Silvio Mario Meloni, Marco Tallarico, Aurea Immacolata Lumbau, Edoardo Baldoni, Milena Pisano

KEY WORDS
Horizontal augmentation, Guided bone regeneration, Resorbable membranes

Cohort study

HORIZONTAL RIDGE AUGMENTATION USING GBR WITH NATIVE COLLAGEN MEMBRANE AND 1:1 RATIO OF PARTICULATE XENOGRAFT AND AUTOLOGOUS BONE: A 5-YEAR PROSPECTIVE CLINICAL STUDY

SILVIO MARIO MELONI, DDS, PhD, MS
Associate Professor, School of Dentistry, University of Sassari, Italy

MARCO TALLARICO, DDS, MS
Assistant Professor, School of Dentistry, University of Sassari, Italy

AUREA IMMACOLATA LUMBAU, DDS, PhD, MS
Assistant Professor, School of Dentistry, University of Sassari, Italy

EDOARDO BALDONI, MD, DDS
Full Professor, School of Dentistry, University of Sassari, Italy

MILENA PISANO, DDS
Adjunct Professor, School of Dentistry, University of Sassari, Italy

Correspondence to:
Milena Pisano
milenapisano@yahoo.it

PURPOSE. To report the 5-year clinical and radiographic data of patients who underwent a two-stage guided bone regeneration (GBR) procedure to reconstruct severe horizontal bony defects (<4 mm) in the posterior areas.

MATERIALS AND METHODS. This study was designed as a prospective single-cohort study. Cawood and Howell class IV horizontal bony defects were augmented seven months before implant placement using a resorbable collagen membrane to protect a 1:1 mixture of anorganic bovine bone mineral (ABBM) and particulated autogenous bone. Patients were followed up for five years after definitive prostheses fitting. Implant and prosthesis survival rates and complications were the primary outcome measures. Secondary outcome measures were horizontal and volumetric dimensional changes, peri-implant marginal bone loss, and periodontal parameters.

RESULTS. Eighteen consecutive patients were enrolled, and 55 implants were inserted. Five years after loading, one patient dropped out. None of the implants or prostheses failed during the entire follow-up. Three minor surgical complications occurred early on in three patients (16.7%). In all of these cases, the collagen membrane was exposed roughly two weeks after augmentation. Two of these patients were moderate smokers (P = 0.559). At initial examination, the mean horizontal alveolar ridge width was 3.07 ± 0.64 mm. At the 7-month follow-up examination, the mean bone width was 8.09 ± 2.16 mm. The mean bone gain was 5.03 (95% CI, 4.13-5.92 mm). The difference was statistically significant (P < 0.001). The mean volume of the grafted bone, calculated using the superimposition technique, was 1.12 (95% CI, 1.01-1.23 CC). Five years after loading, the mean marginal bone loss from implant placement was 1.29 (95% CI, 1.18-1.40 mm), PI was 13.1% ± 3.9% (95% CI, 9.6%-16.6%) and BoP was 6.2% ± 2.8% (95% CI, 4.1%-8.3%).

CONCLUSIONS. Within the limitations of the study, good and stable bone augmentation and high implant survival rate up to 5 years seem to validate the use of resorbable collagen membranes with a 1:1 mixture of particulate ABBM and autogenous bone.

CONFLICT OF INTEREST STATEMENT. This study was not supported by any company, and there are no conflicts of interest to declare.

Doi: 10.36130/CTD.01.2022.04

INTRODUCTION

Implant-supported prostheses are an excellent long-term treatment option for edentulism[1] but their success rate depends on several parameters, including a sufficient amount of bone volume at the implant insertion site[2]. Insufficient healthy bone volumes around implants could negatively compromise the long term prognosis of implant-supported prosthetic restorations[3,4].

In 1988, Cawood and Howell classified alveolar crest atrophy in six degrees[5]. Among these, class IV atrophy, also known as knife-edged ridge, is characterized by a serious horizontal bony defect, often making correct prosthetically driven implant placement impossible[6]. Many techniques have been proposed to reconstruct atrophic alveolar jaws for implant-based rehabilitation, using either a simultaneous or staged approach[7]. For many years, bone blocks have been considered the gold standard for this purpose. However, this surgical technique involved requires harvesting a large amount of bone, often from extra-oral sites, causing high patient morbidity[4,8].

Guided bone regeneration (GBR) with barrier membranes has been proposed to overcome the drawbacks of the bone-block technique[7,9]. In brief, membranes are used to protect a particulated bone graft, preventing the invasion of soft tissues cells and maintaining an adequate biological space for the regeneration of new bone tissue[10]. The use of either non-resorbable or resorbable membranes, in combination with autologous or heterologous particulated bone, haves been investigated in several studies[6,10-12]. Polytetrafluoroethylene (PTFE) membranes have proved very popular, and some articles have reported good results at medium term follow-up[13]. However, with this technique a second surgery is needed, and in the event of exposure in the oral cavity, membranes may become rapidly contaminated by bacteria, potentially causing infection and graft loss[13]. Conversely, resorbable membranes may be less prone to infection[14], and have been used in combination with particulated anorganic bovine bone mineral (ABBM) for the augmentation of horizontally deficient ridges[6,15]. According to several authors, particulated autogenous bone should be mixed with bone substitutes to introduce osteogenic and osteoinductive factors[6,16,17].

The aim of the present prospective study is to report the 5-year clinical and radiographic data pertaining to patients who underwent a two-stage guided bone regeneration procedure using resorbable collagen membrane to protect a mixture of ABBM and particulated autogenous bone in a 1:1 ratio for the reconstruction of severe horizontal bone defects (<4 mm) in the posterior areas. Implants were placed after 7 months, and 1-year and 3-year interim reports revealed a high implant survival rate and high average bone augmentation[6,18]. This paper, the 5-year report, was written in accordance with the Strengthening the Reporting of Observational studies in Epidemiology (STROBE) guidelines[19].

MATERIALS AND METHODS

This study was designed as a single-cohort prospective observational study to assess patients with severe horizontal bone defects in the posterior mandible or maxilla treated with GBR 7 months before implant placement. Patients were selected and treated at one private clinic in Sardinia (Italy) from June 2013 to April 2014. One experienced clinician performed all surgical procedures (S.M.M.), while another clinician (M.P.) fitted all the prosthetic restorations. All patients were duly informed about the nature of the study, and gave their informed written consent.

Any patient aged 18 years or older affected by partial or total posterior edentulism of either the mandible or maxilla, with residual horizontal ridge thickness of 4 mm or less (Cawood-Howell Class IV)[3], who required an implant-supported restoration and was able to under-

stand and sign informed consent was considered eligible for inclusion in this study. Patients were not admitted into the study if any of the following exclusion criteria applied:

- American Society of Anesthesiologist (ASA) class III or IV;
- Pregnancy or nursing;
- Alcohol or drug abuse;
- Heavy smoking (>10 cigarettes/day);
- Radiation therapy to head or neck region within 5 years;
- Absence of teeth/denture in the opposing jaw;
- Untreated periodontitis;
- Immediate post-extraction implants;
- Full-mouth bleeding and full-mouth plaque index of 25% or greater;
- Unavailability for regular follow-ups.

Surgical and prosthetic protocol

Patients' medical history, photographs (**FIG. 1**) and study models were collected at the first visit. Preoperative cone-beam computed tomography (CBCT) scans were obtained for initial screening and evaluation (**FIG. 2**). Smokers were advised to refrain from smoking four weeks before and for four weeks after surgery. Patients received amoxicillin 2 g (Zimox, Pfizer, Rome, Italy) one hour before surgery, and 1 g twice daily for one week thereafter. In the event of penicillin allergy, clindamycin was administered for premedication (600 mg 1 hour before surgery) and after surgery (300 mg four times a day for 1 week). Patients were instructed to rinse with 0.2% chlorhexidine solution (Curasept, Curaden Healthcare, Saronno, Italy) for one minute before surgery, and a sterile surgical drape was applied to minimize potential contamination from extra-oral sources. Oral sedation with triazolam 0.50 mg (Triazolam Ratiopharm, Milan, Italia) was given prior to surgery. Local anaesthesia (Septanest with adrenaline, 1/100000, Septodont, Mataró, Spain) was given.

A midcrestal incision was made in the keratinized tissue using a No. 15 surgical blade, and a full-thickness flap was raised beyond the mucogingival junction, at least 5 mm beyond the bone defect. Two vertical incisions were made at least one tooth mesial and distal from the area to be augmented, while, in edentulous areas, vertical incisions were made into the retromolar pad, at least 5 mm away from the planned surgical site. In the posterior mandible, a lingual flap was elevated beyond the mylohyoid line, protecting sensitive anatomical structures. Before bone harvesting, the recipient site was debrided, removing the soft tissue remnants. Autogenous bone was taken from the retromolar regions of the mandible using a minimally invasive cortical bone collector (Micross, Meta, Reggio Emilia, Italy). In maxillary sites, an additional flap was raised for the bone harvesting procedure. After that, multiple decortication was performed at the recipient site using a 2-mm round bur (**FIG. 3**). Then, a collagen membrane (Bio-gide, Geistlich Biomaterials Italia, Vicenza, Italy) was fixed using two lingual/palatal titanium pins (Supertack, MCbio, Lomazzo, Italy). The particulated harvested autogenous bone material was mixed with ABBM (Bio-OSS, Geistlich Biomaterials Italia) in a 1:1 ratio, and placed at the buccal and lingual/palatal sides of the defect (**FIG. 4**). At this stage, the collagen membrane was trimmed to cover the entire volume of the graft. Two additional titanium pins were placed on the buccal side to fix the membrane. Then, a third tack was placed in the mid-buccal side to prevent apical movement of the bone graft. Where indicated, maxillary cases were given a conventional sinus augmentation procedure to achieve additional apical bone height for subsequent implant placement. Finally, a periosteal incision was made between the two vertical incisions to allow for completely tension-free flap closure. In the mandible, both the lingual and the buccal flaps were released. The flaps were sutured in two

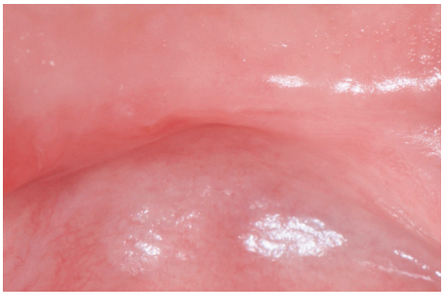

FIG. 1: *Pre-operative photograph, occlusal view.*

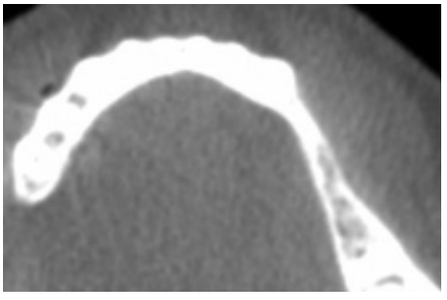

FIG. 2: *Pre-operative CBCT scan, axial view.*

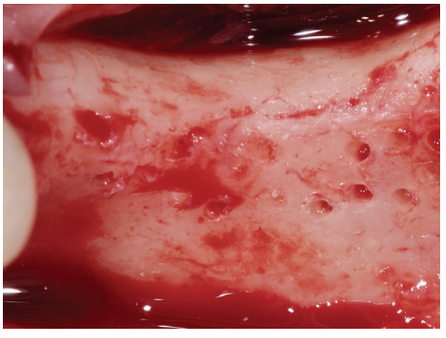

FIG. 3: *Intra-operative photograph, before bone reconstruction.*

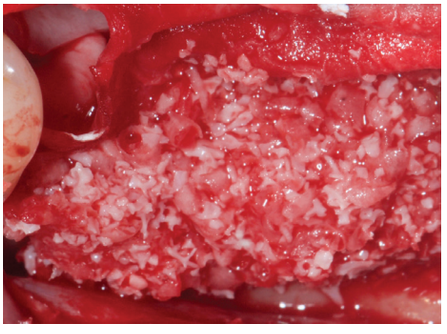

FIG. 4: *Bone reconstruction with 50% autologous bone 50% anorganic bovine bone and collagen membrane.*

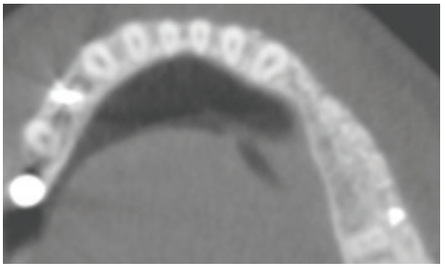

FIG. 5: *CBCT scan 7 months after bone reconstruction.*

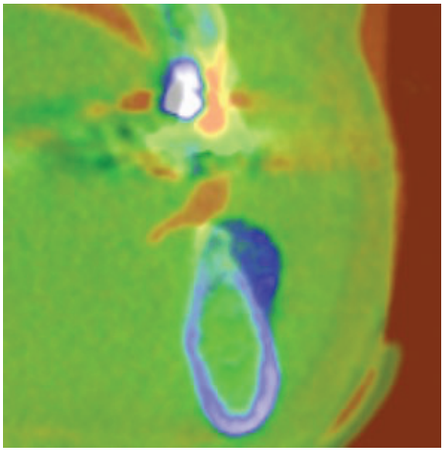

FIG. 6: *Superimposition of CBCT scans taken before and 7 months after surgery.*

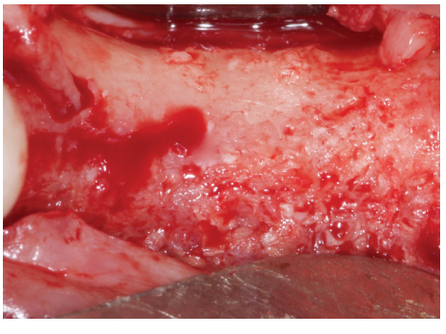

FIG. 7: *Alveolar crest before implant placement.*

layers to prevent exposure of the membrane. Horizontal mattress sutures (4-0 Vycril, Ethicon, Johnson & Johnson, Rome, Italy) were tied 4 mm from the incision line, and then, single interrupted sutures were tied to close the edges of the flap. Vertical incisions were sutured with single interrupted sutures.

Postoperatively, 5 mg of oxycodone hydrochloride (Mundipharma Pharmaceuticals, Milan, Italy) was prescribed twice daily for the first day, and then as needed. Dexamethasone (Desoren, Rekah Pharmaceutical Products, Holon, Israel) 4 mg was administered immediately after surgery. Patients were instructed to continue antibiotic therapy as prescribed, to rinse with 0.2% chlorhexidine for two weeks, and to follow a soft-food diet for 10 days. The single interrupted sutures were removed between 10 and 14 days after surgery, and the mattress sutures were removed two to three weeks after surgery. Seven months after GBR, a second CBCT scan was performed to assess the graft material integration and to measure the horizontal bone remodelling (**FIGS. 5, 6**). Implants with a partially machined collar (PMC, NobelReplace Conical Connection, Nobel Biocare, Kloten, Switzerland) were placed according to the manufacturer's instruction, using an insertion torque ranging between 30 and 45 Ncm, as measured by the surgeon using a manual torque wrench (**FIGS. 7, 8**), and submerged. Three to six months after implant placement, zirconia ceramic definitive crowns were fitted (**FIGS. 9-11**). All patients were followed up for at least five years after loading. Data were collected at implant placement, loading, and at 12, 36 and 60 months after loading (**FIGS. 12, 13**). Hygiene maintenance and occlusal check-ups were scheduled every 6 months.

Outcome measures

Implant and prosthesis survival rates and complications were the primary outcome measures.

- Implant failure was considered any removal of implants dictated by implant mobility, progressive marginal bone loss, infection or implant fracture. The stability of individual implants was measured by the prosthodontist at the time of definitive crown fitting applying a removal torque of 35 Ncm. After loading, implant stability was tested manually by the same prosthodontist using two dental mirror handles.
- Prosthesis failure was considered any prosthesis that had to be refitted for any reason.
- Any surgical complications such as membrane exposure, subsequent infection and/or morbidity associated with the donor site; as well as any prosthetic complications, such as fractures or chipping of the provisional or definitive ceramic crown, or abutment mobility; and any biological complications, such as wound or implant infection, mucositis, abscesses, or peri-implantitis, were recorded. Complications were assessed and treated by the same clinicians who performed the augmentation and implant or prostheses placement procedures.

Secondary outcome measures were horizontal and volumetric dimensional changes, peri-implant marginal bone loss, and periodontal parameters.

- Horizontal and volumetric dimensional changes were measured on CBCT. CBCT scans were performed before ridge reconstruction, and 7 months thereafter. The Digital Imaging and Communication in Medicine (DICOM) data were imported into the OnDemand 3D software (version 1.0.9.3223, Cybermed, Seoul, South Korea) to perform all measurements. The DICOM data was manually aligned on unchanged anatomical areas (e.g., teeth, basal skull, and previous implants) and then automatically matched using the adjunctive Fusion module (Cybermed). Horizontal bone was measured 2 mm below the bone crest at all reconstructed ridges before and after treatment. Bone gain was calculated for each site, and is expressed as a linear difference between pre-regeneration and post-regene-

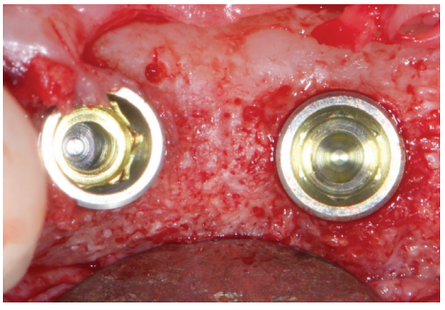

FIG. 8: *Alveolar crest at implant placement.*

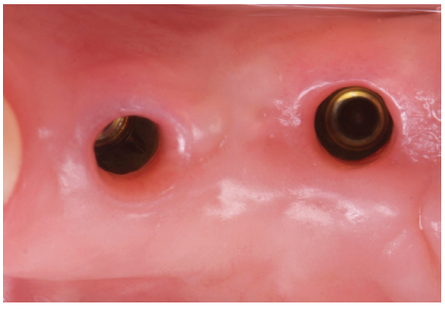

FIG. 9: *Soft tissue healing immediately before loading.*

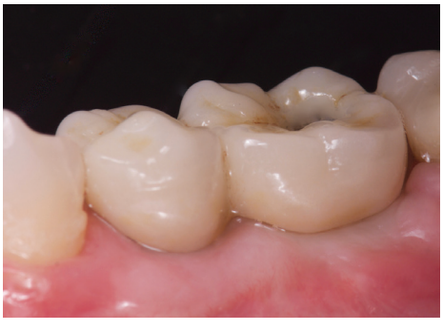

FIG. 10: *Clinical view at loading.*

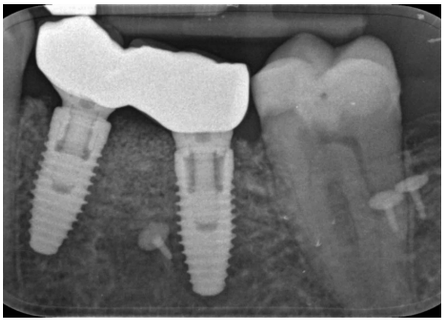

FIG. 11: *Peri-apical x-ray at loading.*

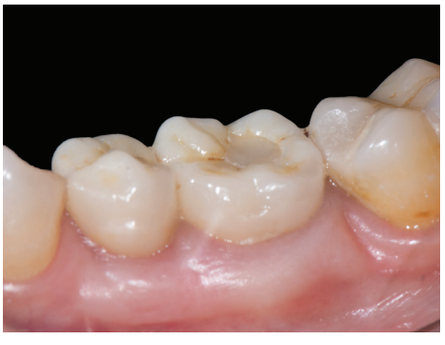

FIG. 12: *Clinical view at 5-year follow-up.*

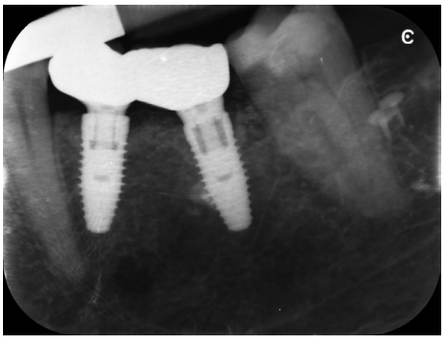

FIG. 13: *Peri-apical x-ray at 5-year follow-up.*

ration measurements. Post-operative volumetric data were subtracted from the original, and the volumes of the grafted material were calculated using automatic tools.

Peri-implant marginal bone loss was calculated on digital periapical radiographs taken with the paralleling technique using a film-holder (Rinn XCP, Dentsply, Elgin, Illinois, USA) at implant placement (baseline) and at 1, 3 and 5 years after definitive loading. The radiographs were accepted or rejected for evaluation based on the clarity of the implant threads. The distance from the most coronal margin of the implant collar to the most coronal point of bone-to-implant contact was calculated. All readable radiographs were displayed in image analysis software (DFW2.8 for Windows, Soredex, Tuusula, Finland) on a 24-inch LCD screen (iMac, Apple, Cupertino, California, USA), and evaluated under standardized conditions (SO 12646:2004). The software was calibrated for every single image

using the known distance between two adjacent implant threads. Measurements of the mesial and distal bone crest level adjacent to each implant were made to the nearest 0.01 mm, and averaged at patient level.

Volumetric dimensional changes and peri-implant marginal bone level changes were evaluated by an expert radiologist (G.F.) not otherwise involved in the study.

Plaque index (PI), defined as plaque absent or present (0/1), and bleeding on probing (BoP), defined as absent or present (0/1), were recorded on six sites per tooth (three buccal and three oral sites, respectively), at 1, 3 and 5 years after loading. Multiple implants were averaged at patient level and the data were expressed as percentages. Another clinician (A.D.), not previously involved in the study, made all the periodontal measurements up to 3 years, after which the measurements were performed by another clinician (M.P.).

Statistical analysis

All analysis was carried out according to a pre-established analysis plan using SPSS software for Mac OS X (version 22.0; SPSS, Chicago, Illinois, USA). A dentist (M.T.) analysed the data. Descriptive analysis was performed for numeric parameters using means ± SD and 95% confidence interval (CI). Continuous outcomes (horizontal and volumetric dimensional changes; peri-implant marginal bone loss; plaque index; and bleeding on probing) were compared using paired t-tests. The patient was the statistical unit of the analyses. Multiple implants were averaged at patient level. All statistical comparisons were conducted at the 0.05 level of significance.

RESULTS

Twenty patients were screened for eligibility, but two patients were not enrolled in the trial as they refused to undergo more than one CBCT scan. Eighteen consecutive patients (seven males and 11 females) with a mean age of 56.8 years (range 24-78) with 22 surgical sites classified as Cawood-Howell Class IV (5) received at least one GBR procedure each. Overall, 55 regular platform implants of 4.3 mm of diameter were inserted. Eight patients were treated in the mandible and 10 in the maxilla. Of these, six procedures (60%) involved sinus lift.

At the follow-up examination 5 years after definitive loading, one patient had dropped out, having moved to another city and being unable to attend the scheduled appointment. No deviation from the original protocol occurred. None of the implants or prostheses failed during the entire follow-up period.

Three early surgical complications occurred in three patients (16.7%). In all of these cases, the collagen membrane became exposed about 2 weeks after augmentation. Although two of these patients were moderate smokers, Fisher's exact test failed to find any significant association ($P = 0.559$) between smoking and early membrane exposure. To resolve the issue in these patients, the affected area was treated by locally applying chlorhexidine gel 0.5% (Curasept ADS 0.5%) twice per day for 3 weeks. Complete soft tissue healing was observed in all three cases. No other biological or technical complications were recorded during the entire follow-up period.

At initial examination, the mean horizontal alveolar ridge width was 3.07 ± 0.64 mm (95% CI, 2.80-3.34 mm). At the 7-month follow-up examination, the mean bone width was 8.09 ± 2.16 mm (95% CI, 7.19-8.99 mm), i.e., a mean bone gain of 5.03 ± 2.15 mm (95% CI, 4.13-5.92 mm). The difference was statistically significant ($P < 0.001$; **TABLE 1**). The mean volume of the grafted bone, calculated using the superimposition technique, was 1.12 ± 0.18 CC (95% CI, 1.01–1.23 CC).

One year after definitive loading, the mean marginal bone loss from implant placement was 1.03 ± 0.21 mm (95% CI, 0.83–1.17 mm). Three years after definitive loading, the mean marginal

TABLE 1 MARGINAL BONE LEVELS

	Implant placement (baseline) (n = 18)	1 year (n = 18)	3 years (n = 18)	5 years (n = 17)
Marginal bone levels (mm)	0.02 ± 0.04; 95% CI: 0.0-0.04	1.05 ± 0.27; 95% CI: 0.93-1.17	1.17 ± 0.26; 95% CI: 1.04-1.29	1.28± 0.23; 95% CI: 1.17-1.38
Marginal bone loss compared with baseline (mm)		1.03 ± 0.26; 95% CI: 0.91-1.15	1.15 ± 0.28; 95% CI: 1.02-1.28	1.29 ± 0.23; 95% CI: 1.18-1.40
P Value		< 0.001	< 0.001	< 0.001

bone loss was 1.15 ± 0.28 mm (95% CI, 0.84–1.22 mm). At the 5-year follow-up, the mean marginal bone loss was 1.29 ± 0.23 mm (95% CI, 1.18–1.40 mm), which was statistically significantly higher than at baseline (P < 0.001).

One year after definitive loading, the mean PI was 11.1% ± 7.1% (95% CI, 7.3%-14.8%), while 5.6% ± 4.4% (95% CI, 3.1%-8.1%) of the implants showed positive BoP. Three years after definitive loading, PI was 11.6% ± 3.5% (95% CI, 8.6%-14.6%) and BoP was 5.2% ± 2.9% (95% CI, 3.3%-7.1%). At the last follow-up examination, PI was 13.1% ± 3.9% (95% CI, 9.6%-16.6%) and BoP was 6.2% ± 2.8% (95% CI, 4.1%-8.3%).

DISCUSSION

The aim of this prospective study was to investigate the 5-year post-loading clinical and radiographic data on GBR procedures using particulate autologous bone and ABBM in a ratio of 1:1 in combination with a resorbable membrane for horizontal augmentation of knife-edged ridges.

Data obtained at 5-year follow-up confirm the 1- and 3-year results[6,18]. Specifically, at 5 years, the mean horizontal bone gain was 5.03 mm (±2.15 mm), with seven sites gaining at least 7 mm or more. This finding is in line with another report supporting the use of GBR procedure with collagen membranes as the standard treatment for knife-edged ridges[16]. Moreover, in a systematic review, Aghaloo and Moy reported a statistically significant reduction in implant survival rates at sites grafted with autogenous bone blocks, as compared to other regenerative techniques[2]. Specifically, their meta-analysis found an implant survival rate of 95.5% for GBR, as compared to 74.4% for iliac crest grafts[2]. However, it is important to note that that review was not based on RCTs.

In the present study, three early collagen membrane exposures were recorded, but the planned treatment was successfull anyway. In contrast, non-resorbable e-PTFE membranes are frequently associated with major complications such as infection due to membrane exposure, and hence need to be removed before the planned time. In our opinion, results reported in this article support the use of only resorbable materials *versus* non-resorbable ones when treating severely resorbed ridges. However, RCTs would be needed to support this view. Indeed, only one controlled trial has compared bone quality after vertical GBR with non-resorbable titanium reinforced barriers *versus* resorbable barriers on titanium mesh, and this reported comparable results[20]. Nonetheless, in our opinion the major advantage of resorbable membranes is the reduced number of major complications, another finding that needs to be confirmed by RCTs. Moreover, the use of 50% ABBM in these procedures reduces the need for large amounts of harvested autogenous bone, which, combined with the use of particulate bone harvested using a scraper, could lead to decreased post-operative morbidity.

The limitations of the present study were the lack of suitable controls, the low number of treated patients, and the inclusion of posterior jaws only. That being said, despite the long interval between surgery and prosthesis fitting, the two-stage procedure seems to be safe and predictable for major reconstructions, and can be applied in daily practice[16].

CONCLUSIONS

Within the limitations of the present study, good and stable augmented bone and high implant survival rate at 5-year follow-up seem to validate the use of collagen resorbable membranes with a 1:1 mixture of particulate ABB and autogenous bone for the reconstruction of severe horizontal ridge defects in posterior jaws.

ACKNOWLEDGEMENTS

The authors wish to thank the radiologist Dr. Giuseppe Fais and the dentist Dr. Alessandro Deledda for their contributions to data collection. The authors also take this opportunity to point out that there was a typing mistake in the 3 year follow-up article, and the clinician involved in collecting periodontal data was A.D. and not G.F.

REFERENCES

1. Pjetursson BE, Thoma D, Jung RE, Zwahlen M, Zembic A. A systematic review of the survival and complication rates of implant-supported fixed dental prostheses (FDPs) after a mean observation period of at least 5 years. Clin Oral Implants Res 2012;12:22-38.
2. Aghaloo TL, Moy PK. Which hard tissue augmentation techniques are the most successful in furnishing bony support for implant placement. Int J Oral Maxillofac Implants 2007;22:49-70.
3. Esposito M, Grusovin MG, Coulthard P, Worthington HV. The efficacy of various bone augmentation procedures for dental implants: a Cochrane systematic review of randomized controlled clinical trials. Int J Oral Maxillofac Implants 2006;21:696-710
4. Simion M, Jovanovic SA, Tinti C, Benfenati SP. Long-term evaluation of osseointegrated implants inserted at the time or after vertical ridge augmentation. A retrospective study on 123 implants with 1-5 year follow-up. Clin Oral Implants Res 2001;12:35-45.
5. Cawood JI, Howell RA. A classification of the edentulous jaws. Int J Oral Maxillofac Implants 1988;17:232-6.
6. Meloni SM, Jovanovic SA, Urban I, Canullo L, Pisano M, Tallarico M. Horizontal ridge augmentation using GBR with a native collagen membrane and 1:1 ratio of particulated xenograft and autologous bone: a 1-year prospective clinical study. Clin Implant Dent Relat Res 2017;19:38-45.
7. Buser D, Ingimarsson S, Dula K, Lussi A, Hirt HP, Belser UC. Long-term stability of osseointegrated implants in augmented bone: a 5-year prospective study in partially edentulous patients. Int J Periodontics Restorative Dent 2002;22:109-17
8. Chiapasco M, Casentini P, Zaniboni M, Corsi E. Evaluation of peri-implant bone resorption around Straumann Bone Level implants placed in areas reconstructed with autogenous vertical onlay bone grafts. Clin Oral Implants Res 2012;23:1012-21.
9. Urban IA, Jovanovic S, Lozada JL. Vertical ridge augmentation using guided bone regeneration (GBR) in three clinical scenarios prior to implant placement: a retrospective study of 35 patients 12 to 72 months after loading. Int J Oral Maxilofac Implants 2009;24:502-10.
10. Urban IA, Caplanis N, Lozada JL. Simultaneous vertical guided bone regeneration (GBR) and guided tissue regeneration (GTR) in the posterior maxilla using recombinant human platelet-derived growth factor (rhPDGF). A case report. J Oral Implantol 2009;35:251-6.
11. Esposito M, Grusovin M, Worthington H, Coulthard P. Interventions for replacing missing teeth: bone augmentation techniques for dental implant treatment. Cochrane Database Syst Rev 2006;CD003607.
12. Wessing B, Urban I, Montero E et al. A multicenter randomized controlled clinical trial using a new resorbable non-cross-linked collagen membrane for guided bone regeneration at dehisced single implant sites: interim results of a bone augmentation procedure. Clin Oral Implants Res 2017;28:218-26.
13. Chiapasco M, Abati S, Romeo E, Vogel G. Clinical outcome of autogenous bone blocks or guided bone regeneration with e-PTFE membranes for the reconstruction of narrow edentulous ridges. Clin Oral Implants Res 1999;10:278-88.
14. Schenk RK, Buser D, Hardwick WR, Dahlin C. Healing pattern of bone regeneration in membrane-protected defects: a histologic study in the canine mandible. Int J Oral Maxillofac Implants 1994;9:13-29.
15. 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;54:420-32.

16. 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 Restorative Dent 2013;33:299-307.
17. Jovanovic SA, Spiekermann H, Richter EJ. Bone regeneration around titanium dental implants in dehisced defect sites: a clinical study. Int J Oral Maxillofac Implants 1992;7:233-45.
18. Meloni SM, Jovanovic SA, Urban I, Baldoni E, Pisano M, Tallarico M. Horizontal ridge augmentation using GBR with a native collagen membrane and 1:1 ratio of particulate xenograft and autologous bone: A 3-year after final loading prospective clinical study. Clin Implant Dent Related Res 2019;23:22-9.
19. von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP. The strengthening the reporting of observational studies in epidemiology (STROBE) statement: guidelines for reporting observational studies. STROBE initiative. Int J Surg 2014;12:1495-9.
20. Cucchi A, Sartori M, Parrilli A, Aldini NN, Vignudelli E, Corinaldesi G. Histological and histomorphometric analysis of bone tissue after guided bone regeneration with non-resorbable membranes *vs* resorbable membranes and titanium mesh. Clin Implant Dent Relat Res 2019;21(4):693-701.