of the control group, which received an autogenous bone transplant. The authors concluded that the application of I-PRF with xenograft may show favor in bone formation over autogenous bone grafts.[38] It is controversial to use CBCT as a method to measure bone density because CBCT images are expected to cause errors when defining the density of scanned structures due to inconsistencies and arbitrariness of gray values, especially when related to abrupt changes of density in the object, x-ray beam hardening effect, scattered radiation, and projection data discontinuity-related effects, making the validity of the measurements obtained questionable.[39]

There are many factors that may have a great impact on the graft prognosis, including cleft bilaterality, cleft size more than 10 mm, and proper wound closure.[40] Patients with bilateral clefts face a five-fold higher risk of postoperative complications, bone loss, or reoperation compared with those with unilateral clefts.[21] The final bone dimension may be significantly influenced by the fibrous inclusion between the bone graft particles.[40]

There are many other factors that should be considered while evaluating ABG. In our opinion, they could also be considered aims rather than factors. They are all related to future events for the concerned patients, including the eruption of teeth (lateral incisor and canine) and their proper placement through bone grafting[41]; nostril base augmentation, also known as intermediate rhinoplasty, which is thought to be best done after orthodontic alignment; and ABG, because it provides a stronger skeletal support for longer-lasting correction.[42] Dental implant stability is another point to be considered, which has the role of supporting dental prostheses, loading augmentation material in the cleft area, and preventing severe bone

Table 3. Pre- and Postoperative Success Scale among the Studied Groups

	Group A	Group B	*P*
Preoperative score	18 (100%)	18 (100%)	—
Postoperative assessment			
Bone height			0.864
H4	8 (44.4%)	6 (33.3%)	
H3	5 (27.8%)	7 (38.9%)	
H2	2 (11.1%)	1 (5.6%)	
H1	2 (11.1%)	2 (11.1%)	
H0	1 (5.6%)	2 (11.1%)	
Bone width			0.730
W2	14 (77.7)	12 (66.7%)	
W1	3 (16.7%)	4 (22.2%)	
W0	1 (5.6%)	2 (11.1%)	
Nasal floor			0.847
N4	15 (83.3%)	13 (72.2%)	
N3	1 (5.6%)	2 (11.1%)	
N2	1 (5.6%)	1 (5.6%)	
N1	0	0	
N0	1 (5.6%)	2 (11.1%)	
Total postoperative score			
Score-0	1 (5.6%)	2 (11.1%)	0.828
Score-6	2 (11.1%)	2 (11.1%)	
Score-7	1 (5.6%)	2 (11.1%)	
Score-8	2 (11.1%)	1 (5.6%)	
Score-9	5 (27.8%)	7 (38.9%)	
Score-10	7 (38.9%)	4 (22.2%)	

Data expressed as frequency (%). The *P* value was significant if it was less than 0.05.
Group A: the autogenous iliac bone graft was used to fill the alveolar defect.
Group B: xenograft with PRF was used to fill the alveolar defect.

atrophy.[43] According to Matsui et al,[44] adequate bone availability is essential for effective implant treatment in this patient group. In the current study, there was no line of demarcation between the alveolar bone and the grafted bone, which means a high degree of stability as well as canine eruption in some cases in both groups.

The limitations of the current study included a relatively small sample size, being conducted in a single center, the short-term follow-up of those patients, and the radiological analysis being performed by one observer. Yet, being a randomized controlled trial is considered a strength point of the study.

CONCLUSIONS

Alveolar clefts should undergo bone grafting to improve the chances for a complete dental rehabilitation. This study revealed that xenograft with PRF is a viable alternative for alveolar cleft reconstruction. The results of the xenograft-PRF combination were similar to those of autogenous ABG, and so it could be used as an alternative when ABG is risky or difficult to harvest. Also, it is associated with considerable successful scores. To our knowledge, this is the first study that compares autologous ICBG versus xenograft with PRF in its gel form in cleft alveolus grafting.

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DISCLOSURE

The authors have no financial interest to declare in relation to the content of this article.

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The current study was registered at clinicaltrials.gov with ID: NCT04693741.

ETHICAL APPROVAL

Ethics statement/confirmation of patients' permission: The study obtained approval from the institutional review board of the Faculty of Medicine, Assiut University, with IRB no. 17101305. The current work was conducted In line with the Declaration of Helsinki.

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