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EVALUATION OF PLATELET-RICH FIBRIN/ BIPHASIC CALCIUM PHOSPHATE EFFECT VERSUS AUTOGENOUS BONE GRAFT ON RECONSTRUCTION OF ALVEOLAR CLEFT DEFECT IN THE MAXILLARY ARCH: A RANDOMIZED CONTROLLED CLINICAL TRIAL

Heba Samra [1], Hamida Refai [2], Hassan Abdel-Ghany [3]

[1.] PhD student, Department of Oral and Maxillofacial Surgery, Faculty of Dentistry, Cairo University, Egypt E-mail**:** hebatallah_samra@yahoo.com Hebatallah.samra@dentistry.cu.edu.eg,

[2.]Professor, Department of Oral and Maxillofacial Surgery, Faculty of Dentistry, Cairo University, Egypt **E-mail:** hamida.refai@dentistry.cu.edu.eg,

[3.] Hassan Abdel-Ghany: Professor, Department of Oral and Maxillofacial Surgery, Faculty of Dentistry, Cairo University, Cairo, Egypt E-mail: hassan_ao@yahoo.com

*Corresponding author: Heba Samra PhD student, Department of Oral and Maxillofacial Surgery, Faculty of Dentistry, Cairo University, Egypt E-mail: Hebatallah.samra@dentistry.cu.edu.eg

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ABSTRACT

Background: Autogenous iliac bone is considered the gold standard grafting material for reconstruction of alveolar cleft defect. However, its donor side morbidity nictitates searching for an alternative. Biphasic calcium phosphate combined platelets rich fibrin (BCP/PRF) has been actively investigated as a grafting material for reconstruction of other bony defects with promising results.

Purpose: the purpose of this study was to investigate whether BCP/PRF can be proper alternative to autogenous bone graft in reconstruction of alveolar cleft defect.

Study Design: This study is a parallel randomized controlled clinical trial. The study population was composed of 18 patients with alveolar cleft recruited at outpatient clinic of oral and maxillofacial surgery department, Faculty of Dentistry, Cairo University, Egypt from November 2017 to January 2023. They were randomly allocated to one of two study arms: the intervention (BCP + PRF) group in which the alveolar cleft defect was grafted with BCP/PRF or the control group in which the alveolar cleft defect was grafted with autogenous iliac bone graft. Predictable variable grafting material (BCP/PRF) versus iliac graft.

Main outcome Variable(s): The primary outcome was bone height (distance between the alveolar ridge and the most coronal part of grafted region). The secondary outcomes were volume of bone bridge (summation of multiplying area by thickness) and operative duration (time elapsed between using the scalable for incision and the last stitch).

Covariates: Covariates included patient demographics, operated side, type of cleft, previous bone grafting, volume of preoperative bone defect and volume of grafting material.

Analysis: The used tests were Chi-square test, Fisher's Exact, Student t-test Pearson coefficient, Paired t-test. Statistical significance was defined as $p \leq 0.05$.

Results: No statistically significant difference was noted after 6 months in bone height between the two groups (MD -1.88; 95% CI - 4.67 to 0.91; p = 0.172). The iliac bone graft group had significant larger volume of bone bridging compared with the BCP +PRF group (MD -121.64; 95% CI-226.67 to -16.60; p = 0.026). The operative time in BCP +PRF group is significantly lower than that in the iliac bone graft group (MD - 0.99; 95% CI -1.19 to - 0.79; p = 0.001).

Conclusion: Autogenous bones graft is still the first choice for alveolar bone grafting. This clinical trial suggested that application of BCP/PRF composite in alveolar cleft reconstruction was safe and effective and could be a bone substitute candidate instead of autologous bone graft.

Key words: PRF, alveolar cleft reconstruction, Biphasic calcium phosphate, synthetic bone substitutes, Platelets concentrate.

1 INTRODUCTION

Alveolar cleft grafting is a constant step in 75% of patients with cleft lip and palate. One of the challenges facing maxillofacial surgeons during management of this anomaly is the choice of bone graft material. The most common used graft is autogenous bone harvested from iliac crest. Donor side morbidities motivate researchers to find an alternative bone substitute[1]. Biphasic calcium phosphate combined platelets concentrate has been recognized as bone substitute materials possessing osteoconductivity and biodegradation properties. This composite was used in cases of sinus floor elevation, socket preservation, intrabony defect repair with promising results[2'3'4'5'6]. The aim of this study was to evaluate the effectiveness of biphasic calcium phosphate combined PRF in reconstruction of alveolar cleft defect in randomized controlled clinical trial.

2.PATIENTS AND METHODS

2.1. study design

This study is a parallel randomized controlled single blinded clinical trial. The study population was composed of 18 patients with alveolar cleft recruited at outpatient clinic of oral and maxillofacial surgery department, Faculty of Dentistry, Cairo University, Egypt from November 2017 to January 2023. The inclusion criteria were patients with maxillary alveolar cleft defect, aged from 17 to 22 years old, free from systemic diseases and with adequate oral hygiene. Syndromic cases and patients with platelets disorders, hemoglobin less than 10 severe wide defects and metabolic bone disease were excluded.

2.2 Ethical Approval

The Research Ethics Committee at Faculty of Dentistry; Cairo University, Egypt approved this prospective randomized controlled clinical trial with an approval number 17119. The protocol of this study was also registered on Clinical Trials.gov with identifier: NCT03302429. The study was designed and conducted according to Helisiniki- Ethical Principles for medical research involving human participants. The patients were informed about the treatment procedure and its possible risks.

2.3. Randomization

After informed consent was obtained, each patient was randomly assigned into 1 of 2 equal groups; the intervention (BCP + PRF) group in which the alveolar cleft defect was grafted with BCP/PRF or the control group in which the alveolar cleft defect was grafted with autogenous iliac bone graft. Randomization was achieved through three steps sequence generation, allocation, concealment and implementation. Sequence generation was performed by generating numbers from 1:18 using Random Integer Set Generator, Randomness and Integrity Service Ltd (http://www.random.org/). Each generated random number represented the number of patients with a letter A (for intervention) or B (for control) in a random manner.

Allocation concealment had been done using opaque sealed envelopes. The envelope's content was 8 times folded to ensure that the contents will not be visible when held up to a light source. In the implementation step, the participants chose between opaque sealed envelopes. Then the personal information (patient's name, ID no), and the assigned group had been recorded and written on the envelope.

2.4. Preoperative procedures

The demographic data, past medical and dental history, extra-oral and intra-oral examination**,** CBCT examination for each patient were documented in his/her diagnostic sheet. Orthodontic treatment was performed prior to bone grafting to correct the rotated central incisors and cross bite, and to provide the surgeon with better access for graft placement and soft tissue closure. Routine laboratory investigations including complete blood picture (CBC), coagulation profile (PT, PTT, and INR), liver function tests and kidney function tests were performed. Chest radiograph was mandatory to detect covid 19 cases.

2.5. Operative procedures

All patients were operated on by the same surgeon under general anesthesia using naso-endotracheal intubation. Immediately after induction of General Anaesthesia, intravenous injection of 1.5 gm Sulbactam / Ampicillin (Unsayn 1.5 gm, Pfizer, Egypt). and dexamethasone Naph 8 mg/ml (Dexamethasone 8mg/mL EIPICO) was performed. With the patient in supine position, the surgical field was scrubbed with Betadine (Povidone iodine 10% The Nile Co. for pharmaceuticles and chemical industries- Cairo A.R.E) and the patient was draped according to regular surgical standers.

Local anesthetic solution (Mepivicaine 2% and levonordefrin 1:20000) (Mepvicaine -L Alexandria pharmaceuticals-A.R. E) was infiltrated at the incision lines for hemostasis. Sulcular incision was performed using no.15 blade scalpel, around the neck of teeth adjacent to the cleft defect and extends up to the first molar on the lesser segment and at least two teeth distal to the canine on the greater segment. Releasing incision distal to the first molar was performed to achieve further access and facilitate tension free primary closure above the grafted defect. A vertical incision was made mid-way along the buco-palatal width of the cleft margin. Full thickness

mucoperiosteal flaps were reflected up to the pyriform exposing the labial bone and the alveolar cleft defect. The labial mucosa was separated sharply from the nasal mucosa and soft tissue pocket was created by closing the nasal floor and the palatal mucoperiosteum across the cleft site with simple interrupted sutures using 5/0 vicryl sutures (Assucryl,Assut sutures, Switzerland).

2.5.1. BCP + PRF Preparation: Patient's venous blood was drawn by the anesthetist into two 10 ml sterile vacutainer tubes without anticoagulant. Then the vacutainer tubes were placed in the rotor of the centrifuge machine (80-1, Desktop, Low speed, Electronic Centrifuge, China). To balance the centrifuge, a vacutainer filled with saline was placed opposite to each vacutainer filled with blood in the centrifuge rotor. Centrifugation parameters were set to 3000 rpm, and the centrifugation time was 12 minutes. The centrifuge spun and separated the blood in each vacutainer into three distinct layers; lower layer of red blood cells, middle layer containing fibrin clot and the upper layer containing acellular plasma. The fibrin clot was detached from the centrifuged blood and then squeezed between two sterile glass slaps to mold it into membrane.

Biphasic calcium phosphate (BCP) products (Guidor Easy-graft CRYSTAL products, Sunstar) are bioresorbable, completely synthetic bone graft substitutes. They consist of two components: Granules and BioLinker. The granules are biphasic calcium phosphate (BCP) [60% hydroxyapatite (HA) and 40% beta-tricalcium phosphate (ß-TCP)] with a particle size 450-1000µm and contained in 3x0, 25ml syringe. The biolinker is N-Methyl-2-pyrrolidone-solution contained in ampulla combining these two components, the easy-graft material becomes a putty-like biomaterial and can be applied directly from the syringe into the bone defect.

2.5.2. Harvesting of iliac graft:

Grafting from the iliac crest was always performed in a two-team approach. The patient was placed in the supine position; a rolled towel was placed beneath the buttock to elevate and rotate the anterior iliac crest. The surgical field was decontaminated with Betadine (Povidone iodine 10% The Nile Co. for pharmaceuticles and chemical industries- Cairo A.R.E.) and a sterile drape was applied. Hypotensive general anaesthesia was used to decrease blood loss from the donor site. The antero-superior iliac spine was palpated. The skin was pulled over the crest laterally to keep the incision away from the bony prominences and belt line. The incision was 5cm in length and started 2cm posterior to the anterior superior iliac spine to avoid damaging the lateral femoral cutaneous nerve and it was parallel to the anterosuperior part of the crest .The initial incision was performed through subcutaneous tissue to the superficial fascia. A white line of periosteum between the gluteal and abdominal muscles was identified, and the incision was continued down to the bone. Subperiosteal dissection was carried out medially to insert oblique and transverse muscles retractors to expose the donor site and protect the abdominal cavity. Cortico-cancellous block was harvested by osteotomising the medial side of the crest. Two parallel vertical cuts were made with a surgical bur and continued with a chisel and mallet (Split technique). Extra cancellous bone had been harvested once the blocks have been removed. Debridement of the wound was then performed with normal saline solution and sutured in layers (muscles and subcutaneous tissues were sutured with 4/0 vicryl (Assucryl,Assut sutures,Switzerland) and the skin incision was sutured with simple interrupted suture using Prolene (Polypropylene, Assut sutures,Switzerland). A compressive dressing was applied on the iliac crest wound and maintained for 48 hours postoperatively.

2.5.3. Grafting procedures:

In the study group PRF membrane was placed on the nasal mucosa. The BCP (Guidor Easy-graft CRYSTAL products, Sunstar) was applied directly from the syringe into the defect condensed well and molded to cover bone edges of the cleft defect finally PRF membrane cover BCP material. The mucoperiosteal flaps were repositioned and sutured in a tension free manner with interrupted suture. In the control group Corticocancellous block was placed to the two segments of then the cancellous harvested bone was packed into the soft tissue pocket. The flaps were repositioned and sutured with 5-0 vicryl.

Grafting procedures in the study group, (A) PRF membrane covering nasal mucosa,(B) easy graft apply directly from the syringe into the defect (C) BCP packed and condensed to fill the alveolar defect,(D) PRF membrane covering biphasic calcium phosphate bone graft, (E&F) Watertight tension free closure of the alveolar cleft after grafting (E)labial and (F) palatal mucosal closure with 5-0 vicryl

Post-operative care and instruction

Hospital discharge occurred the same day of the surgical procedure in both groups. Postoperative medications included Intramuscular antibiotic 1.5 gm Ampicillin/sulbactam vials (Unasyn, Pfizer Egypt/ vial) twice daily for the first two days followed by oral antibiotics Sultamicillin 375 mg tablets (Unasyn, Pfizer Egypt/ tablet) every 8 hours for 5 days. Patients in control group were advised to apply topical antibiotic Fusidic acid 2% (Fucidin 2%,

Minapharm,Egypt) on the iliac crest wound after removal of the overlying dressing for 7 days. Non-steroidal anti-inflammatory analgesic ibuprofen 400 mg tab was prescribed twice daily after meal. Intramuscular dexamethasone phosphate 8mg amp (Dexamethazone 8mg/mL EIPICO.)
once after surgery and Fexofenadine 120 mg tab (Telfast,Aventis,Egtpt.) once daily for 5 days before sleeping. Xylometazoline hydrochloride one drop in each nostril was advised three times per day for five days only. Oral hygiene is encouraged after each meal by rinsing their mouths with 0.12% chlorohexidine gluconate solution (Antiseptol,Kahira Pharma,Cairo,Egypt.) starting the day after surgery.

Patients in control group were instructed to minimize ambulation for the first 48 hours. The patients in both groups were instructed to avoid blowing the nose, drinking using straw, spitting and breathing down. Coughing and sneezing should be done with an open mouth until the stitch-out and using cold liquid diet for a week. After that they shift to mechanical soft diet for 4 weeks. They were advised to avoid biting with their incisors for 4 weeks.

Data collection

4.1. Operation duration: The time elapsed between using the scalable for incision and the last stitch was measured by watch in hours.

4.2. Clinical assessment Period: Patients were clinically assessed weekly in the first month, then monthly up to six months postoperatively. In each visit, patients were assessed for pain; signs of fever, edema, wound dehiscence, pus discharge, potential graft exposure, nasal regurgitation and regarding healing of donor site, clinical assessment include gait disturbance, numbness, itching and pain. After 3 months, patients resumed periodic evaluations with the orthodontic team.

4.3. Radiographic assessment:

Cone beam computed tomography (CBCT) scan was performed, one week preoperative, two weeks and 6 months postoperatively CBCT machine used in this study was characterized by the followings: The X-ray tube used to scan the samples possesses a current intensity 14 mA, Kilovoltage 90 Kvp. The scanning time was 9 seconds of pulsed exposure resulting in an effective exposure time 2.5 seconds to scan FOV of 8 cm Height x 11cm and Width x 10 cm Depth, FOV adjustment was guided by three laser light beams to centralize the area of interest within the scanning field. The raw DICOM data set obtained from the CBCT scanning was imported to special third-party software for secondary reconstruction.

All measurements were taken by a single rater with the same center and device at three different times. The outcome assessor was blinded to avoid biased treatment effect estimations.

In coronal plane, the vertical bone height at the cleft site after 6 months was measured in millimeters through drawing two tangents parallel to each other and parallel to the floor; one line tangent to the alveolar ridge and the second line tangent to the most coronal part of grafted region. Then a perpendicular was drawn between the two tangents the distance between the two tangents represents the height of bony bridge in the 6 postoperative months (Fig. 1).

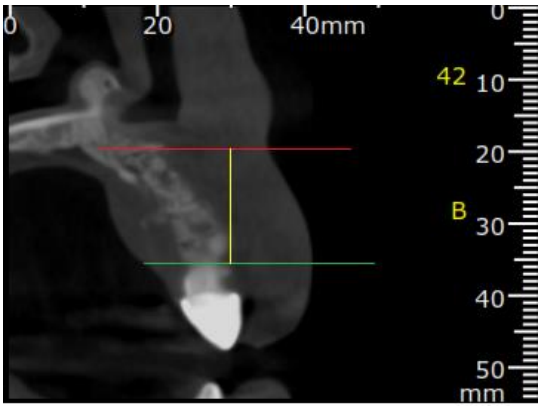

Figure 1. CBCT radiograph showing measuring the vertical bone height at the cleft site 6 months postoperatively in the study group; the red line tangent to the most coronal part of the bony bridge, the green line tangent to the most crestal part of bone bridge and the yellow line perpendicular on both tangents represent the height of bone bridge.

According to Feichtinger. et al., (2006)[7] the volumes of alveolar cleft defect in both groups were calculated in two steps; first by free hand tracing to the area of interest on axial cuts using the drawing tools of the navigation system (Fig.2).

The traced boundary of cleft area was the width of the cleft which extend between adjacent teeth of the cleft extending to the lower margin of the anterior nasal aperture to the crest of the alveolar ridge

The navigation system calculated the area. Secondly the volume was calculated (in cubic millimeters) using the following formula: V= (A1xT) + (A2 xT) + ……. + (An xT) where: V= volume, A= area, N=number of slices and T= thickness of the axial C.T slice. The volume of the packed grafting materials at the 2nd postoperative week and the volume of bone bridging the alveolar cleft at the 6th postoperative month were calculated in the same way. The percentage of grafting material packing was calculated using the formula volume of the packed grafting materials/volume of preoperative cleft defect × 100. The percentage of bone fill was calculated using the formula volume of bone bridge/volume of preoperative cleft defect × 100. The measurements

were performed three times with a time gap of two weeks. The measurements were performed with a single assessor to prevent interoperator errors. The assessor was blinded to the treatment group to prevent bias.

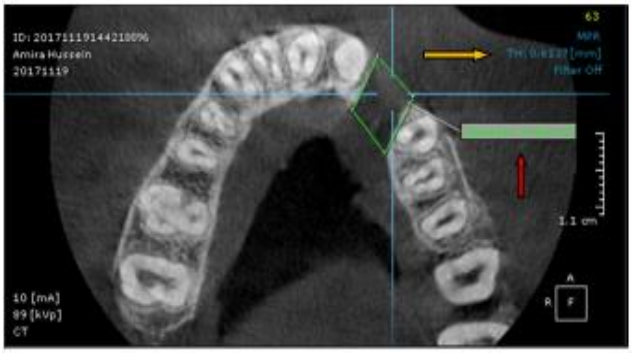

Figure 2. Axial cut CBCT radiograph showing tracing of the cleft defect area to calculate volume. Red arrow refers to surface area measure (A) and yellow arrow refers to thickness of axial C.T slice (T).

Statistical analysis

Data was fed to the computer and analyzed using IBM SPSS software package version 20.0. (Armonk, NY: IBM Corp). Qualitative data were described using number and percentage. The Shapiro-Wilk Test was used to verify the normality of distribution Quantitative data were described using range (minimum and maximum), mean, standard deviation, median and interquartile range (IQR). The significance of the results obtained was judged at the 5% level .

The tests used were - Chi-square test. For categorical variables, to compare between different groups; Fisher's Exact correction for chi-square when more than 20% of the cells have expected count less than 5; Student t-test for normally distributed quantitative variables, to compare between two studied groups - Pearson coefficient to correlate between two normally distributed quantitative variables Paired t-test for normally distributed quantitative variables, to compare between two defects.

3.Results

The flow diagram of the study is shown in figure 3. The demographic characteristics and statistical comparison of the two groups are illustrated in Table 1. Among the 9 patients in BCP + PRF group, there were 3 male patients and 6 female patients and in the iliac bone graft group there were 4 male patients and 5 female patients. The mean age of patients in both groups was 20.11 years. Among the type of clefts in BCP + PRF group, there were 7 unilateral and 2 bilateral cleft cases whereas in iliac bone graft group there were 6 unilateral and 3 bilateral cleft cases. However, the bilateral cases were previously operated, and one side was failed. Six patients in BCP + PRF group had previous bone grafting of the alveolar cleft versus 5 patients in iliac bone graft group. There was statistically non-significant difference between the two groups regarding the gender distributions, age and type, operated side and previous bone grafting of the alveolar cleft.

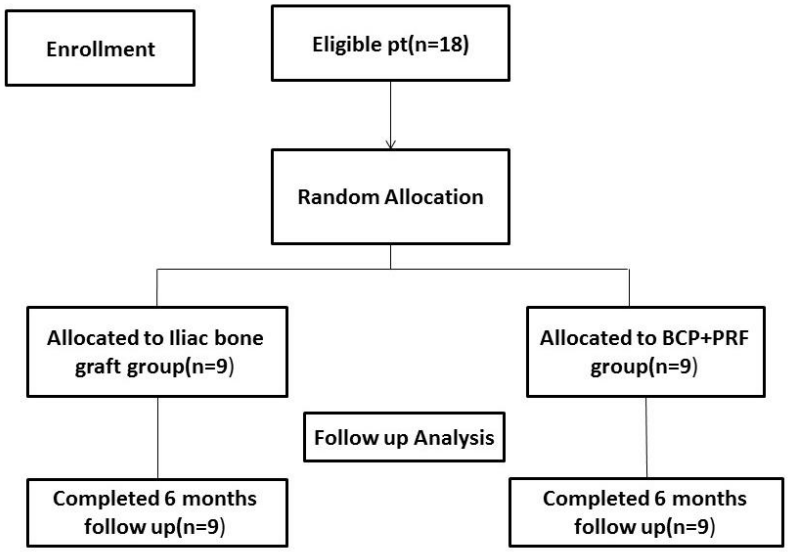

Figure 3. Flow diagram of the study. n number of patients, BCP biphasic calcium phosphate, PRF platelet-rich fibrin.

Table 1. BIVARIATE ANALYSIS OF PRIMARY PREDICTOR VARIABLE VERSUS COVARIATES

	BCP + PRF group (n = 9)		**Iliac bone graft group (n = 9)**		**Test of Sig.**	**P**
	No.	**%**	**No.**	**%**		
sex Male Female	3 6	33.3 66.7	4 5	44.4 55.6	χ^2= 0.234	^{FE}p= 1.000
Age (years) Min. – Max. Mean ± SD. Median (IQR)	17.0 – 22.0 20.11±1.83 20.0 (19.0 – 22.0)		18.0 – 22.0 20.11±1.54 20.0 (19.0 – 21.0)		t= 0.000	1.000
Mean diff. (LL–UL 95%C. I)	0.0 (-1.69 – 1.69)					
Operated side Right Left	3 6	33.3 66.7	4 5	44.4 55.6	χ^2= 0.234	^{FE}p= 1.000
Type of cleft Unilateral Bilateral	7 2	77.8 22.2	6 3	66.7 33.3	χ^2= 0.277	^{FE}p= 1.000
Previous bone grafting Absent Present	3 6	33.3 66.7	4 5	44.4 55.6	χ^2= 0.234	^{FE}p= 1.000

IQR: **Inter quartile range** SD: **Standard deviation** **t: Student t-test.**
χ^2: Chi **square test** FE**: Fisher Exact**
C.I: Confidence interval LL: Lower limit UL: Upper Limit
p: p value for comparing between the studied groups.

Primary wound healing was observed in all patients in the iliac bone graft group, whereas in BCP + PRF group, primary healing was noted in 7 patients. Wound dehiscence and infection occurred 2 weeks postoperatively in the remaining two patients in this group. Frequent irrigation and local dressing were used to promote secondary healing which was achieved in one of them after one month of follow-up. The other patient had pus discharge and unclosed fistula by the end of the study.

Clinical examination of donor site in the iliac bone graft group one week postoperatively revealed minimal edema and moderate pain without any sign of infection. The time taken to return to normal activities ranged from ten days to two weeks.

The duration of surgical procedures ranged from 1.92 - 2.50 h in BCP + PRF group with a mean of 2.20 ± 0.21 h, whereas they ranged from 2.92 - 3.42 h in the iliac bone graft group with a mean of 3.19 ± 0.18 h.

The student t-test comparing the two groups revealed that the operation time in BCP +PRF group is significantly lower than that in the iliac bone graft group (MD - 0.99; 95% CI -1.19 to - 0.79; p = 0.001). Table 3 summarizes the comparison of the duration of the surgical procedures between the groups.

Table 2 clarified the assessment of bone height at the cleft site after 6 months. Their means for study group and control group were 8.33 ± 3.26 and 10.21 ± 2.23mm, respectively. No statistically significant difference was noted after 6 months between the two groups (MD -1.88; 95% CI - 4.67 to 0.91; p = 0.172)

Table 2. BIVARIATE ANALYSIS OF PRIMARY PREDICTOR VARIABLE VERSUS PRIMARY OUTCOME VARIABLES

	BCP + PRF group (n = 9)	Iliac bone graft group (n = 9)	t	p	Mean diff. (LL–UL 95%C. I)
Bone height (mm)					
Min. – Max.	3.0 – 12.01	6.15 – 13.01	1.431	0.172	-1.88 (-4.67 – 0.91)
Mean ± SD.	8.33 ± 3.26	10.21 ± 2.23			
Median (IQR)	9.25(7.0 – 10.5)	10.55(9.4–11.8)			

IQR: **Inter quartile range** SD: **Standard deviation** **t: Student t-test.**
C.I: Confidence interval LL: Lower limit UL: Upper Limit
p: p value for comparing between the studied groups.
*: Statistically significant at $p \leq 0.05$

Table 3 summarizes the volumetric analysis of the bone bridging the alveolar cleft at the sixth postoperative month. Their means for BCP + PRF group and iliac bone graft group were 364.6 ± 84.45 and 486.2 ± 122.3 $mm^{3,}$ respectively. The iliac bone graft group had a significantly larger volume of bone bridging compared with the BCP + PRF group (MD -121.64; 95% CI-226.67 to -16.60; p = 0.026).

Table 3. BIVARIATE ANALYSIS OF PRIMARY PREDICTOR VARIABLE VERSUS SECONDARY OUTCOME VARIABLES

	BCP + PRF group (n = 9)	Iliac bone graft group (n = 9)	t	p	Mean diff. (LL–UL 95%C. I)
Bone bridging Volume (mm^3)					
Min. – Max.	267.3 – 515.3	331.3 – 661.3	2.455*	0.026*	-121.64 (-226.67 – -16.60)
Mean ± SD.	364.6 ± 84.45	486.2 ± 122.3			
Median (IQR)	350.2 (301.6 – 415.2)	440.4 (425.7 – 601.1)			
Duration of operation (hrs.)					
Min. – Max.	1.92 – 2.50	2.92 – 3.42	10.534	<0.001*	-0.99 (-1.19 – -0.79)
Mean ± SD.	2.20 ± 0.21	3.19 ± 0.18			
Median (IQR)	2.17 (2.0 – 2.3)	3.25 (3.0 – 3.3)			

IQR: **Inter quartile range** SD: **Standard deviation** **t: Student t-test.**
C.I: Confidence interval LL: Lower limit UL: Upper Limit
p: p value for comparing between the studied groups.
*: Statistically significant at $p \leq 0.05$

4.DISCUSSION

Alveolar cleft defect grafting is considered an obligatory step in management of patients with cleft lip / palate. It generally accepted that bone autograft is the gold standard grafting material. The iliac crest is the most frequently used site for harvesting bone autograft. However, autogenous bone graft has limitations, including donor-site morbidity, such as pain, infection, and nerve injury; volume limited quantity; blood loss; and prolonged operating time. The ideal substitute has not been identified yet, but the investigative search continues. In hopes of finding an alternative to bone autograft, the use of synthetic bone substitutes is becoming increasingly popular because of their biocompatibility, availability, sterility and bioactivity.

Most of information available regarding the use of synthetic bone substitutes in alveolar cleft defect is unreliable and questionable because it is derived from case reports or experimental animal models. More standardized clinical trials are needed to be performed

to assess the viability of synthetic bone substitutes in alveolar cleft reconstruction.

The aim of this randomized controlled clinical trial was to compare between BCP combined PRF and autogenous bone graft regarding bone volume and bone height and duration of surgical procedure in reconstruction of alveolar cleft defect. The results of this study showed that after 6 months, insignificant difference was noted in bone height between the two groups (MD -1.88; 95% CI - 4.67 to 0.91; p = 0.172), the iliac bone graft group had significant larger volume of bone bridging compared with the BCP +PRF group (MD -121.64; 95% CI-226.67 to -16.60; p = 0.026) and that the operative time in BCP +PRF group is significantly lower than that in the iliac bone graft group (MD - 0.99; 95% CI -1.19 to - 0.79; p = 0.001).

Our findings cannot be compared with previous studies because using combination of BCP with PRF has not been previously reported in alveolar cleft grafting except recent study published in 2023 by El-Rawee et al[8], but even this study performed on different age group and without using growth factors.

The present study investigated the outcome of alveolar bone grafting in adult patients. Their mean age was 20.11 years, ranging from 18-22 years. Tertiary bone grafting is not an option included when setting up the management protocol of cleft lip and palate patient, but it is a reality facing the maxillofacial surgeon who must treat the patient and achieve the goals available during this age stage. Preserving lateral incisor and permanent canine may not be rewarded during this age, but bridging the alveolar cleft defect with sufficient bone volume will improve nasal aesthetic and allow implant placement[9].

Primary wound healing was observed in all patients in the iliac bone graft group. This finding complements studies on alveolar bone grafting with iliac bone graft that showed successful outcome[10,11] Contrary, studies on larger samples reported several postoperative complications[12,13,14,15] . This difference may be attributed to the variations in methodology and sample size. In a retrospective study, 71 patients underwent alveolar bone grafting with anterior iliac crest or intraoral corticocancellous bone autografts (particulate, block, or mixed) found exposure of the graft associated with wound dehiscence (n = 13), infection of the wound with purulent discharge (n = 8), and resorption of the graft as reported at the orthodontic follow-up (n = 8)[12].

Primary healing was noted in 7 out of 9 patients in BCP + PRF group. Wound dehiscence and infection were observed 2 weeks postoperatively in the remaining two patients that could be attributed to poor oral hygiene. This observation supports that of Lundberg[16] who found that poor oral hygiene was associated with an increased risk of surgical failure after secondary alveolar bone grafting and highlighted the impact of local infection on healing and the importance of maintaining good oral hygiene during bone graft healing. Wound dehiscence with subsequent infection or exposure of the graft was previously reported regardless the type of grafting materials used for reconstruction of cleft and was attributed to several reasons including over packing of grafting material into the cleft, difficulty to find sufficient soft tissues to achieve watertight and tension-free closure of the grafted cleft, preoperative bone quality around the cleft-related teeth, scar from previous surgical procedures, poor compliance with postoperative oral hygiene and the presence of direct exposure to the contaminated oral and nasal environments[12,14,15,16]

One of the rationales behind the search for alternatives to autografts is to reduce the surgical time. The present study confirms this concept. Since the operation time in BCP+PRF group was significantly lower than that in the control group although grafting from the iliac crest was always performed in a two-team approach. The mean of operating time in BCP + PRF group was 2.20 ± 0.21 h, whereas it was 3.19 ± 0.18 h in the iliac bone graft group. This finding is somewhat different with that of Balaji[17], who compared in a retrospective study between rhBMP2 and iliac crest autograft for alveolar cleft repair and found that the difference between rhBMP2 and iliac crest graft treated cases in term of surgical time was statistically insignificant with the mean length of surgery for rhBMP2 group was 86.50 ± 20.18 minutes and that for iliac crest group was 97.17 ± 24.24 minutes[17]. The young ages of the patients at surgery in Balaji's study (8.26 ± 2.61 years) could explain this difference because of their relative smaller volume of alveolar cleft defects that entailed harvesting smaller amount of iliac grafting material thus reducing the time needed.

Bone height measurements and volumetric analysis are almost constant outcomes measured in alveolar cleft reconstruction procedures. Unfortunately, a wide variety of measuring methods and units has been used making accurate comparison between studies unreliable. Different measuring methods have been used for the assessment of bone bridge height in the alveolar region including absolute value in mm and Bergland and Chelsea scales[18,19]. In the present study, the mean bone height in iliac bone graft group 6 months postoperatively was 10.21 ± 2.23 mm which is shorter when compared with that observed by Alonso et al[18] who found the mean bone height was 13.5 mm ± 2.0. This may be due to the difference in demographic characteristics of the

participants in their study; aged 8 to 12 years with no previous alveolar surgery.

In the present study, the observed insignificant difference between the two groups at baseline regarding the covariates and the establishment of specific inclusion and exclusion criteria are important when judging the results. In the present study, no statistically significant differences in bone height and bone filling percentage were noted after 6 months between the two groups and the iliac bone graft group had significant larger volume of bone bridging than that of the BCP +PRF group. These findings are in general agreement with those of other previous studies comparing alloplastic grafting materials with autologous iliac bone graft in alveolar cleft reconstruction. A systematic review and meta-analysis of four randomized controlled trials focused on the effectiveness of autologous and alloplastic secondary alveolar bone grafting in children with cleft lip and palate found that autologous bone graft showed statistically significant higher bone formation after 6-month follow-up but no statistically significant difference was noted after a 1-year follow-up and no statistically significant difference in bone height was noted after 6-month and 1-year follow-up[19].

Comparing the two groups, the present study revealed a beneficial effect for the iliac bone graft group which had significant larger volume of bone bridging than that of the BCP +PRF group. Logistic issues also must be considered when comparing between these grafting materials that gives BCP +PRF some benefit over iliac bone graft including shorter operating time and sparing patients from the procedure of iliac crest harvesting is in itself a compelling reason to favor BCP + PRF use.

5.CONCLUSION

This clinical trial suggested that application of BCP/PRF composite in alveolar cleft reconstruction was safe and effective and could be a bone substitute candidate instead of autologous bone**.**

DECLARATIONS

Ethics approval and consent to participate

The study received ethical approval from the Ethics Committee of Dr. Soetomo General Hospital (approval number: 1152/KEPK/XI/2024).

Consent for publication

Not applicable.

Competing interests

The authors declare no conflict of interest.

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