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Evaluation of Guided Bone Regeneration Using Xenograft/A-PRF Mixture in Atrophic Posterior Mandible (Clinical and Radiographic study)

Ramy Richa
Oral Surgical Sciences Department, Division of Periodontology,
Faculty of Dentistry, Beirut Arab University, Beirut, Lebanon
Essam Osman
Dental Biomaterial Department, Faculty of Dentistry, Alexandria, Egypt
Nahed Attia
Periodontology Department, Faculty of Dentistry, Alexandria, Egypt
Hani Arakji
Oral Surgical Sciences Department, Division of Oral Surgery,
Faculty of Dentistry, Beirut Arab University, Beirut, Lebanon
Mohamed Shokry
Oral and Maxillofacial Surgery Department,
Faculty of Dentistry, Alexandria, Egypt

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Abstract

Introduction: The rehabilitation of posterior mandible with dental implants represents today a hard challenge for clinicians due to the lack of supporting bone. Different surgical techniques are currently being used to augment the posterior mandible where GBR is considered most commonly used. Materials and Methods: Fifteen patients were selected to treat mandibular alveolar ridge resorption with guided bone regeneration using titanium reinforced membrane and a filling mixture of xenograft bovine bone/PRF. The membrane was fixed using meisinger pin control kit and profix 3mm microscrews. A PRF membrane was used to cover the Ti d-ptfe. Results: Using the mixture of PRF/xenograft as well as PRF membranes

showed promising results in term of primary wound healing, whereas a significant bone quantity with a mean bone volume of 5.78 ± 0.81 was reported. The primary implant stability recorded high values and significantly increased at a period of 6 months post insertion p=0.037 Conclusion: It could be concluded that PFR/ xenograft mixture can be promising when used with the titanium reinforced d-ptfe membrane in 3D ridge reconstruction of atrophic posterior mandible, moreover using PRF membrane to cover the TI- d-ptfe membrane could enhance soft tissue healing as well as it can prevent soft tissue dehiscence due to the concentration of the growth factors that can be released during primary wound healing. Xenograft/PRf mixture can be consistent to be utilized for creation of new bone in severely atrophic ridges if used in GBR. The high ISQ at primary implant placement and at a period of 6 months post insertion according to Osstell can explain the successful application of this mixture in 3D bone augmentation of atrophic posterior mandible.

Keywords: Guided bone regeneration, A-PRF, Xenograft, Posterior mandible, implant stability

Introduction

After tooth loss, the alveolar ridge resorption proceeds. Following the extraction of a tooth, the alveolar ridge width and height decrease at a high rate during the first year and mainly during the first few months (Kingsmill, 1999). During the healing phase after extraction, the mean changes recorded based on data from several studies show that the clinical loss in width to be greater than the loss in height (Van der Weijden & Dell'Acqua, 2009).

Dental implants are currently the treatment of choice for restoration of edentulous areas. Depending on the edentulous period, the difficulty of the implant surgery varies. According to the width, height, and quality of bone, the surgeon would assess the possibility of placing the implants. In long periods of edentulism, it is often mandatory to perform hard tissue ridge augmentation to enhance bone volume before implant placement (Toscano, et al., 2010).

The reconstruction of alveolar ridge abnormalities concurrently with or staged before implant placement has been extensively documented using guided bone regeneration, where the function of the barrier membrane aims to promote bone formation while acting as a passive barrier to preclude soft tissue in- growth. Moreover, the effect of the barrier membrane has been further shown to promote bone formation, as it induces molecular and cellular events. (Urban, et al., 2022)

Guided bone regeneration for vertical ridge augmentation is a highly technique-sensitive therapy (Rocchietta, et al., 2008). The application of a

moldable barrier membrane in conjunction with a bone substitute that can securely build up a durable biological structure that mimics native tissues and provides enough volume is required for space creation and maintenance to function reliably. These requirements are met by non-resorbable titanium-reinforced barrier membranes, which have been proposed as a successful means of achieving vertical ridge augmentation in big defects (Merli, et al., 2014). Non resorbable (frequently polytetrafluoroethylene-PTFE) or resorbable (frequently collagen based) membranes are usually used to contain the grafting material, preventing graft resorption, and preventing the surrounding soft tissues to migrate and infiltrate into the surgery site (Urban & Monje, 2019). The local anatomy and desired clinical outcome, type of graft used and the healing biology, all these factors drive the choice of specific membrane. However, the main disadvantages faced using this technique are the anatomical limitations and the high resorption rate of the graft material (Drăgan, 2022)

Vertical GBR is technique sensitive that limits the clinical success, failure is usually associated with wound dehiscence. The ability to develop bone along the axis of applied forces is another limitation (Rocchietta, Fontana, & Simion, 2008). Although, titanium membrane shows specific problem where the fibrous tissues grow into the wide holes of the membrane leading to its exposure. (Urban, et al., 2014) (Rakhmatia, et al., 2013)

(Choukroun, et al., 2006) developed platelet rich fibrin (PRF), a second-generation platelet concentrate that promotes hard and soft tissue repair. It contains large quantities of collected platelets, allowing for the delayed release of growth factors (GFs) (Kang, et al., 2011). These GFs include vascular endothelium growth factor (VEGF), platelet-derived growth factor (PDGF), fibroblast growth factor (FGF), epidermal growth factor (EGF), hepatocyte growth factor (HGF), insulin-like growth factor (IGF), and transforming growth factor-β (TGF-β). All of this help to replace damaged tissue, resurface wounds, and restore vascular integrity. In comparison to other platelet concentrates, PRF releases these factors at a slower pace over a longer period of time, improving wound healing (Blair & Flaumenhaft, 2009)

PRF has been demonstrated to enhance the formation of osteoblasts and periodontal ligament cells, both of which are important for periodontal defect healing (Ehrenfest, et al., 2010); (Sharma & Pradeep, 2011); (Mazor, et al., 2009); (Simonpieri, et al., 2011).

For more predictable regeneration of bone, autografts can be combined with platelet concentrates. This clinical case letter reports a case of Siebert's class I ridge defect which was treated with the staged guided bone regeneration (GBR) approach using autogenous block graft and platelet-rich fibrin that demonstrates the efficacy of using a block graft along with PRF,

which stimulation of new bone formation and successful placement of dental implant in the augmented site (Datla, et al., 2018)

Therefore, the rationale of this study is to evaluate clinically and radiographically the efficiency of using xenograft mixed with A-PRF for guided bone regeneration in posterior mandibular defects.

Material and Methods:

This study was accomplished as a randomized clinical trial following the consort guidelines. The study was carried out at the Oral Surgery Division, Faculty of Dentistry, Beirut Arab University, Lebanon, between February 2022 till September 2023. Ethical approval was obtained by the institutional review board (2023-H-0121-D-P-0534) before the start of the study. The study was completed in accordance with the Helsinki Declaration of 1975, revised in 2013. Before the initiation of the work, patients who participated in this trial signed an informed consent and were well-informed about all the steps of the procedure and any complications that might result during or after the procedure.

Sample size was estimated using the sample size calculator website; http://epitools.ausvet.com.au, by adjusting the power of the study to 80% and regulating the alpha error to 5%. This yielded a total of 13 patients; two patients were added to the final calculated sample size to avoid sample attrition that might occur throughout the follow-up period of the study. A total of 15 patients of both genders with an age range of 30–60 years fulfilling the inclusion and exclusion criteria. Patients who were included in this trial should have unilateral or bilateral mandibular posterior partial edentulism, a bone height crestal to the canal <7mm, good oral hygiene. Whereas patients that have uncontrolled or untreated periodontal disease involving residual dentition, uncontrolled systemic condition that jeopardize the surgery, radiotherapy to the head/neck district performed within the past 24 months, chemotherapy for treatment of malignant tumors at the time of the surgical procedure, patients with present or past treatment with intravenous bisphosphonates, patients having psychological problems, heavy smoking (>10 cigarettes per day), and alcohol or drug abuse, pregnant patients were excluded from this study. (Ronda, et al., 2014) :

All patients underwent thorough clinical examination; health of the periodontium, oral hygiene level was inspected. Prosthetic assessment was performed for the future prosthesis. Preoperative cone beam CT were requested from all patients to measure quantitatively the available bone, and the distance between the alveolar crest and the mandibular canal (**Figure 1**). Moreover, all patients received proper prophylactic treatment and were given adequate oral hygiene instructions.

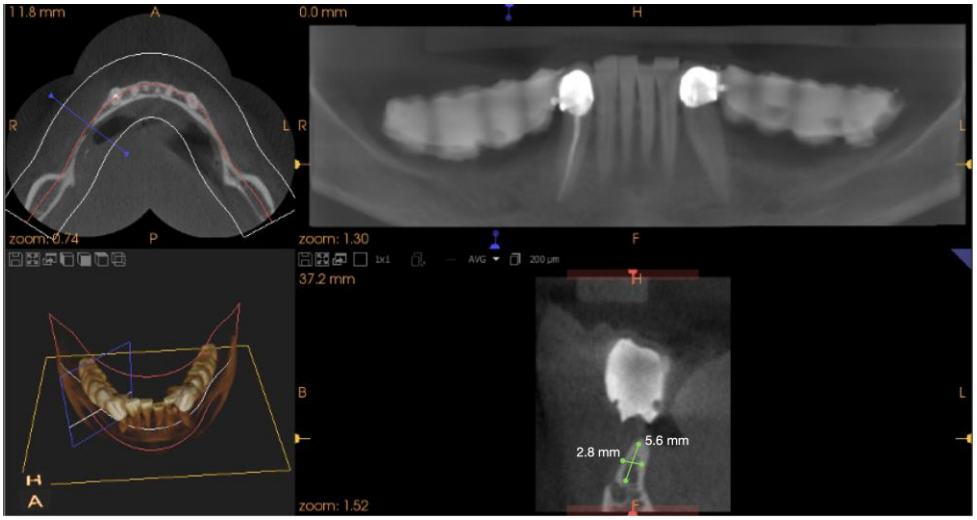

Figure 1. Preoperative CBCT showing the mandibular deficiency

One hour prior to the surgical procedure, all patients were instructed to take 2 g of antibiotics (875 mg amoxicillin, 125 mg clavulanic acid). As for patients allergic to penicillin, 600 mg clindamycin was prescribed. All patients were told to rinse their mouth with Chlorhexidine gluconate 0.2% mouthwash 30 min before the initiation of the procedure.

Under complete aseptic and sterile conditions, the patients received inferior alveolar and buccal block anesthesia using Articaine 4%, 1:100,000 epinephrine (Septanest, Septodont). At the recipient site, crestal incisions was made over the edentulous alveolar ridge and was extended from the retromolar area (distally) till the mesial aspect of the adjacent tooth. A full thickness flap was reflected on the buccal and lingual side exposing the posterior atrophic mandible. With a 1mm round bur mounted on a straight surgical handpiece the bone was decorticated under copious irrigation **(Figure 2)**. Afterwards, A-PRF was prepared (Choukroun, et al., 2006) by withdrawing the patients' own blood from the median cubital or cephalic vein into empty plastic vaccumed tubes, and they were immediately centrifuged at a speed of 1300 rpm for 7 mins. A-PRF were collected and were placed in their specific box to produce the A-PRF membrane. A-PRF membranes were cut and together with serum exudates were mixed with the graft material (Cerabone – Botiss – Germany).

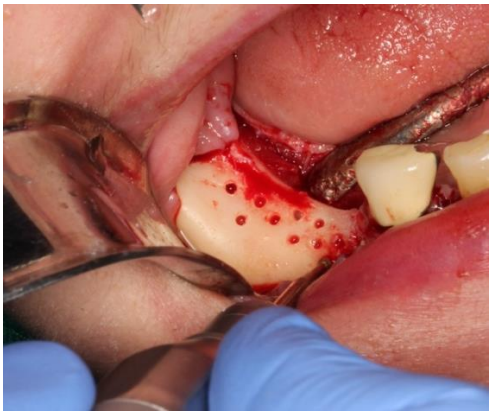

Figure (2). Preparation of the recipient site with decortication

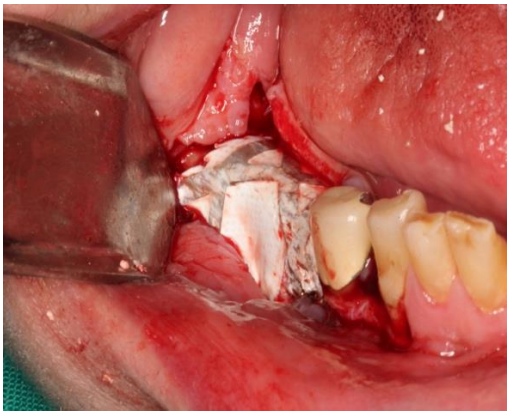

Figure (3). Total fixation of the membrane overlying the A-PRF/Xenograft mixture

After choosing the appropriate size, shaping and fixing of the non-resorbable titanium reinforced membrane (Cytoplast – Osteogenics Biomedicals – USA) using bone tacs (Meisinger Master pin kit – Germany), Profix kit and fixation screws (3mm length) (Osteogenics Biomedicals – USA) on the lingual side of the mandible. Furthermore, the (Xenograft - A-PRF) mixture was delivered to the recipient site using bone carrier to fill under the membrane and the titanium reinforced membrane was properly adapted over the bone graft material ensuring that no empty spaces are present (Figure 3).

The membrane was then fixed on the crestal and buccal side using the membrane tacs and fixation screws. The non-resorbable titanium reinforced membrane was trimmed 1 mm away from the adjacent tooth and the previously prepared membrane was adapted over the non-resorbable titanium reinforced membrane (Figure 4). After proper releasing of the flaps, horizontal mattress sutures at 5mm with interrupted sutures to ensure primary closure of the surgical site.

Patients were directed to strictly follow the standard post-operative instructions. Dexamethasone 8mg injection was prescribed immediately post operatively. Antibiotics were continued and NSAID medication (Bruffen 400 mg) were administered to all patients twice daily for 5 days. Patients were requested to continue the chlorhexidine mouthwash for the following 10 days. All patients did postoperative CBCT to check the augmented site as a baseline (Figure 5).

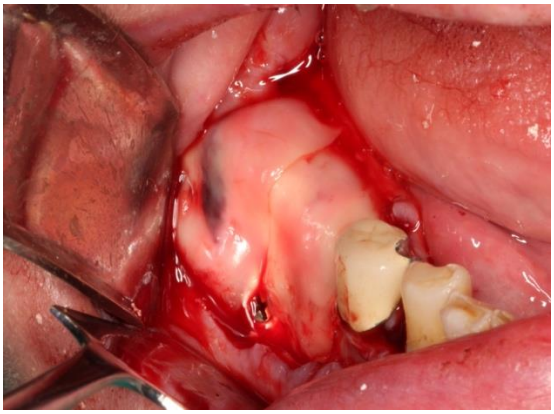

Figure (4). Application of A-PRF the membrane overlying Ti d-ptfe

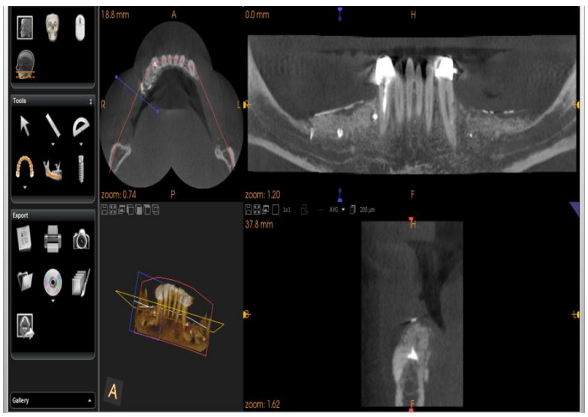

Figure (5). Immediate postoperative CBCT (baseline)

Clinically, soft tissue healing (presence or absence of infection and dehiscence of the flap) was evaluated on a period of two weeks postoperatively. Also, swelling was assessed on the 4th, 7th, and 14th postoperative days. Evaluation of pain was performed using visual analogue scale (VAS) on the 2nd, 7th and 14th postoperative days. As for paresthesia, it was evaluated according to the Two Point Discrimination Test (TPD) on the 2nd, 7th and 14th postoperative days.

6 months postoperative, reentry to the augmented for the purpose of removal of the titanium reinforced membrane, clinical evaluation of the grafted site for volume as well as bone formation, implants placement according to the surgical protocol of zimvie 3i implant system.

Primary implant stability was measured using RFA (radio frequency analysis) by mean of Osstell system at the time of placing the implants, while delayed measurement of implants stability was performed 4 months later.

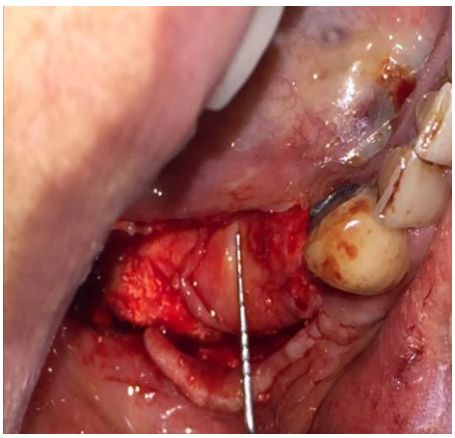

Figure (7). Healed mature bone

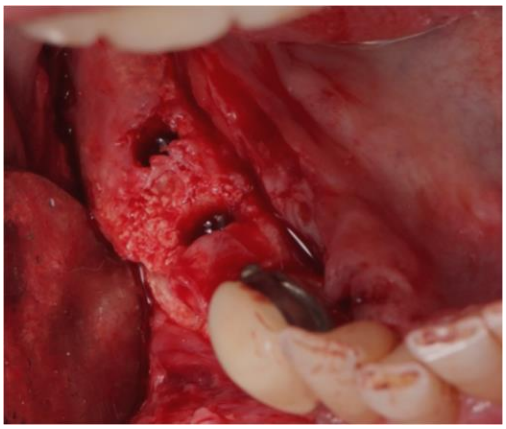

Figure (8). Implant placement

Radiographically, Cone beam computed tomography (CBCT) was done directly postoperatively (baseline) and after 6 months to check the amount of new gained bone volume before implant placement. All radiographs were evaluated by the same investigator. CBCT analysis was executed using a software program (CS 9600, Carestream, Atlanta, USA). Same sagittal cut on the area with the greatest defect was used at all follow up period to measure the bone width and height until the inferior alveolar nerve canal. Figure (9)

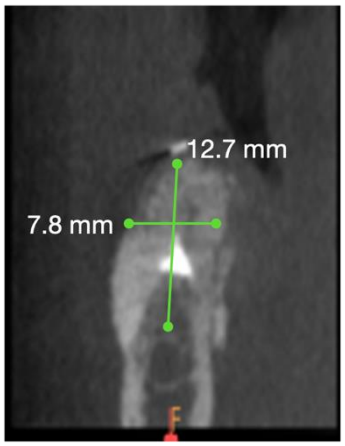

Figure (9). 6 months postoperative CBCT to evaluate bone density and volume before implant placement

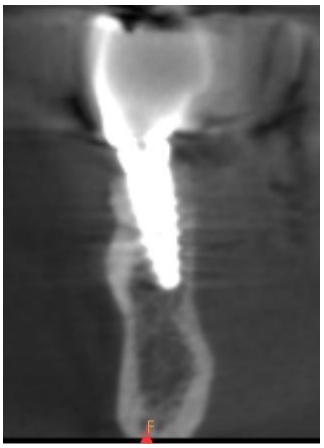

Figure (10). 6 months CBCT after implant placement showing stable bone in 3D

Furthermore, a CBCT was performed at 6 months to evaluate the stability of grafted bone around implants. Figure (10)

The obtained data were fed to the computer using the IBM SPSS software package, version 24.0 to analyze be interpreted (Armonk, NY: IBM Corp.). Numbers and percentages were used to describe qualitative data. The Kolmogorov-Smirnov test was employed to ensure that the distribution was normal. Range (minimum and maximum), mean, standard deviation, and median were used to characterize quantitative data. The significance of the acquired results was assessed at a 5% level.

Results

The fifteen participants consisted of 8 females and 7 males ranging in age from 42 to 55 years with a mean of 47.76 ± 3.65 years. All the surgeries were done without facing any complication. All operative sites showed uneventful healing without infection or flap dehiscence during the follow up period.

Figure 11 compares swelling over the follow-up period, statistically significant difference existed in swelling values between baseline (postoperative swelling measures) and all the follow up periods. Non-statistically significant difference existed between 4th and 7th days, while there was statistically significant difference between 4th and 14th days and 7th and 14th days.

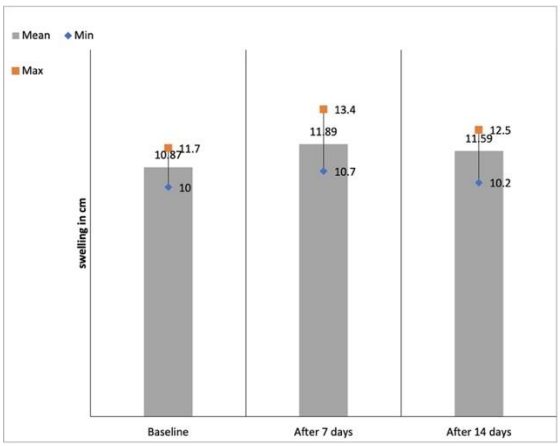

Figure 11. Comparison between the different studied periods according to swelling

Figure 12 compares pain over the two weeks follow up period, statistically significant difference between all the follow up periods. Pain reached a maximum value score (8) on the 2nd postoperative day and started to decrease gradually on the 7th and 14th days respectively.

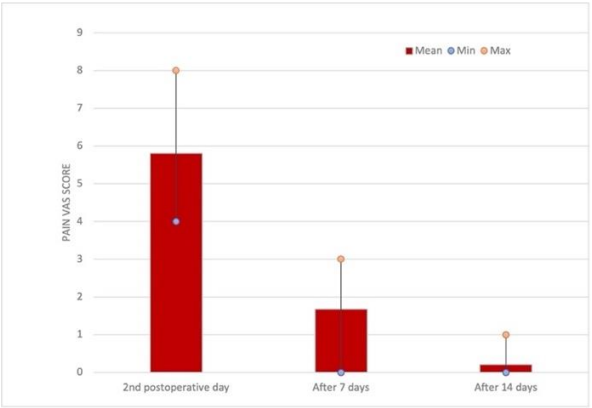

Figure 12. Comparison between the different studied periods according to pain

Table 1 shows the comparison of paresthesia throughout the follow up. Statistically significant differences existed between all tested periods. All patients had a full sensation recovery after 2 months.

Table 1. Comparison between the three studied periods according to numbness

	Numbness		
	4th post-operative	**After 7 days**	**After 14 days**
(n = 15)			
Mean ± SD.	3.47 ± 0.61	3.22 ± 0.47	2.93 ± 0.41
Median (Min. – Max.)	3.50 (2.50 – 4.50)	3.0 (2.50 – 4.0)	3.0 (2.50 – 4.0)
Sig. bet. periods.	$p_1=0.026^*$,$p_2=0.010^*$,$p_3=0.025^*$		

p_1: p value for comparing between **4th post-operative** and **After 7 days**, p_2: p value for comparing between **4th post-operative** and **After 14 days**, p_3: p value for comparing between **After 7 days** and **After 14 days**, *: Statistically significant at $p \leq 0.05$

Table 2 evaluates the bone quantity between three studied periods. Comparing preoperative bone quantity to baseline (immediate postoperative) and after 6 months, statistically significant difference existed. Non-statistical significant difference was present between the readings of bone quantity between baseline and 6 months.

Table 2. Comparison between the three studied periods according to bone quantity

	Bone quantity		
	Pre-operative	**Baseline**	**6 months post-operative**
(n = 15)			
Mean ± SD.	6.04 ± 0.97	11.92 ± 0.85	11.82 ± 0.81
Median (Min. – Max.)	6.0 (4.0 – 7.0)	12.0 (10.0 – 13.0)	12.0 (10.0 – 13.0)
Sig. bet. Periods.	$P_1<0.001^*$,$p_2<0.001^*$,$p_3=0.206$		

p_1: p value for comparing between Pre-operative and Baseline, p_2: p value for comparing between Pre-operative and 6 months post-operative, p_3: p value for comparing between Baseline and 6 months post-operative, *:Statistically significant at $p \leq 0.05$

Table 3, compares the ISQ values at implant placement and after 6 months Statistically significant differences existed between the two-time intervals. ISQ values increased after 6 months, showing increased implant stability.

Table 3. Comparison between the two different periods for implant stability according to ISQ

	ISQ at implant placement(n = 15)	**ISQ 6 months after implant placement (n = 15)**	**p**
ISQ			
Mean ± SD.	61.07 ± 1.39	78.33 ± 1.95	0.0370*
Median (Min. – Max.)	63.0 (59.0 – 66.0)	81.0 (72.0 – 85.0)	

*:Statistically significant at $p \leq 0.05$

Discussion

The lack of sufficient bone quantity in sites selected for implant placement is a challenge that frequently faces the implantologists (Garaicoa-Pazmiño, et al., 2014). However, several surgical methods to create sufficient bone volume have been developed such as autogenous onlay bone blocks, guided bone regeneration, distraction osteogenesis, and ridge expansion as well as many other techniques that have been shown successful in reconstruction of atrophic posterior mandible.

This Study is a randomized controlled clinical trial. Fifteen consecutive patients from Outpatient clinic of Oral Surgical Sciences Department, Faculty of Dentistry, Beirut Arab University, Beirut, Lebanon, needing dental implants in the posterior mandible was enrolled in this study with an age range from 30 to 60 years. Mandibular partial edentulism involving the premolar/molar area, associated with the presence of crestal bone height <7 mm coronal to the mandibular canal. The sample was randomly allocated to receive 3D ridge reconstruction that was performed using conventional GBR technique with the use of A-PRF-Cerabone mixture as a filling material which was covered with non-resosrbable titanium reinforced d-PTFE (dense polytetrafluoroethylene) the membrane was fixed with bone tacs and fixation screws then A-PRF membranes used overlying the d-PTFE.

Assessment of soft tissue healing took place by evaluating the color of mucosa, soft tissue dehiscence, as well as infection over different follow up periods. No statistically significant difference regarding the change in color throughout the evaluation period of this study.

This outcome can be agreed with (Al-Hamed, et al., 2019) who suggest that enhancing the biological capacities, tissue creation, and healing of the regenerated region through the increased concentration of growth

factors and other molecules associated to angiogenesis, stem cell migration, and osteogenic differentiation is what makes PRF biologically plausible.

Furthermore (Miron, et al., 2017) who conducted a study to evaluate the benefits of using PRF in alveolar ridge augmentation came out to demonstrate that the presence of A-PRF membrane can improve soft-tissue healing and reduce tissue dehiscence

Upon evaluating swelling, the results revealed a statistically significant difference between the follow up period $4^{th,}$ 7^{th} and 14. That was agreed with (Romanos, 2010) who suggested that the Incisions periosteal and vertically releasing are frequently employed in vertical GBR to raise a tensionless flap. However, depending on the augmentation approach, this flap design frequently leads to problems such as flap perforation and graft exfoliation in 2.5–10% of instances, as well as edema, bleeding, and patient discomfort (Ogata, et al., 2013). The location of deep periosteal incisions, which disrupts periosteal blood vessel circulation, is likely one of the primary causes of severe problems. Tension at the crestal incision site is caused by increased tissue swelling brought on by postoperative blood stasis. This tension can hinder wound healing and cause premature membrane exposure (Maridati, et al., 2016).

A statistically significant difference was recorded among patients at different time intervals, as pain was manageable and subsided at day 14 in all patients. Pain scored its maximum value on the second postoperative day, and this is due to the body reaction to the surgical procedure and the release of prostaglandin and cytokines. Pain score started to decrease gradually throughout the follow up period. These results run in parallel with (Windisch, et al., 2021), the authors found that pain was moderate in all GBR cases.

(Pacifici, et al., 2015) suggested that the use of plasma rich fibrin membranes is indicated to improve soft-tissue healing and reduce tissue dehiscence, re duce postoperative pain and swelling, and minimize infection in the surgical area

A statistically significant difference was noticed while assessing the bone quantity) at baseline and at 6 months in comparison to preoperative bone quantity. These results run parallel with (Tunkel, et al., 2021) who showed comparable results regarding vertical and horizontal augmentation gain when using the autologous and allogenic bone shells. However, a systematic review and meta-analysis, (Urban, et al., 2019) affirmed that GBR and bone shells can both significantly increase bone quantity in the augmented sites, also, devices that are form-stable growth such as titanium-reinforced non-resorbable membranes may increase vertical bone may enhance vertical bone gain.

In a review article (Urban, et al., 2023) the authors stated that the majority of trials using titanium-reinforced polytetrafluoroethylene

membranes, which are thought to be perfect for 3D augmentation surgery since they can create a private zone for a long-time space maintenance and can halt the soft tissue to collapse.

Resonance frequency analysis (RFA), which evaluates the lateral support of the implant in bone, was used for more accountable and trustworthy results that were patient-friendly according to (Huang, et al., 2020).

Implant stability quotient was compared at the time of implant placement as well as at 6 months post implant insertion, the results yielded significant differences in the ISQ values which explain the better bone maturation and integration with implants over time. Both periods showed high ISQ readings where the implants placed had high primary stability, which means that the bone was hard and mature and it can predict a successful survival of the implants if the prosthetic part is well planned and oral hygiene is well maintained.

Moreover, (Mendoza-Azpur, et al., 2019) conducted a randomized controlled clinical trial comparing guided bone regeneration with xenograft and bone blocks with xenografts, the authors declared that implants were 100% successful after a follow up period of 18 months.

Conclusion

Within the limitation of this study, it could be concluded that PFR/ xenograft mixture can be promising when used with the titanium reinforced d-ptfe membrane in 3D ridge reconstruction of atrophic posterior mandible, moreover using PRF membrane to cover the TI- d-ptfe membrane could enhance soft tissue healing as well as it can prevent soft tissue dehiscence due to the concentration of the growth factors that can be released during primary wound healing. Xenograft/PRf mixture can be consistent to be utilized for creation of new bone in severely atrophic ridges if used in GBR.

Implant stability showed promising and reliable readings at primary implant placement. However, implant stability was significantly higher at a period of 6 months post placement according to Osstell.

Conflict of Interest: The authors declare that there was no conflict of interest during conducting this research work.

Data availability: All of the data are included in the content of the paper.

Funding statement: The authors did not obtain any funding for this research

Declaration for human participants/ Ethical Approval: This study was approved by the international review board at Beirut Arab University, code: (2023-H-0121-D-P-0534).

Ethical principles of research: This research was completed in accordance with the Helsinki Declaration of 1975, revised in 2013.

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