Received: 12 April 2020 | Revised: 19 June 2020 | Accepted: 22 June 2020

DOI: 10.1111/cid.12935

WILEY

ORIGINAL ARTICLE

Radiological and histological evaluation of horizontal ridge augmentation using corticocancellous freeze-dried bone allograft with and without autogenous bone: A randomized controlled clinical trial

Mahtab Hashemipoor DDS, MSc[1] | Najmeh Asghari DMD[2] | Mohammad Mohammadi DDS, MSc[3] | Mahsa Kalantari DDS, MSc[4] | Mohaddese Arabsolghar DDS, MSc[3] | Hadi Ranjbar PhD[5]

[1]Department of Periodontics, Kashan Dental School, Kashan University of Medical Sciences, Kashan, Iran

[2]Henry M. Goldman School of Dental Medicine, Boston University, Boston, Massachusetts

[3]Oral and Dental Diseases Research Center and Department of Periodontics, Kerman Dental School, Kerman University of Medical Sciences, Kerman, Iran

[4]Department of Oral and Maxillofacial Pathology, and Oral and Dental Diseases Research Center, Kerman Dental School, Kerman University of Medical Sciences, Kerman, Iran

[5]Mental Health Research Center, Psychosocial Health Research Institute, Iran University of Medical Sciences, Tehran, Iran

Correspondence
Mohammad Mohammadi, Oral and Dental Diseases Research Center and Department of Periodontics, Kerman Dental School, Kerman University of Medical Sciences, Kerman, Iran.
Email: m_mohammadi@kmu.ac.ir, mmohammadi28@yahoo.com

Funding information
Kerman University of Medical Sciences, Grant/Award Number: 1

Abstract

Purpose: The purpose of this study was radiological and histological evaluation of horizontal ridge augmentation using corticocancellous freeze-dried bone allograft (FDBA) with and without autogenous bone (AB).

Materials and methods: The present research was conducted on 42 patients (27 females and 15 males) with insufficient width of edentulous ridge. The patients were randomly assigned into two groups, FDBA alone + collagen membrane (n = 21) and the combined FDBA and AB + collagen membrane (n = 21). The horizontal alveolar ridge dimensions were measured using cone-beam computerized tomography before and 6 months after alveolar ridge augmentation. At the time of insertion of implants, biopsy of new bone was taken from 11 patients in each group and was analyzed histologically. The obtained data were statistically analyzed with paired *t* test and two-sample *t* test. The registration number was IRCT201109165305N3.

Results: The mean ± SD ridge width gain after 6 months at the distance of 0, 2, 4, and 6 mm from crest of alveolar ridge was 2.78 ± 1.44, 3.05 ± 1.21, 2.82 ± 1.62, and 2.23 ± 1.95 mm in the FDBA group and 2.40 ± 1.60, 3.10 ± 1.80, 3.60 ± 1.87, and 2.65 ± 2.39 mm in the combined group, respectively, which was statistically significant in both groups using paired *t* test ($P < .001$). However, the difference between two groups analyzed by two-sample *t* test was not statistically significant ($P > .05$). Amount of new bone generation, remained particles, and connective tissue was not statistically different between two groups ($P = .367$, $P = .428$, and $P = .598$, respectively).

Conclusion: Based on the results of this study, corticocancellous FDBA granules along with collagen membrane can successfully be used for horizontal augmentation of edentulous ridge, and adding AB to the granules of FDBA does not significantly increase the quality and quantity of regenerated bone.

KEYWORDS

allograft, bone graft, bone regeneration, collagen membrane

1 | INTRODUCTION

Osseointegrated implants are an ideal alternative to missing teeth; however, their success is directly related to the quantity and quality of bone in edentulous areas.[1,2] During the first year, loss of teeth results in a 25% reduction in bone width and a decrease of 4 mm in vertical bone height.[3] There are several proposed surgical procedures to reconstruct bone before insertion of the implant, including distraction osteogenesis, ridge splitting, maxillary sinus augmentation, autogenous bone (AB) block, and guided bone regeneration (GBR).[4-7]

Among the above-mentioned methods, GBR has been frequently studied for treating local defects of jawbones.[8] The success rate of implant treatment in the area restored by the GBR technique is similar to that of implant treatment in the healthy native bone region.[8]ABs, allografts, ceramics, and xenografts are usual biomaterials used to perform GBR.

The AB grafts are known as the gold standard due to the nature of osteogenesis, osteoinduction, and osteoconduction. However, problems such as delayed resorption of augmented bone, increasing the surgery time, pain, and morbidity in the donor site have limited their application. They are also doubtful about their cell vitality.[9-11] Allografts have no osteogenic properties, but they are widely used because of sufficient amounts and no need for donor site. Demineralized freeze-dried bone allograft (DFDBA) and FDBA are the known allografts.[12] FDBA is in the mineralized form; therefore, it matures faster than DFDBA and suffers atrophy at a lower rate.[9] The FDBA either in particulate[13-16] or block[17] form has been used in bone augmentation processes with successful histological and clinical results.[12]

Due to the different mechanical and biological properties of various graft materials, a combination of these materials can be used to optimize the environment for bone regeneration. If osteoinductivity and osteogenesis are required along with increased mineral density, the FDBA can be used in combination with AB. Beitlitum et al showed that using AB along with FDBA in a layered technique did not increase the treatment results in comparison with FDBA alone.[4]

Regarding the controversial and insufficient information on the advantages of combining these biomaterials and the existence of only one study comparing FDBA alone with FDBA + AB,[4] the present study was conducted to investigate histologically and radiographically horizontal ridge augmentation using corticocancellous FDBA with and without AB in a randomized controlled clinical trial (RCT).

2 | MATERIALS AND METHODS

This was a randomized, controlled clinical trial. This RCT was registered on the Iranian Registry of Clinical Trials (IRCT) with registration number of IRCT201109165305N3 at https://irct.ir/trial/38904. In this study, we considered the CONSORT guidelines.

The study population included patients who were continuously referred to the Dental School of Kerman University of Medical Sciences, Iran. The sample size was calculated considering α = .05, 1-β = 0.2, d = 1.5, and in view of the SD acquired in the Beitlitum's study[4] which was 1.28, the result was 19 cases in each group; and by taking into account the 10% possibility of sample loss, sample size was set on 21 in each group.

The location of this study was the Periodontics Department of Kerman Dental School. This research was approved by Ethical Committee of Kerman University of Medical Sciences and the Ethical approval Code was IR.KMU.REC.1396.1098.

The patients were recruited with nonprobability sampling technique (convenience sampling). The study was conducted on these subjects after obtaining their written consent. Considering inclusion criteria, a periodontist who was not blind to the study determined the need for bone augmentation in these individuals with the help of cone-beam computerized tomography (CBCT). The patients were randomly assigned into two parallel groups of corticocancellous FDBA (FDBA group) alone and corticocancellous FDBA + AB (combined group) by minimization method. Minimization is a dynamic randomization method in relatively small randomized clinical trials.[18] At the beginning, the first few participants were assigned into these two groups through tossing coin (simple randomization), then the next participants were allocated to these two groups considering sex variable to balance. In this method, clinician can predict the allocation of the next participants by knowing the factor levels of a previously enrolled participants and knowing the characteristics of the next participant. Because of the entity of this randomization method, allocation concealment was not performed.[18,19]

2.1 | Inclusion and exclusion criteria

To enroll in the study, these individuals had to be at least 18 years old and require a horizontal bone augmentation for the implant treatment in an edentulous ridge with two to three lost teeth, bordered by at least one tooth and 2.5 to 4 mm width in the posterior of maxilla or mandible. Exclusion criteria were heavy smoking (over 10 cigarettes per day), pregnancy, uncontrolled periodontal disease, known allergy to FDBA, collagen membrane, or medication used in this study, and any medication (such as corticosteroid and bisphosphonate) or systematic diseases (such as uncontrolled diabetes, osteoporosis, and immune deficiency), and medical treatments such as the chemotherapy and radiotherapy that could interfere with treatment. Oral hygiene should also be good (plaque index less than 20%). If necessary, dental calculus removal was performed prior to surgery. The exclusion criteria after starting the treatment were infection, loss of graft materials in cases with wound opening, and failing to follow up the cases.

2.2 | Preoperative measurements

Edentulous ridge width measurements in the implant sites were performed at a distance of 0, 2, 4, and 6 mm from the crest of the alveolar ridge. These measurements were done in the distance of 5 mm

from the distal of tooth root located anterior of the deficient ridge by using CBCT. These measurements were done only at one site for each patient. We decided to use CBCTs to measure the width of edentulous ridge in this study, because several studies have proven the accuracy of the linear measurements of dento-facial structures by CBCTs.[20,21] All measurements (baseline and 6 months after surgery) were done by two periodontists who were educated and calibrated by an experienced radiologist. Both of them were blind to the study groups. For blindness, the demographic information of each patient was removed from CBCTs and a code was given to each CBCT.

2.3 | Surgical procedures

One hour before surgery, 1 g of amoxicillin and 800 mg of ibuprofen were given to the patients for prophylaxis of wound infection and postoperative pain. The technique of bone augmentation was performed in one session by a periodontist who was not blind to the study. First, an injection of a local anesthetic was performed using lidocaine 2% with epinephrine 1:80000 (Darou Pakhsh, Tehran, Iran) in the affected areas (infiltration or block). After achieving the local anesthesia, a mid-crestal incision and two vertical releasing incisions with one tooth further than the site being treated in each side were made, followed by a full thickness mucoperiosteal flap to get the perfect access to the target area. Soft tissue remnants were detached from the bone surface, and cortical perforation was done during irrigation with saline to ensure vascularization. The combined group was treated by the combination of the 1 to 1.5 cc FDBA granules of 1000 to 2000 μm (Tissue Regeneration Corporation, Kish, Iran) and AB with a ratio of 1:1[22] prepared from the ramus or chin region by Bonesier (Jeil medical Co, Seoul, Korea) (Figure 1). Bonesier is a rotary collecting bone instrument to harvest bone with less trauma to adjacent tissues. FDBA group was treated by the 2 to 3 cc FDBA granules of 1000 to 2000 μm alone (Figure 2). The bone graft materials were moisturized and hydrated by sterile normal saline before use. Knowing that one third of the augmented ridge width will be lost after regeneration,[23] we grafted the ridge to about 8 to 9 mm horizontally to obtain sufficient width to place regular implants. After putting the graft materials on the target area in both groups, they were completely covered by a resorbable collagen membrane (Jason membrane, botiss biomaterials GmbH, Berlin, Germany). To fix the graft materials, a 5-0 absorbable suture of Vicryl (Supa, Tehran, Iran) was applied on the membrane using the horizontal mattress technique by taking anchorage from the remained periosteum on the bone in the apical region of facial flap. A periosteal releasing incision was created in order to tension-free closure of the flap. The primary soft tissue closure was performed by nylon suture (5-0) (Supa, Tehran, Iran) with horizontal mattress, interrupted, and criss-cross techniques. Six months after the augmentation procedure, the implants were inserted during the second surgical procedure.

2.4 | Postoperative cares

The patients were instructed not to brush in the transplanted area for the first 2 weeks after surgery. The chlorhexidine mouthwash 0.2% was administered twice daily for 2 weeks, ibuprofen 400 mg every 6 hours as needed and amoxicillin 500 mg every 8 hours for 1 week. The patients were also instructed to have a soft diet. After the first 14 days, sutures were removed and patients were educated to start the mechanical plaque control adjacent to operated area.[6] All postoperative instructions were explained to the patients and also a copy was handed to them to make sure they act accordingly.

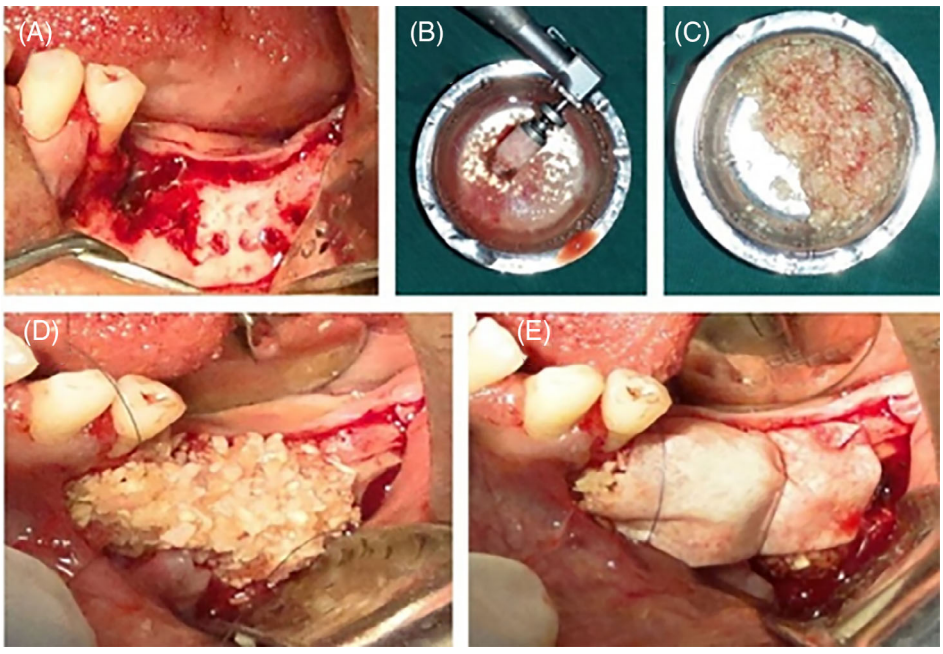

FIGURE 1 Surgical procedures by graft material of FDBA with autogenous bone. A, Clinical view after flap elevation and cortical perforation. B, Autogenous bone harvesting with bonesier. C, Combination of FDBA and autogenous bone. D, Placement of graft materials in the target area. E, Coating the graft materials with collagen membrane and fixing with horizontal mattress suture. FDBA, freeze-dried bone allograft

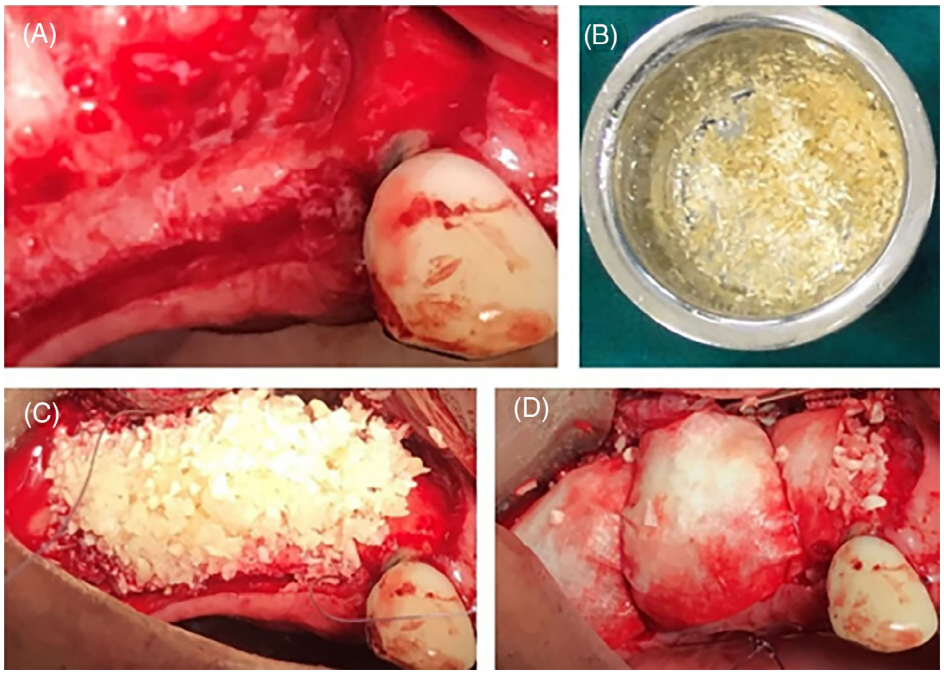

FIGURE 2 Surgical procedures by graft material of FDBA. A, Clinical view after flap elevation and cortical perforation, B, FDBA, C, placement of graft materials in the target area, and, D, coating the graft materials with collagen membrane and fixing with a horizontal mattress suture. FDBA, freeze-dried bone allograft

2.5 | Postoperative measurements

The re-measurements of ridge width at the distance of 0, 2, 4, and 6 mm from the crest of the alveolar ridge were performed in the same areas as previously measured through another CBCT taken 6 months after the bone augmentation, at the time of the implant surgery.

2.6 | Histological assessments

At the time of insertion of implants, a bone biopsy with 2 mm diameter and 6 mm length was performed using Trephine bur (Hu-Friedy) from 22 patients (11 in each group).

Because of lateral augmentation of the edentulous ridge, the biopsies were prepared from the buccal of augmented ridge between the implant sites or distal to the last implant site. Because of the site of taking biopsy, probability of bone traumatization during trephine biopsy, and patients consent, histological evaluation was limited to 11 cases in combined group. Therefore, the biopsies from FDBA group were also limited to 11 cases to balance the number of participants in each group.

The bone samples were placed in 10% formalin for fixation for 24 hours. After decalcification with nitric acid 13%, the samples were sectioned in parallel with the diameter of the sample and embedded in the paraffin. Multiple sections of 3 to 5 μm were prepared from the samples and stained by hematoxylin and eosin to be observed under Olympus Optical Microscope (YX-100, Japan). In this phase, all samples were evaluated in terms of new viable bone formation, presence of remaining bone graft particles, presentation of acute and chronic inflammation, and granulomatous inflammatory response to a foreign body.

2.7 | Histomorphometrical assessments

For histomorphometrical analysis, micrographs were prepared from each slide under the light microscope (Olympus BX-41 connected to Olympus camera DP12-2, Japan) at magnifications of 40× and 100×. For each sample, a micrograph was prepared at a magnification of 40× and three micrographs at a magnification of 100× (from the upper, middle, and lower boarders of the sample). The micrographs were encoded according to the slide code and saved on the computer, and then evaluated with the Adobe photo shop software program.[24] For each sample, the areas of new bone region, remaining graft particles, and soft tissue were calculated separately. Then, the sum of each of these areas was calculated in all samples, and a total area was obtained for each one. In the next stage, the area of each region (new bone, remaining graft particles and soft tissue) was divided by the total area and was reported as percentage.[25,26] The histomorphometrical evaluation of all samples was done at a magnification of 100× and all samples were matched in length, width, and pixel. To prevent sampling bias, five slides from each sample were randomly selected and analyzed for histology and histomorphometry and then their average was calculated.

The following criteria were used to differentiate a new bone from native bone:

1. The absence of organized mature lamellar bone
2. Increased new cellularity and vascularity
3. Observations of multiple osteocytes
4. Higher staining due to hematoxicillin vs eosin

Also, the differentiation of new bone from allograft particles was based on the presence of cells in new bone lacunas (unlike FDBA, where lacunas lack cells) and the difference in staining intensity.[13,25]

The histological and histomorphometrical examinations of all samples were performed by a pathologist who was blind to the study. A code was given to each prepared slide to blind the assessor.

2.8 | Statistical analysis

Data were analyzed by SPSS 20 software. Kolmogorov-Simonov statistical test showed normal distribution of the data. Therefore, two-sample *t* test was used to analyze the results between the two groups, and the paired *t* test was applied to analyze the preoperative and postoperative differences for the two groups. The reliability between two examiners was determined by Pearson's correlation coefficient.

3 | RESULTS

The present research was conducted on 42 patients. The FDBA group consisted of 21 patients (13 females and 8 males) and the combined group also had 21 patients (14 females and 7 males). Recruitment, surgery, and data gathering were performed between May 2017 and April 2018. Two of the 21 participants in the FDBA + AB group did not show up to complete the treatment, so the results were analyzed based on 40 remaining participants (Figure 3). Only two patients in the present study who were both from the FDBA group needed to receive complementary GBR in the implant insertion session due to insufficient quantity of bone regeneration.

A small membrane exposure occurred only in one surgical site related to the FDBA group, which healed completely without loss of graft materials. All patients reported some extent of inflammation, pain, and bruises during the healing process. Any harm did not occur to the participants during operation and after follow-up in both groups.

3.1 | Radiological findings

Inter-examiner reliability was excellent (r = 0.89). In the FDBA group (Figure 4), the mean ridge width at the distance of 0, 2, 4, and 6 mm from the crest of the alveolar ridge in CBCT was 2.22 ± 1.02, 3.90 ± 0.75, 5.36 ± 1.59, and 6.31 ± 2.07 mm, respectively, before treatment. This amount was increased by 5.00 ± 1.15, 6.95 ± 0.21, 8.18 ± 1.56, and 8.54 ± 1.65 mm, 6 months after treatment; this increase was statistically significant (P < .001) (Table 1).

In the combined group (Figure 5), the mean ridge width at the distance of 0, 2, 4, and 6 mm from the crest of the alveolar ridge in CBCT was 1.90 ± 0.78, 3.55 ± 1.05, 5.10 ± 2.12, and 6.60 ± 2.25 mm, respectively, before treatment. This amount was increased by 4.30 ± 1.68, 6.65 ± 1.75, 8.70 ± 1.68, and 9.25 ± 1.58 mm after 6 months; this increase was statistically significant (P < .001) (Table 1).

The difference between the two groups was not statistically significant in any of the measurements performed at the distance of 0, 2, 4, and 6 mm from the alveolar crest before (P = .255, P = 1.28,

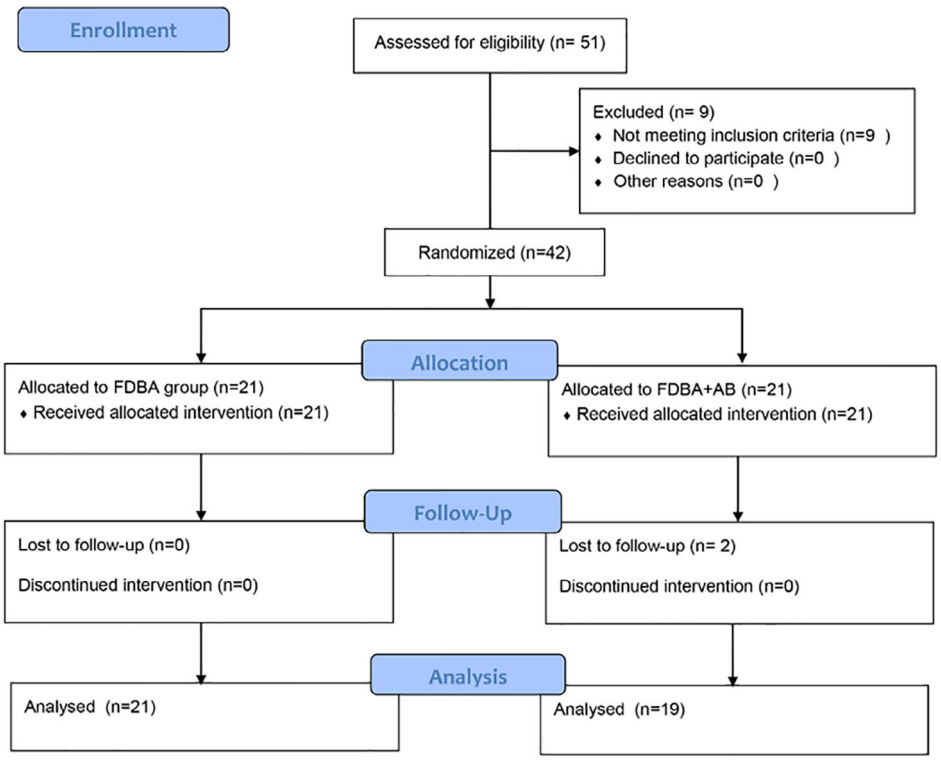

FIGURE 3 Consort fellow diagram of participants

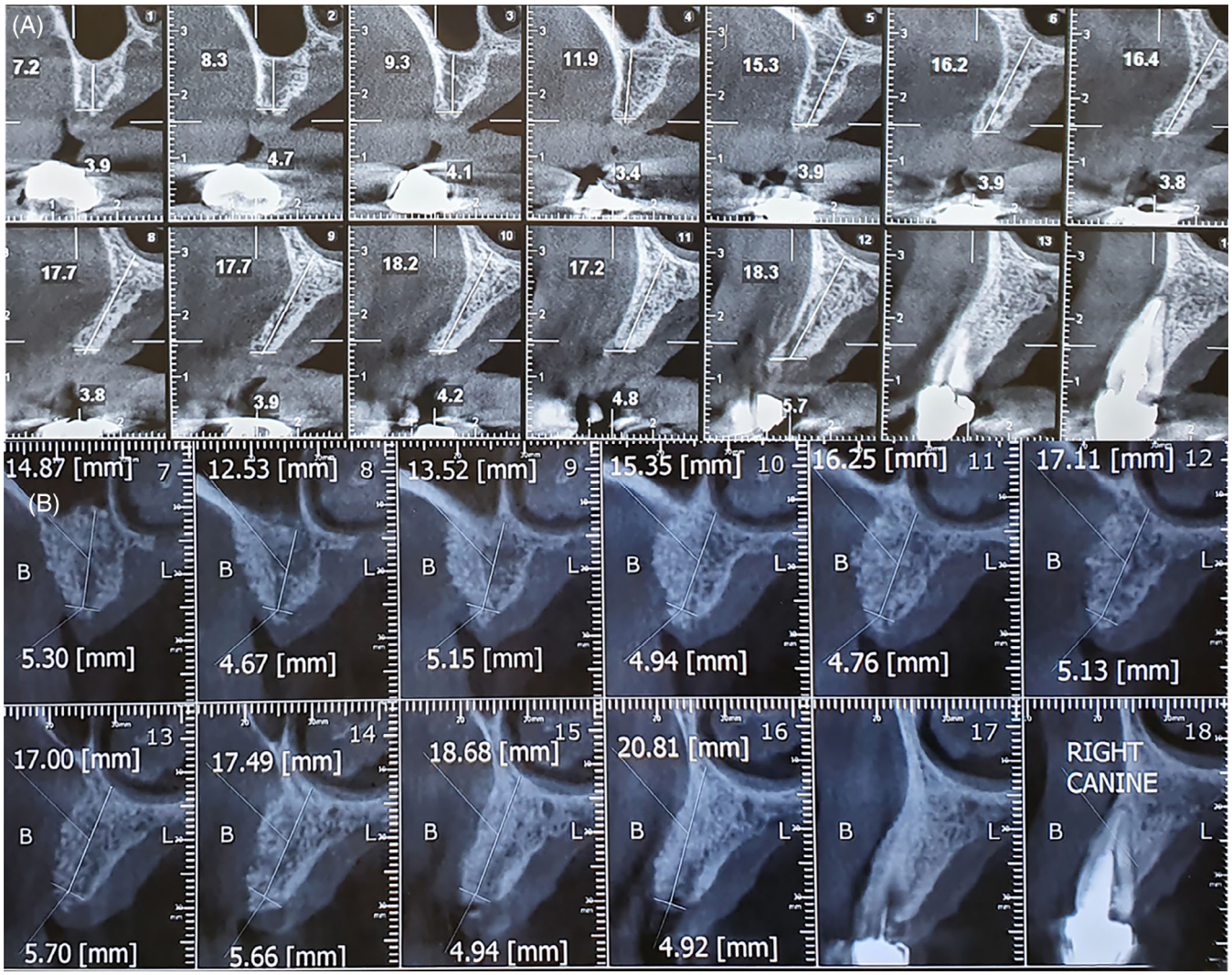

FIGURE 4 CBCT before, A, and after, B, augmentation in a patient from FDBA group. CBCT, cone-beam computerized tomography; FDBA, freeze-dried bone allograft

TABLE 1 Comparison of horizontal alveolar ridge dimensions at the distance of 0, 2, 4, and 6 mm from crest of alveolar ridge before and after ridge augmentation in each group by the means of CBCT and the effect size of treatment type on horizontal ridge augmentation in each group

Group	Distance from the crest	Preoperative mean ± SD	Postoperative mean ± SD	Paired T test	Effect size
FDBA	0 mm	2.22 ± 1.02	5.00 ± 1.15	t (21) = −8.99 P < .001	2.72
	2 mm	3.90 ± 0.75	6.95 ± 1.21	t (21) = −11.76 P < .001	4.06
	4 mm	5.36 ± 1.59	8.18 ± 1.56	t (21) = −8.14 P < .001	1.77
	6 mm	6.31 ± 2.07	8.54 ± 1.65	t (21) = −5.35 P < .001	1.07
FDBA + AB	0 mm	1.90 ± 0.78	4.30 ± 1.68	t (19) = −6.69 P < .001	3.07
	2 mm	3.55 ± 1.05	6.65 ± 1.75	t (19) = −7.69 P < .001	2.95
	4 mm	5.10 ± 2.12	8.70 ± 1.68	t (19) = −8.58 P < .001	1.69
	6 mm	6.60 ± 2.25	9.25 ± 1.58	t (19) = −4.95 P < .001	1.17

Note: P value <.05 is statistically significant.
Abbreviations: AB, autogenous bone; CBCT, cone-beam computerized tomography; FDBA, freeze-dried bone allograft.

P = .649, and P = .676, respectively) and after the treatment (P = .122, P = .514, P = .308, and P = .167, respectively) (Table 2).

To assess the effect size (ES), the difference in the mean of ridge width from baseline to 6 months after operation was calculated and divided by the SD at baseline. In all distances from the crest, the ES was high in both groups (>0.8). This means that both treatments had very good outcomes in regeneration of barely sufficient ridges (Table 1).

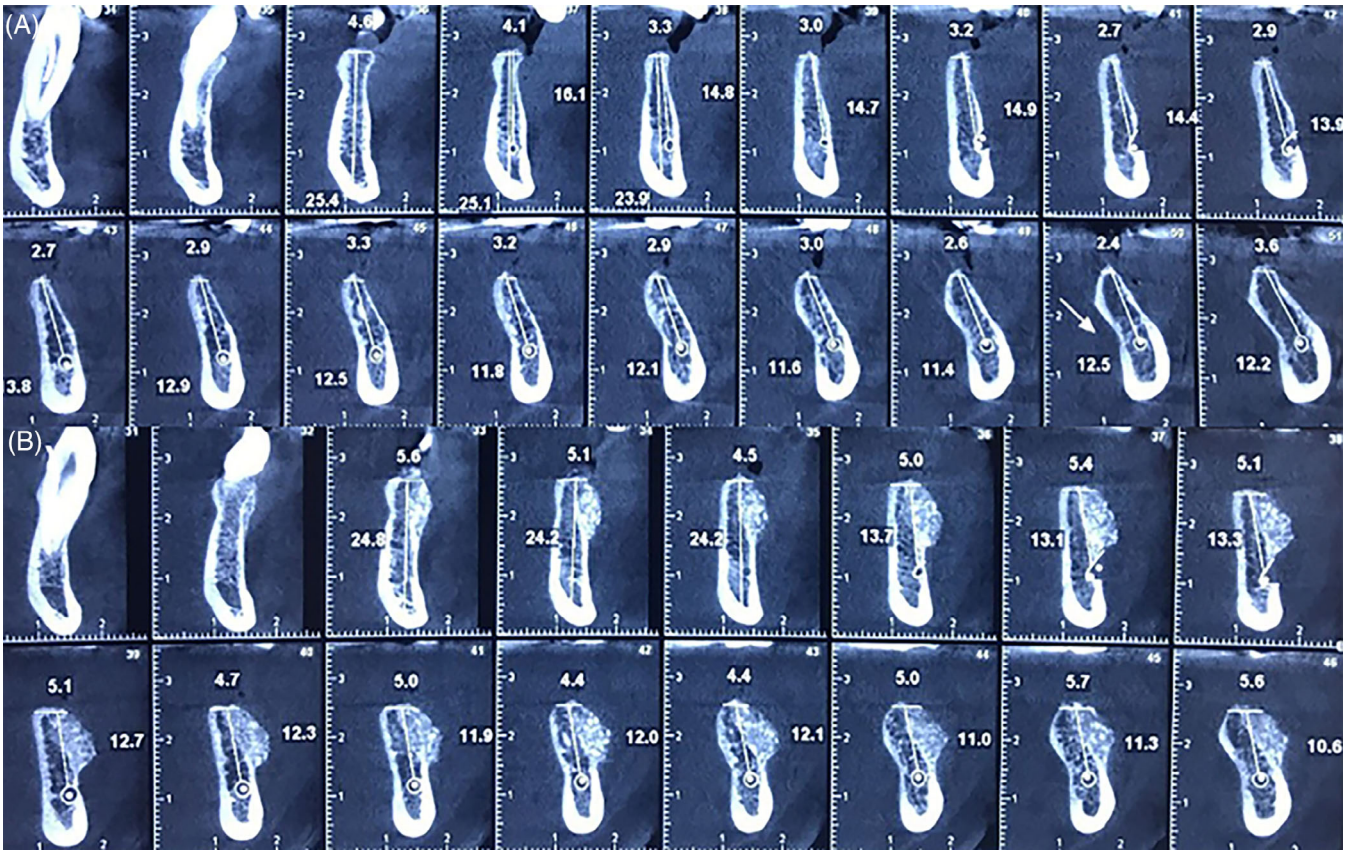

FIGURE 5 CBCT before, A, and after, B, augmentation in a patient of FDBA + autogenous bone group. CBCT, cone-beam computerized tomography; FDBA, freeze-dried bone allograft

TABLE 2 Comparison of horizontal alveolar ridge dimensions at the distance of 0, 2, 4, and 6 mm from crest of alveolar ridge before and after ridge augmentation between the two groups by CBCT

	Time	FDBA	FDBA + AB	Independent *t*-test
0 mm	Preoperative	2.22 ± 1.02	1.90 ± 0.78	t (40) = 1.15 P = .255
	Postoperative	5.00 ± 1.15	4.30 ± 1.68	t (40) = 1.58 P = .122
2 mm	Preoperative	3.90 ± 0.75	3.55 ± 1.05	t (40) = 0.206 P = 1.28
	Postoperative	6.95 ± 1.21	6.65 ± 1.75	t (40) = 0.65 P = .514
4 mm	Preoperative	5.36 ± 1.59	5.10 ± 2.12	t (40) = 0.45 P = .649
	Postoperative	8.18 ± 1.56	8.70 ± 1.68	t (40) = −1.03 P = .308
6 mm	Preoperative	6.31 ± 2.07	6.60 ± 2.25	t (40) = −0.42 P = .676
	Postoperative	8.54 ± 1.65	9.25 ± 1.58	t (40) = −1.40 P = .167

Note: P value <.05 is statistically significant.
Abbreviations: AB, autogenous bone; CBCT, cone-beam computerized tomography; FDBA, freeze-dried bone allograft.

3.2 | Histological findings

In the histological examination of 11 samples in both groups, evidence was found from a new viable bone in the form of broad bone trabeculae and more delicate lace-like regions adjacent to graft. The graft particles were surrounded by new bone (containing numerous osteocytes and osteoblasts) and were in close contact with the new bone. No evidence of acute or chronic inflammation and granulomatous inflammatory response to a foreign body was observed in any of the samples (Figures 6-8).

3.3 | Histomorphometrical findings

The mean new bone was 43.71 ± 5.63% in the FDBA group and 46.07 ± 6.34% in the combined group, and the difference between the two groups was not statistically significant (P = .367). The mean remaining graft particles were 9.86 ± 2.16% in the FDBA and 9.08 ± 2.33% in the combined group, and the difference between the two groups was not statistically significant (P = .428). The mean soft tissue was 46.42 ± 7.33% in the FDBA group and 44.83 ± 6.55% in the combined group, and the

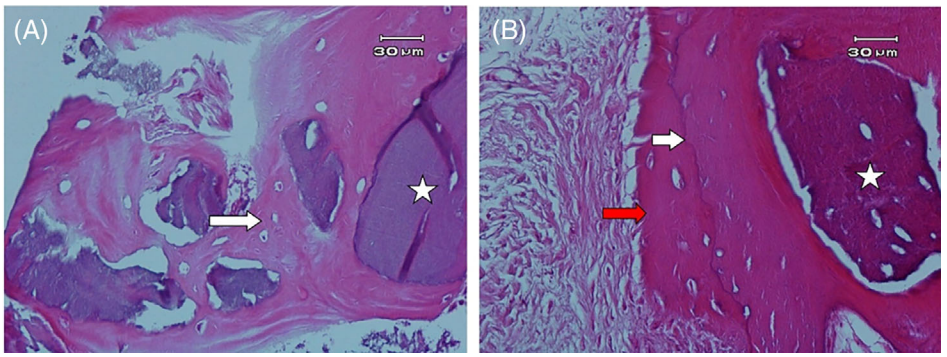

FIGURE 6 A new bone consisting of multiple lacunas containing osteocyte (arrow) adjacent to connective tissue (star) in FDBA group (right image) and combined group (left image) (400×). FDBA, freeze-dried bone allograft

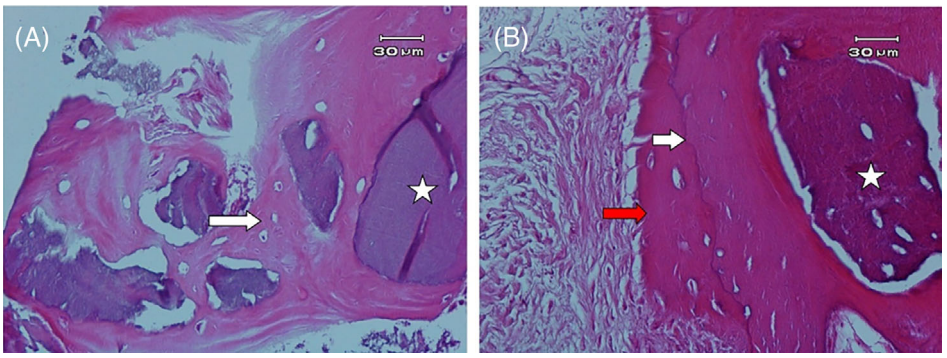

FIGURE 7 Remaining graft particles (star) surrounded by new bone (red arrow) containing osteoblast rhyme (white arrow) in FDBA group (right image) and combined group (left image) (400×). FDBA, freeze-dried bone allograft. FDBA, freeze-dried bone allograft

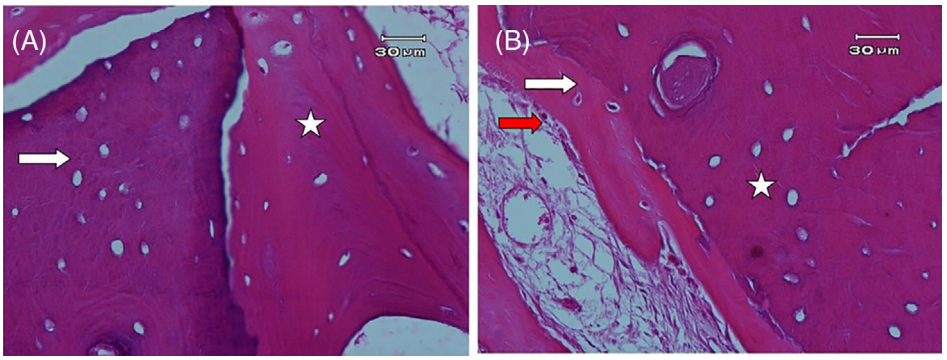

FIGURE 8 New bone (red arrow) containing osteoblast rhyme (white arrow) adjacent to native mature lamellar bone (star) in FDBA group (right image) and the combined group (left image) (400×). FDBA, freeze-dried bone allograft

Variable	FDBA	FDBA + AB	Independent *t*-test
Soft tissue	46.42 ± 7.33%	44.83 ± 6.55%	*P* = .598
New bone	43.71 ± 5.63%	46.07 ± 6.34%	*P* = .367
Remaining graft particles	9.86 ± 2.16%	9.08 ± 2.33%	*P* = .428

TABLE 3 Histomorphometric comparison of soft tissue, new bone, and remaining graft particles in the two groups after bone augmentation

Note: P value <.05 is statistically significant.
Abbreviations: AB, autogenous bone; FDBA, freeze-dried bone allograft.

difference between the two groups was not statistically significant (*P* = .598) (Table 3).

4 | DISCUSSION

The aim of this study was histological and radiological evaluation of horizontal ridge augmentation using corticocancellous FDBA with and without AB.

Based on the results of this study, the horizontal ridge dimension at the baseline was almost the same in both groups, and there was no statistically significant difference, indicating the homogeneity of the two groups at the start of the study. The ridge dimensions showed no significant difference between the two groups after 6 months of intervention. Accordingly, the ridge width in the FDBA group was 0.7 and 0.3 mm more than that of the combined group in the distance of 0 and 2 mm from the crest of the alveolar ridge, but this difference was not statistically significant (*P* = .122 and *P* = .514, respectively). In

the distance of 4 and 6 mm from the crest of the alveolar ridge, the ridge width in the combined group was, respectively, 0.52 and 0.71 mm more than that of the FDBA group, which was not statistically significant (P = .308 and .167, respectively).

Feuille et al (2003) reported the mean horizontal ridge width gain at the distance of 3 to 5 mm from the crest of the alveolar ridge 6 months after augmentation with FDBA alone was 2.3 ± 1.0 mm, which was statistically significant (P < .05). This result was almost the same as the mean horizontal ridge width gain by FDBA alone in our study at the distance of 2 and 4 mm from the crest of the alveolar ridge (3.05 and 2.82 mm, respectively), with the difference that they used nonresorbable e-PTFE membrane. Due to the similar results, the high exposure probability, and the problems associated with these membranes, it can be concluded that the resorbable collagen membranes are suitable alternative to them.

According to the results of Beitlitum's study, the use of a layer of AB has no significant effect on regeneration of horizontal or vertical ridge defects, and the horizontal or vertical ridge deficiencies may be treated with FDBA alone and cross-linked collagen barrier membranes with clinically successful outcomes, which is in line with the results of our study.[4]

Eskan et al showed the mean gain of crestal ridge width was 2 ± 1.2 mm in particulate cancellous allograft group.[23] This was less than that of our study with a mean gain of 2.78 mm. The causes of this difference may be the smaller size of allograft granules (500-800 μm vs 1000-2000 μm) and the type of allograft (cancellous vs corticocancellous) used in Eskan's study; hence, more resorption of allograft and less space maintenance can be expected while using cancellous allograft with smaller particles.

In all distances from the crest, the ES was high in both groups (>0.8). This means that lateral ridge augmentation with FDBA + collagen membrane or FDBA + AB + collagen membrane had very good outcomes in regeneration of barely sufficient ridges in comparison to the baseline.

No evidence of acute or chronic inflammation was observed in any of the samples. Solakoglu et al also demonstrated no signs of inflammatory reactions with using allogenic bone materials.[27] In the present study, all biopsies were prepared form the buccal region of the augmented ridge; thus, the probability of native bone existence in prepared biopsies decreased. Taking biopsy from the implant site increases the percentage of native bone to regenerated bone in the biopsy core; therefore, it may affect the histological results as a confounder variable in such studies.

According to histomorphometrical analysis, the mean new bone in the combined group was more than that of the FDBA group (46.07 ± 6.34% and 43.71 ± 5.63%, respectively), which can be due to BMP in the AB and its role in osteogenesis, but their difference was not statistically significant (P = .367).

The mean remaining graft particles in the FDBA group were more than in the combined group (9.86 ± 2.16% and 9.08 ± 2.33%, respectively) which could be due to the higher resorption rate in AB, but their difference was not statistically significant (P = .428). The mean soft tissue was higher in the FDBA group than in the combined group (46.42 ± 7.33% and 44.83 ± 6.55%, respectively) but the difference was not statistically significant either (P = .598).

According to histomorphometrical analyses in the Feuille's study, the mean new bone was 47.6%, similar to the results of our study. The mean remaining graft particles were 52.4%, much more than ours (9.86%), which may be due to the fact that all biopsy samples in this study were prepared at the time of the removal of the membranes, earlier than the time of biopsy in our study (6 months after augmentation).[13]

In a study by Cammack et al in 2005, the mean new bone regenerated in the FDBA group was 41.89%, which was similar to that found in our study in the FDBA group (43.71%). The mean remaining graft particles and soft tissue in the FDBA group were 7.29% and 49.57%, consistent to those obtained in our study in the FDBA group (9.86% and 46.42%, respectively).[25]

Based on the results of a systematic review and meta-analysis by Sanchez et al, the use of bone substitute materials and AB in the ridge augmentation process had similar results.[28] They also reported that the sample size of all included studies was relatively low.[28] After back calculating the needed sample size considering the mean (SD) obtained in the present study, the sample size of this study had enough power to show significant results.

The shorter healing time by using AB is another scientific subject, which is because of osteoinductive property of AB. As a result, bone regeneration can be assumed to be delayed by the use of bone substitute materials alone, and the implant inserting and loading will be postponed.[29]

The economic aspect should not be ignored regarding the graft materials. The AB grafting process has been lengthening the process time, especially in cases of extra-oral donor graft sites, which will impose more cost for long periods of general surgery and general anesthesia. Cost-effectiveness analyses are needed to characterize this aspect.[29]

One of the limitations of this study was the size of bone defects. Patients with 2 to 3 lost teeth were enrolled in the present study; therefore, the results of this study should be interpreted with caution and may not be generalized to larger defects. The next limitation of present study was not using of stent during taking CBCT. Another limitation of this study was randomization method. At the start of the study, all patients were not on the access and assessing of the patients based on inclusion criteria and entering them to the study was performed during the study. In addition, to balance the participants in the study groups based on sex variable, minimization method was used for allocation. Allocation concealment was not applied because of the entity of this randomization method.

The results of this study showed that the quantity and quality of regenerated bone by using FDBA alone or FDBA + AB were statistically similar. Therefore, using of FDBA alone for reconstruction of small to moderate ridge deficiencies is suggested resulting in less cost, time, and postoperative complications.

5 | CONCLUSION

The results obtained from the present study demonstrated that the amount of increase of ridge width after augmentation between the two groups of FDBA and FDBA + AB were not statistically significant. Based on histomorphometrical analysis, there was no significant difference between the two groups in terms of new bone, remaining graft particles, and soft tissue. Considering the similar clinical and histological results of the two groups, the FDBA alone can be used for horizontal augmentation of edentulous ridge, and adding AB to corticocancellous FDBA granules does not significantly increase the quality and quantity of regenerated bone 6 months after operation.

ACKNOWLEDGMENT

This study was supported by a grant from Kerman Oral and Dental Diseases Research Center, Kerman University of Medical Sciences.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

ORCID

Mohammad Mohammadi https://orcid.org/0000-0001-6257-6126

REFERENCES

1. Adeyemo W, Reuther T, Bloch W, et al. Healing of onlay mandibular bone grafts covered with collagen membrane or bovine bone substitutes: a microscopical and immunohistochemical study in the sheep. *Int J Oral Maxillofac Surg*. 2008;37(7):651-659.
2. Borie E, Fuentes R, Del Sol M, Oporto G, Engelke W. The influence of FDBA and autogenous bone particles on regeneration of calvaria defects in the rabbit: a pilot study. *Ann Anat Anatomischer Anzeiger*. 2011;193(5):412-417.
3. Carlsson G, Persson G. Morphologic changes of the mandible after extraction and wearing of dentures. A longitudinal, clinical, and X-ray cephalometric study covering 5 years. *Odontol Revy*. 1967;18(1):27-54.
4. Beitlitum I, Artzi Z, Nemcovsky CE. Clinical evaluation of particulate allogeneic with and without autogenous bone grafts and resorbable collagen membranes for bone augmentation of atrophic alveolar ridges. *Clin Oral Implants Res*. 2010;21(11):1242-1250.
5. Block MS. Treatment of the single tooth extraction site. *Oral Maxillofacial Surg Clin*. 2004;16(1):41-63.
6. Buser D, Dula K, Hirt HP, Schenk RK. Lateral ridge augmentation using autografts and barrier membranes: a clinical study with 40 partially edentulous patients. *J Oral Maxillofac Surg*. 1996;54(4):420-432.
7. Inchingolo F, Tatullo M, Marrelli M, et al. Trial with platelet-rich fibrin and bio-Oss used as grafting materials in the treatment of the severe maxillar bone atrophy: clinical and radiological evaluations. *Eur Rev Med Pharmacol Sci*. 2010;14(12):1075-1084.
8. Hämmerle CH, Jung RE, Feloutzis A. A systematic review of the survival of implants in bone sites augmented with barrier membranes (guided bone regeneration) in partially edentulous patients. *J Clin Periodontol*. 2002;29(S3):226-231.
9. Ahn Y-S, Kim S-G, Kim C-S, Oh J-S, Lim S-C. Effect of guided bone regeneration with or without pericardium bioabsorbable membrane on bone formation. *Oral Surg Oral Med Oral Pathol Oral Radiol*. 2012;114(5):S126-S131.
10. Block MS, Kelley B. Horizontal posterior ridge augmentation: the use of a collagen membrane over a bovine particulate graft: technique note. *J Oral Maxillofac Surg*. 2013;71(9):1513-1519.
11. Zerbo IR, De lange GL, Joldersma M, Bronckers AL, Burger EH. Fate of monocortical bone blocks grafted in the human maxilla: a histological and histomorphometric study. *Clin Oral Implants Res*. 2003;14(6):759-766.
12. Rummelhart J, Mellonig J, Gray J, Towle H. A comparison of freeze–dried bone allograft and demineralized freeze–dried bone allograft in human periodontal osseous defects. *J Periodontol*. 1989;60(12):655-663.
13. Feuille F, Knapp CI, Brunsvold MA, Mellonig JT. Clinical and histologic evaluation of bone-replacement grafts in the treatment of localized alveolar ridge defects. Part 1: mineralized freeze-dried bone allograft. *Int J Periodontics Restor Dent*. 2003;23(1):28–35.
14. Froum SJ, Wallace SS, Elian N, Cho SC, Tarnow DP. Comparison of mineralized cancellous bone allograft (Puros) and anorganic bovine bone matrix (bio-Oss) for sinus augmentation: histomorphometry at 26 to 32weeks after grafting. *Int J Periodontics Restor Dent*. 2006;26(6):542–551.
15. Gapski R, Neiva R, Oh T-J, Wang H-L. Histologic analyses of human mineralized bone grafting material in sinus elevation procedures: a case series. *Int J Periodontics Restor Dent*. 2006;26(1):58–69.
16. Kolerman R, Tal H, Moses O. Histomorphometric analysis of newly formed bone after maxillary sinus floor augmentation using ground cortical bone allograft and internal collagen membrane. *J Periodontol*. 2008;79(11):2104-2111.
17. Nissan J, Ghelfan O, Mardinger O, Calderon S, Chaushu G. Efficacy of cancellous block allograft augmentation prior to implant placement in the posterior atrophic mandible. *Clin Implant Dent Relat Res*. 2011;13(4):279-285.
18. Scott NW, McPherson GC, Ramsay CR, Campbell MK. The method of minimization for allocation to clinical trials: a review. *Control Clin Trials*. 2002;23(6):662-674.
19. Pandis N. Randomization. Part 2: minimization. *Am J Orthod Dentofacial Orthop*. 2011;140(6):902-904.
20. Lamichane M, Anderson NK, Rigali PH, Seldin EB, Will LA. Accuracy of reconstructed images from cone-beam computed tomography scans. *Am J Orthod Dentofacial Orthop*. 2009;136(2):156.e151-156.e156.
21. Suomalainen A, Vehmas T, Kortesniemi M, Robinson S, Peltola J. Accuracy of linear measurements using dental cone beam and conventional multislice computed tomography. *Dentomaxillofacial Radiol*. 2008;37(1):10-17.
22. Urban IA, Nagursky H, Lozada JL, Nagy K. Horizontal ridge augmentation with a collagen membrane and a combination of particulated autogenous bone and anorganic bovine bone-derived mineral: a prospective case series in 25 patients. *Int J Periodontics Restor Dent*. 2013;33(3):299-307.
23. Eskan MA, Greenwell H, Hill M, et al. Platelet-rich plasma–assisted guided bone regeneration for ridge augmentation: a randomized, controlled clinical trial. *J Periodontol*. 2014;85(5):661-668.
24. Farhad AR, Razavi SM, Rozati AR, Shekarchizade N, Manshaei M. Selective nitric oxide synthase inhibitor promotes bone healing. *Dent Res J*. 2017;14(5):306.
25. Cammack GV, Nevins M, Dr C, Hatch JP, Mellonig JT. Histologic evaluation of mineralized and demineralized freeze-dried bone allograft for ridge and sinus augmentations. *Int J Periodontics Restorative Dent*. 2005;25(3):231-237.
26. von Arx T, Cochran DL, Hermann JS, Schenk RK, Higginbottom FL, Buser D. Lateral ridge augmentation and implant placement: an experimental study evaluating implant osseointegration in different augmentation materials in the canine mandible. *Int J Oral Maxillofacial Implants*. 2001;16(3):343–354.

27. Solakoglu Ö, Götz W, Heydecke G, Schwarzenbach H. Histological and immunohistochemical comparison of two different allogeneic bone grafting materials for alveolar ridge reconstruction: a prospective randomized trial in humans. *Clin Implant Dent Relat Res*. 2019;21(5):1002-1016.
28. Sanz-Sanchez I, Ortiz-Vigon A, Sanz-Martin I, Figuero E, Sanz M. Effectiveness of lateral bone augmentation on the alveolar crest dimension: a systematic review and meta-analysis. *J Dent Res*. 2015; 94(9 suppl):128S-142S.
29. Al-Nawas B, Schiegnitz E. Augmentation procedures using bone substitute materials or autogenous bone—a systematic review and meta-analysis. *Eur J Oral Implantol*. 2014;7(suppl 2):S219-S234.

How to cite this article: Hashemipoor M, Asghari N, Mohammadi M, Kalantari M, Arabsolghar M, Ranjbar H. Radiological and histological evaluation of horizontal ridge augmentation using corticocancellous freeze-dried bone allograft with and without autogenous bone: A randomized controlled clinical trial. *Clin Implant Dent Relat Res*. 2020;1–11. https://doi.org/10.1111/cid.12935