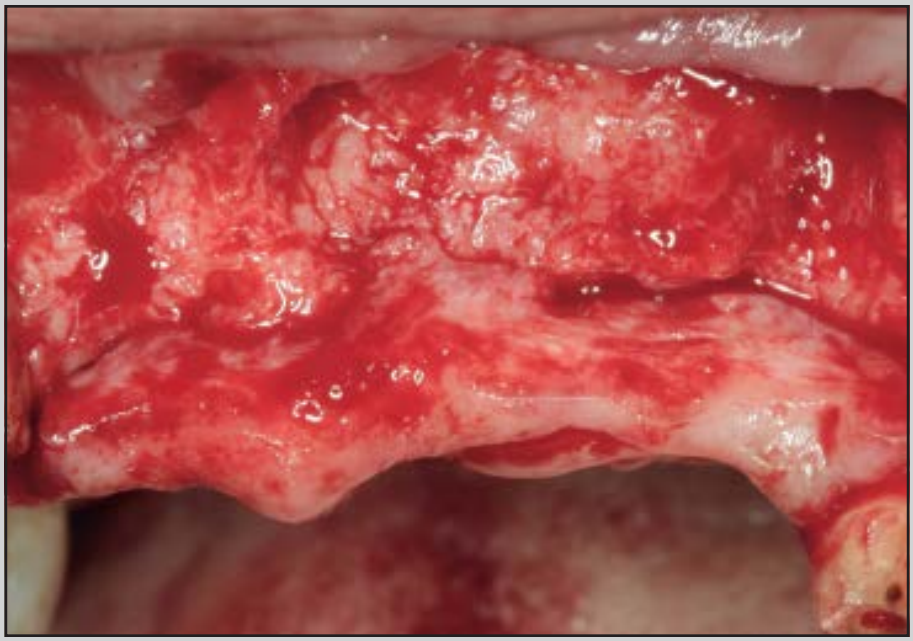

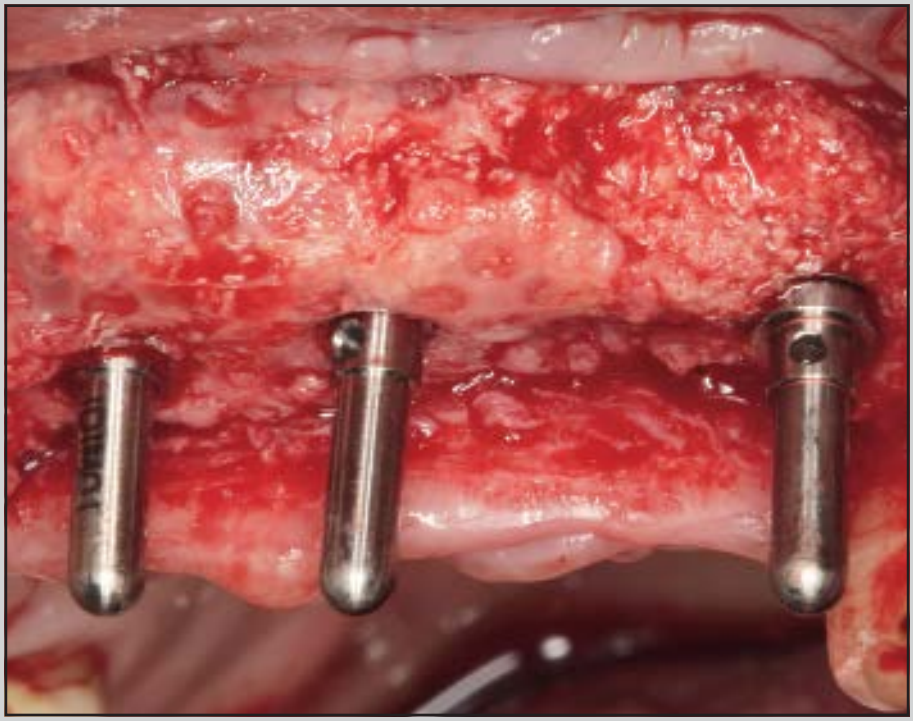

A Novel Combined Surgical Approach to Vertical Alveolar Ridge Augmentation with Titanium Mesh, Resorbable Membrane, and rhPDGF-BB: A Retrospective Consecutive Case Series

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The purpose of this case series was to report the clinical outcomes and histologic findings of vertical ridge augmentation using a combination of titanium mesh, resorbable collagen membrane, and recombinant human platelet-derived growth factor BB (rhPDGF-BB). Nineteen patients were included, and autogenous bone and anorganic bovine bone particles were used. The bone graft was mixed with rhPDGF-BB and loaded onto the bony defect up to the level of the adjacent alveolar crest. A pre-adapted titanium mesh was placed over the grafted region and covered with a resorbable collagen membrane, leaving no areas of the grafted region exposed. Seventeen patients exhibited good soft tissue healing. Postoperative flap dehiscence occurred relatively early in the healing period in one patient, whereas the covering collagen membrane was exposed during the later phase of the healing period in another. During reentry surgery for removal of the titanium mesh, three patients with favorable soft and hard tissue healing underwent bone biopsies for histologic evaluation of the augmented tissue just below the titanium mesh. The mean vertical height of augmented bone was 8.6 ± 4.0 mm. This report demonstrates the remarkable efficacy of guided bone regeneration using a combination of titanium mesh, resorbable collagen membrane, and rhPDGF for vertical ridge augmentation, thus expanding the indications for implant therapy and allowing recovery of the three-dimensional esthetic architecture in a severely absorbed alveolar ridge.
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In the field of implant dentistry, vertical ridge augmentation is a clinical challenge with respect to expanded indications for implant therapy and the final esthetic results. Many clinical reports have demonstrated predictable and controllable bone augmentation using a titanium mesh in combination with extra- or intraoral autogenous bone combined with a xenograft in vertical bony defects.[1–3] However, a titanium mesh has some inherent drawbacks when used in a local ridge augmentation procedure. It is technically difficult to completely cover bone graft materials positioned on the complex form of a resorbed alveolar arch with a titanium mesh, which sometimes results in compromised outcomes. Alveolar augmentation with a titanium mesh often results in wound dehiscence and mesh exposure, thus increasing the risk of infection in the grafted region.[3–8] Holes in the titanium mesh also allow leakage of liquid factors, such as exogenous growth factors added to the grafted region.

Recently, the inherent problems associated with the use of a titanium mesh were overcome by

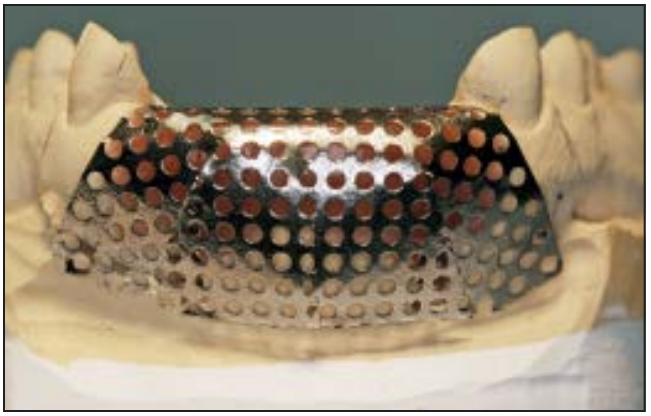


Fig 1 *Pre-adaptation of titanium mesh to a recipient site using a sterilized study cast prior to surgery.*

pre-adapting the mesh before surgery and combining its use with a cross-linked collagen membrane that has excellent biocompatibility, resistance to infection,[9] and a prolonged bioabsorption period (over 24 weeks).[10,11] A combination of titanium mesh and a cross-linked collagen membrane theoretically leads to complementary and synergistic effects and yields many technical and biologic improvements compared with conventional methods.[12,13] Fibrous in-growth from the gingival flaps occurs in the covering collagen membrane and prevents wound dehiscence.[14] In addition, the membrane is expected to prevent invasion of soft tissue into the grafted region and leakage of bone graft materials and exogenous growth factors, such as recombinant human platelet-derived growth factor BB (rhPDGF-BB), through any gaps between titanium mesh units, which plays an important role in wound repair processes such as cell proliferation, chemotaxis, and matrix synthesis.[15,16] The purpose of this retrospective case series was to use visual measurements and histologic evaluations of the regenerative bone to demonstrate the effectiveness of staged GBR using a titanium mesh, a cross-linked collagen membrane, and rhPDGF-BB for vertical ridge augmentation.

Method and materials

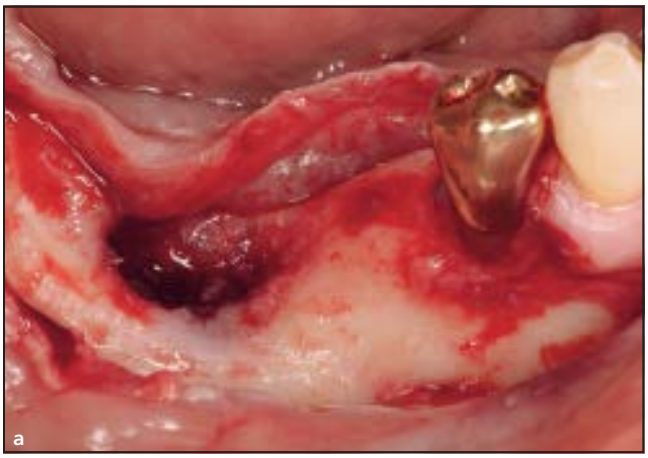
Patient selection

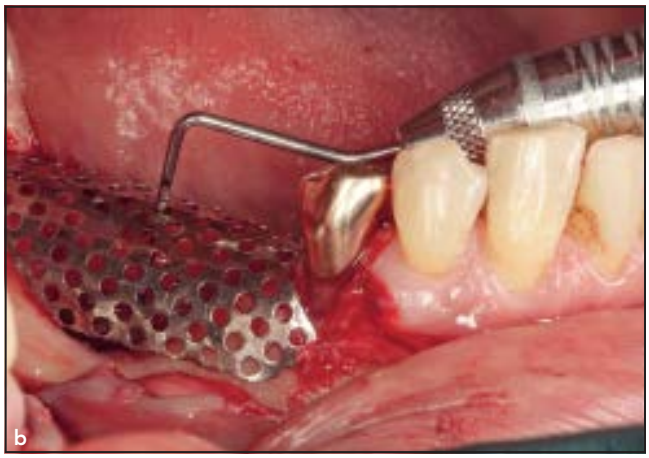
A total of nineteen edentulous ridges (10 maxillary anterior, 4 maxillary posterior, 2 mandibular anterior, and 3 mandibular posterior) of 19 patients (10 women and 9 men) with a mean age of 50.2 ± 14.4 years (range, 17 to 68 years) were augmented by staged GBR at three private clinics between April 2007 and October 2009. All patients requested dental implants to replace their missing teeth. Upon comprehensive examination and treatment planning, a staged approach for vertical alveolar ridge augmentation and subsequent implant placement was recommended because of the severity of defects in the proposed implant sites. All patients were in good general health with no contraindications for surgical treatment. The treatment plan and sequence were described in detail to all patients, who also signed a consent form.

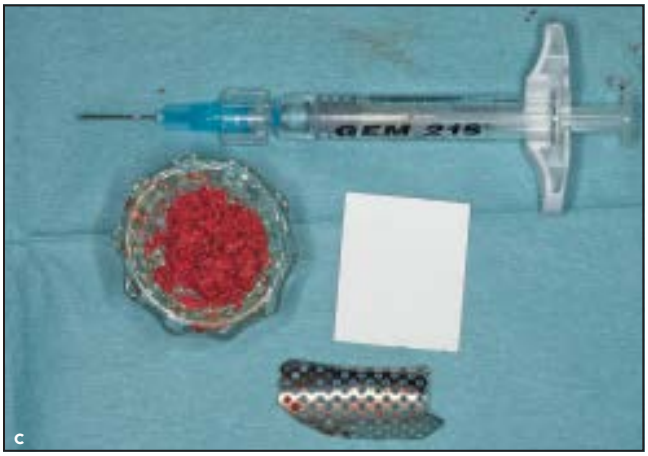
Surgery

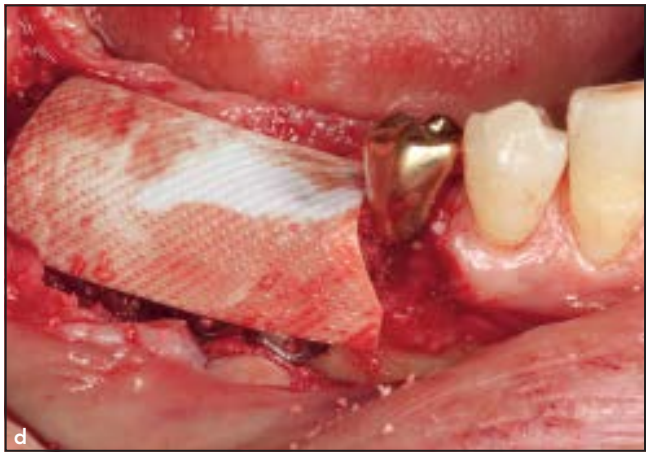
The thickness of the titanium mesh was 0.1 mm (Jeil Medical). The titanium mesh was preshaped using a sterilized study cast before surgery (Fig 1). After local anesthesia, a crestal incision, buccal and lingual mucoperiosteal flap elevation, and removal of residual soft tissue on the bone surface, the cortical bone was perforated up to the intramarrow space to allow vascular and cellular access into the augmentation site. A periosteal releasing incision was placed to achieve primary closure of the augmentation site with tension-free coronal flap advancement.

In all cases, autogenous bone was harvested from the mandibular ramus with a bone scraper (Safescraper Twist, META) and mixed with blood aspirated from the patient's surgical site. Anorganic









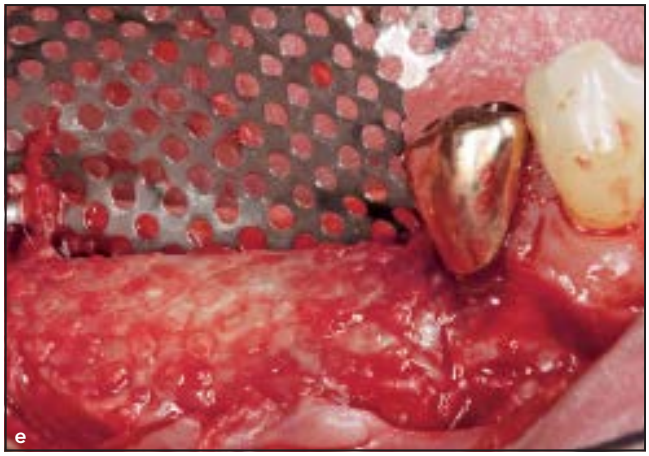


Fig 2a (left) *View of severe bone resorption in the right posterior region of the mandible.*

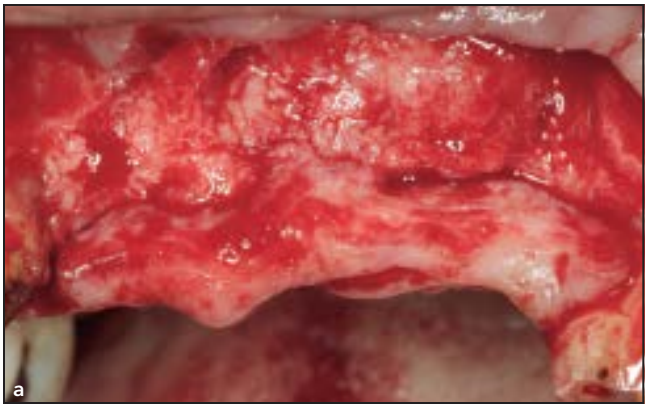
Fig 2b (right) *Vertical measurement of the depth of the bone defect from the deepest point of the defect to the most coronal hole of the titanium mesh using a periodontal probe.*

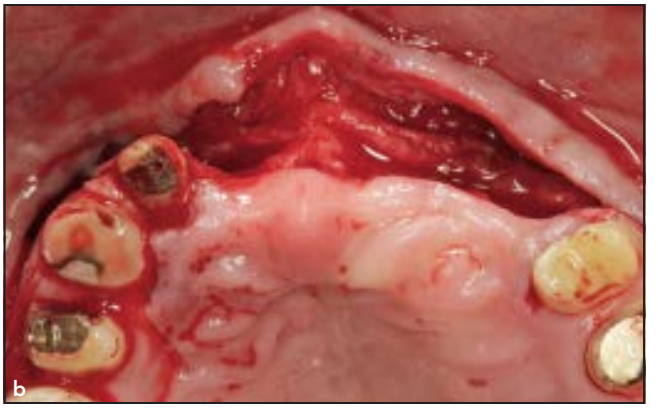
Fig 2c *A mixture of anorganic bovine bone and autogenous bone particles harvested from the mandibular ramus and mixed with rhPDGF-BB.*

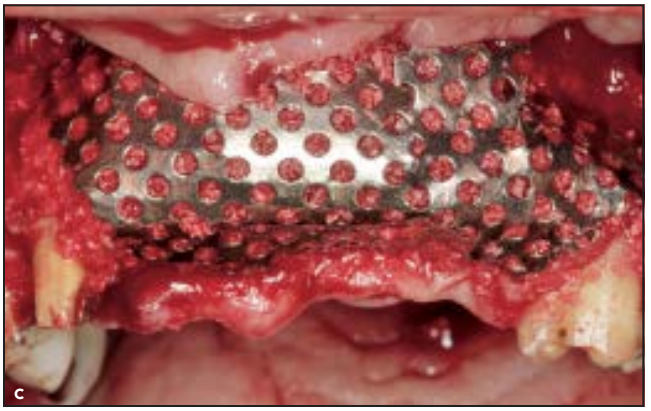
Fig 2d *Complete coverage of the bone-grafted region with an enzymatically cross-linked collagen membrane.*

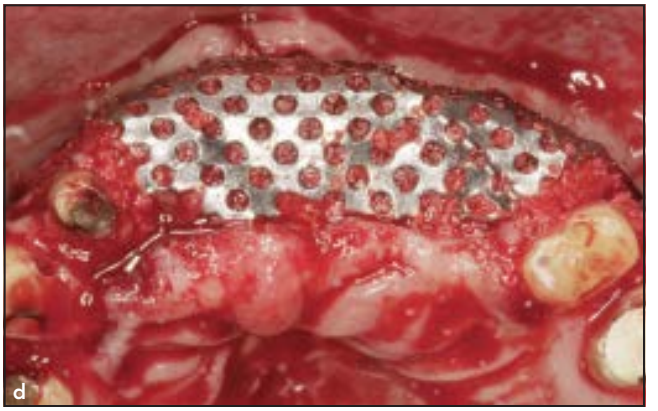
Fig 2e *Augmented bone beneath the titanium mesh after 6 months of healing; note that the entire top surface of the augmented bone has reached a level equivalent to the top of the adjacent bone crest.*

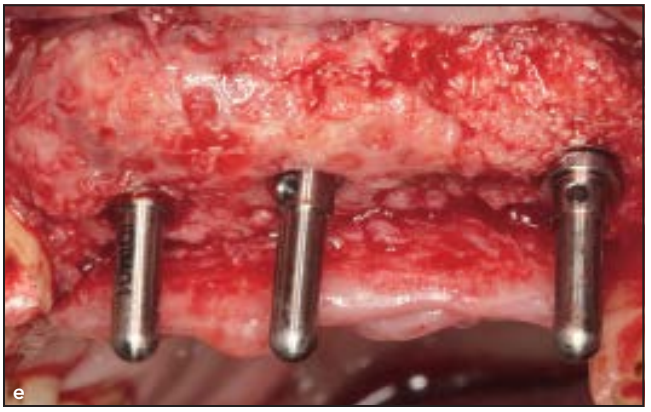
bovine bone (0.25- to 1-mm particles; Bio-Oss, Osteohealth) was mixed with the autogenous bone in a ratio of 1:1 or 4:1. The bone graft mixture was soaked in rhPDGF (Gem 21S, Osteohelth) for 10 minutes (Fig 2) and packed into and/or loaded onto the highly absorbed alveolar ridge up to the level of the adjacent alveolar crest (Fig 3). A pre-adapted titanium mesh was then positioned and stabilized











Figs 3a and 3b (a) *Frontal and* (b) *occlusal views showing severe bone resorption in the anterior maxillary region.*

Figs 3c and 3d (c) *Frontal and* (d) *occlusal views showing bone substitute and autogenous bone particles mixed with rhPDGF-BB and covered with the pre-adapted titanium mesh.*

Fig 3e *Frontal views showing the preparation of implant holes in the augmented ridge; note that apparently solid bone-like tissue is formed.*

over the grafted region. As required, fixation screws (Jeil Medical) were used for stabilization of the titanium mesh. The bone graft mixture and titanium mesh were then completely covered with a cross-linked resorbable collagen membrane (Ossix Plus, Orapharma), and the wound was closed with horizontal mattress and simple interrupted sutures using 5-0 monofilament synthetic absorbable material. Patients were instructed to avoid brushing the treated site for 2 weeks until suture removal, to rinse with 0.12% chlorhexidine gluconate twice daily, and to take azithromycin (500 mg/day for 3 days) and loxonin (180 mg/day for 7 days). Considerable care was taken to protect the augmented sites

from any external forces exerted by the fixed or removable provisional restorations during the entire healing period.

Clinical measurement and data analysis

Cases with small areas of soft tissue dehiscence and no signs of infection (late exposure) underwent irrigation of the region with minocycline once per week. The titanium mesh was left in place for at least 6 months in cases with no complications (nonexposure) or late exposure. These groups underwent titanium mesh removal and simultaneous implant placement when satisfactory ridge augmentation was observed. On both GBR and reentry surgeries, the following parameters were acquired using a University of North Carolina 15-mm periodontal probe (UNC 15, Hu-Friedy): DD1, the depth of the bone defect, which was the distance from the deepest point of the defect to the most coronal hole of the titanium mesh at the intraoral trial of the titanium mesh (Fig 2b); DD2, the depth from the top of the augmented bone to the titanium mesh by measuring the probe through the corresponding hole of the titanium mesh at the second surgery for mesh removal; VHAB, the vertical height of the augmented bone calculated by subtracting DD2 from DD1; and VHAB/DD1, the percentage of augmented bone height calculated by dividing VHAB by DD1. The Mann-Whitney *U* test was used to examine differences in the mean healing time and VHAB/DD1 between the two groups using a statistical software package (SPSS, IBM). $P < .05$ was considered statistically significant.

Histologic preparation

Surplus augmented tissue obtained as a result of bone contouring for implant placement was used as a biopsy sample for histologic evaluation, with the patients' agreement, and was taken from the most coronal portion of the augmentation site just below the titanium mesh from three patients in the nonexposure group. Samples were fixed in 10% neutral buffered formalin and decalcified in 5% formic acid for 6 weeks. Decalcified samples were dehydrated with ascending grades of ethanol and embedded in paraffin wax. Histologic sections were cut with a microtome (3.5-μm serial sections) in the sagittal direction, stained with hematoxylin-eosin, and analyzed histologically under a light microscope.

Results

Clinical measurement

Of the 19 patients, 17 exhibited primary closure of the soft tissue over the augmentation sites without any complications during the entire healing period (nonexposure group) (Figs 2 and 3). These 17 cases underwent implant placement simultaneously with removal of the titanium mesh. The maximum and minimum depth of the bone defect in these patients was 15.0 mm and 2.3 mm, respectively. Vertical formation of new bone tissue up to the height equivalent to that of the adjacent bone was observed in 11 patients in the nonexposure group. The mean healing period before titanium mesh removal was 8.0 ± 1.4 months. In the majority of patients, the site undergoing GBR was the maxillary anterior region (Table 1). Mean DD1 was 10.0 ± 3.8 mm, and mean VHAB was 8.6 ± 4.0 mm in all patients and 8.8 ± 4.2 mm in the nonexposure patients. Mean VHAB/DD1 was 85.8% ± 25.6% in all patients and 87.3% ± 25.6% in the nonexposure patients.

One patient exhibited exposure of the titanium mesh through a small wound dehiscence late in the healing period (late exposure); however, there were no signs of infection. This site had a 7.3-mm alveolar defect and was in the region of the maxillary central incisors. A substantial volume of new bone that was sufficient for implant placement without any additional bone augmentation was observed in this patient (Figs 4a and 4b). A large wound dehiscence with mild wound infection occurred in one patient 4 weeks after surgery in the maxillary left lateral incisor region that had a 11.5-mm bone defect (early exposure). This necessitated immediate removal of the titanium mesh. After thorough irrigation with minocycline and saline, the flap was sutured without removing

Table 1 **The distribution and number of sites subjected to GBR, DD1, healing period until the removal of the titanium mesh, VHAB, and VHAB/DD1 for all patients**

	No. of patients					Mean ± SD				
		Maxillary		Mandibular						
	Total	Anterior	Molar	Anterior	Molar	Age (y)	DD1 (mm)	Healing time (mo)	VHAB (mm)	VHAB/ DD1 (%)
Nonexposure	17	8	4	2	3	49.5 ± 15.1	9.8 ± 3.8	8.0 ± 1.5	8.8 ± 4.2	87.3 ± 25.0
Exposure	2	2	0	0	0	55.5 ± 6.4	11.1 ± 5.4	7.8 ± 0.7	7.2 ± 0.2	73.4 ± 37.7
Total	19	10	4	2	3	50.2 ± 14.4	10.0 ± 3.8	8.0 ± 1.4	8.6 ± 4.0	85.8 ± 25.6

SD = standard deviation; DD1 = depth of bone defect; VHAB = vertical height of the augmented bone; VHAB/DD1 = percentage of augmented bone.

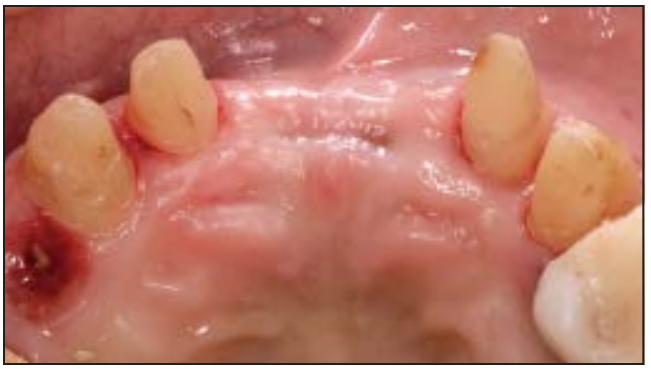


Fig 4a *Slight exposure of the titanium mesh through the gingival flaps in the late exposure patient.*

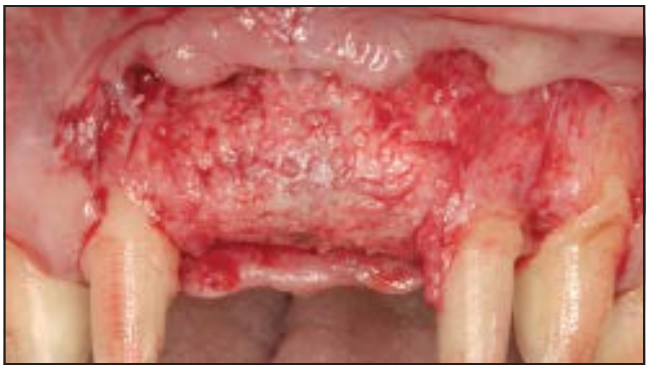


Fig 4b *Favorable and substantial bone regeneration in the late exposure patient.*

the underlying granulation tissue. Seven months after removal of the titanium mesh, approximately 7 mm of vertical bone augmentation was observed. One patient in the nonexposure group experienced occupation by connective tissue containing Bio-Oss particles without bone formation at a site having an alveolar defect of 6.5 mm in the mandibular anterior region. The site was treated by a repeat GBR procedure with the same technique; this resulted in successful vertical bone augmentation sufficient for implant placement 6 months after surgery.

The number of patients with a median DD1 of > 8.5 mm and < 8.5 mm was 9 and 10, respectively (Table 2). The mean healing time was 8 months for both groups, with no significant difference between groups ($P > .05$). The group with a median DD1 of > 8.5 mm had a mean DD1 of 13.1 ± 2.3 mm, while the group with a median DD1 of ≤ 8.5 mm had a mean DD1 of 6.5 ± 1.3 mm. In the former group, 88% of the defect height was filled with augmented bone (VHAB/DD1), whereas in the latter group, 80% of the defect height was filled with augmented bone; mean VHAB in both groups was 11.0 mm and 5.5 mm, respectively. VHAB/DD1 was thus compatible between the two groups.

Histology

Specimens of the regenerated tissue after vertical ridge augmentation were subjected to hematoxylin-eosin staining (Fig 5). Representative images viewed under an original magnification of ×4 (Fig 5b) and ×20 (Fig 5c) are presented. Regenerated tissue in the grafted area largely comprised

Table 2 **DD1, healing period until the removal of the titanium mesh, VHAB, and VHAB/DD1 for all patients with DD1 > 8.5 mm and DD1 ≤ 8.5 mm**

			Mean ± SD			
		No. of patients	DD1 (mm)	Healing time (mo)	VHAB (mm)	VHAB/DD1 (%)
DD1 (mm)	> 8.5	9	13.1 ± 2.3	8.2 ± 1.7	11.4 ± 2.8	88.0 ± 17.1
	≤ 8.5	10	6.5 ± 1.3	7.8 ± 1.2	5.5 ± 2.5	83.4 ± 33.7
Total		19	10.0 ± 3.8	8.0 ± 1.4	8.6 ± 4.0	85.8 ± 25.6

SD = standard deviation; DD1 = depth of bone defect; VHAB = vertical height of the augmented bone; VHAB/DD1 = percentage of augmented bone.

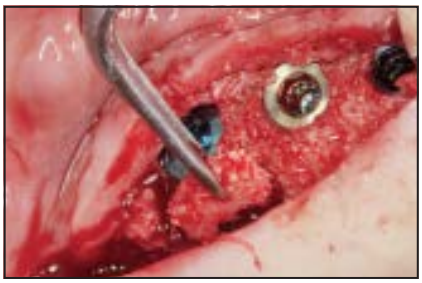
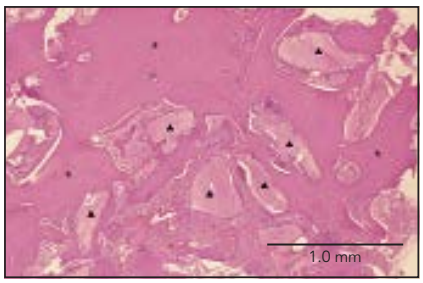
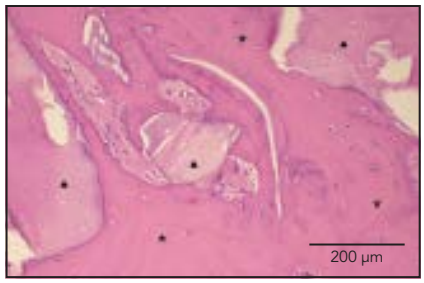


Fig 5a *Histologic samples were obtained from the most coronal portion of the augmentation site.*





Figs 5b and 5c *Histologic images of the regenerated tissue after vertical ridge augmentation; note the extensive and dense bone formation* (asterisks) *surrounding and filling the gaps between the grafts* (triangles), *Bio-Oss particles, and autogenous bone chips (hematoxylin-eosin).*

bone tissue with a small amount of dense connective tissue (Fig 5b) surrounding and connecting the Bio-Oss graft particles and autogenous bone chips, which could be identified as paler-staining amorphous structures (Fig 5b). Newly formed trabeculae were densely calcified and had developed a lamellar structure with osteocytes embedded in their lacunae (Fig 5c). The graft particles and noncellular bone-like matrix (Fig 5c) were directly attached to and partially incorporated into de novo bone.

Discussion

This retrospective case series demonstrated an overall VHAB of 8.6 ± 4.0 mm. Previous clinical reports on vertical ridge augmentation with a nonresorbable membrane and autogenous bone or allograft materials showed 2 to 8 mm of vertical bone augmentation.[17,18] Although a direct comparison of clinical outcomes between this study and previous studies needs careful interpretation because of the differences in evaluation methods, the staged GBR approach may enable substantial vertical bone regeneration equal to or surpassing that reported in previous studies. Moreover, overall, GBR resulted in vertical bone augmentation that was > 80% of the height of the defect (VHAB/DD1) not only in defects of ≤ 8.5 mm but also in those of a greater depth. These results indicate that this GBR procedure has the potential to achieve assured and complete bone regeneration irrespective of the size of the bone defect and deformities.

Previous clinical reports on vertical ridge augmentation with a titanium mesh for bone defects with a mean depth of approximately

3 to 6 mm showed a high occurrence of postoperative mesh exposure (17.3% to 100% in 7 to 23 patients).[3–8] In contrast, this GBR method resulted in membrane exposure in only 2 of 19 patients (a 10.5% incidence rate) even though the bone defects treated in this study were much larger (10.0 ± 3.8 mm in height). More importantly, substantial bone regeneration was observed in the exposure cases in this study. In the patient with late exposure, a bone defect that was 7.3 mm in height was almost completely filled by new bone (Figs 4a and 4b), whereas in the early exposure patient, VHAB was 7.0 mm (47%) after removal of the titanium mesh.

Extensive and dense new bone surrounding and connecting the bone graft particles was observed in all histologic samples. This indicated that the GBR procedure for vertical ridge augmentation resulted in the formation of well-mineralized living lamellar bone that was integrated with grafts, implying inherent bone homeostasis and longitudinal stability of newly formed tissue. Previous in vitro studies demonstrated that osteoblasts can generate a harder, stiffer, and more mineralized matrix on a titanium surface compared with other bioinert materials,[19,20] which indicated advantages of titanium mesh in volume maintenance as well as osteocompatibility. In addition, rhPDGF is expected to function as a chemo-attractant and mitogen for mesenchymal cells and for promoting angiogenesis.[16,21] Despite the debate about blocking of cellular supply from periosteum,[16,22–24] the use of a barrier collagen membrane might help the pharmacologic effect of rhPDGF-BB on osteogenic cellular migration and angiogenesis from bone marrow. However, some basic research showed no direct effect of PDGF-BB on osteoblastic differentiation and bone regeneration.[25,26] Determination of the clinical benefits of rhPDGF-BB in GBR procedures is an interesting topic for future research, including controlled clinical trials.

Conclusions

Within the limitations of this retrospective consecutive case series, this GBR procedure using a cross-linked collagen membrane and titanium mesh in conjunction with rhPDGF-BB yielded three-dimensional alveolar bone regeneration irrespective of the size of the bone defect; however, long-term evaluation is required to assess the clinical outcome.

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