

The Outcomes of Vertical Alveolar Bone Augmentation by Guided Bone Regeneration with Titanium Mesh: A Systematic Review

Nedal A Abu-Mostafa¹, Yasser N Alotaibi², Rose N Alkahtani³, Farah K Almutairi⁴, Amjad A Alfaifi⁵, Osama D Alshahrani⁶

ABSTRACT

Aim: This study aimed to systematically review the published studies on vertical alveolar bone augmentation (VABA) by guided bone regeneration (GBR) with titanium mesh (TM).

Background: Guided bone regeneration is a procedure that can be used for VABA of the alveolar ridge. Titanium mesh is used as a barrier due to its ability to maintain a space that the newly formed bone will occupy.

Materials and methods: A computerized literature search was conducted on the databases PubMed, SCOPUS, Science Direct, and Cochrane Library to review the published article on VABA by TM from 2011 to 2021.

Review results: Eight out of 574 retrieved articles were included in the qualitative analysis, three randomized clinical trials, two prospective clinical trials, and three retrospective trials. They were assessed for risk of bias using the critical appraisal skills program checklist. Titanium mesh was utilized as a barrier in three different ways, adapted directly on the alveolar bone, bent preoperatively on three-dimensional (3D) models, and 3D-printed. Two randomized clinical trials (RCTs) reported 20.8% bone gain, while the other studies reported the means ranging from 2.56 to 4.78 mm. All studies reported TM exposure that ranged from 7.69 to 66.66%. Exposure during the four postoperative weeks led to inadequate bone regeneration. However, late exposure had no effect or caused only slight bone resorption. Early TM removal was performed in two studies, one case per each, ranging from 2.4 to 11.1%. Infection was presented in three studies, one case per each, and the percentages were 5, 11.1, and 25%.

Conclusion: All types of TM had exposure, which was the most common complication, but early removal was indicated only in a few cases. Titanium mesh showed reliability and efficacy as a barrier for VABA by GBR.

Clinical significance: By this procedure, bone height can be restored, however, meticulous follow-up is recommended for the detection and management of TM exposures.

Keywords: Alveolar bone, Guided bone regeneration, Titanium mesh, Vertical bone augmentation.

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BACKGROUND

Implant dentistry has progressed dramatically over the years, with a contemporary success rate of roughly 95%. However, if bone height and width are deficient, implantation may not always be ideal.¹ Alveolar bone loss can be caused by multiple reasons, including periodontitis, traumatic tooth extraction, infection, dentoalveolar trauma, and orthodontic treatment.² Medication use, systemic illnesses, tobacco use, and genetics are all additional risk factors for alveolar bone resorption.³ Furthermore, patients with specific disorders, such as cleft palate syndrome, anodontia, and ectodermal dysplasia, may have insufficient alveolar bone growth.⁴

Short implants may be viable for replacing teeth on the alveolar bone with a vertical defect.⁵ However, bone regeneration is frequently required to offer cosmetic and functional restorations.⁶ A deficient alveolar ridge can be reconstructed using several methods, including guided bone regeneration, inlay and autogenic bone block grafting from intraoral or extraoral sites, bone splitting, and distraction osteogenesis.⁷

Guided bone regeneration is achieved by placing a bone graft on a created space to generate bone mixed with blood and protected by a mechanical barrier from the invasion of fibroblasts and epithelial cells and facilitates the growth of osteoblasts and blood vessels to start bone regeneration. The stability of the barrier, appropriate soft tissue covering, and enough blood supply are essentials for a successful bone generation.⁸ Different biomaterials are used for

¹Department of Oral and Maxillofacial Surgery and Diagnostic Science, Riyadh Elm University, Kingdom of Saudi Arabia

²King Saud University, Kingdom of Saudi Arabia

³King Saud bin Abdulaziz University for Health Sciences, Kingdom of Saudi Arabia

⁴Majmaah University, Riyadh City, Kingdom of Saudi Arabia

^{5,6}Riyadh Elm University, Kingdom of Saudi Arabia

Corresponding Author: Nedal A Abu-Mostafa, Department of Oral and Maxillofacial Surgery and Diagnostic Science, Riyadh Elm University, Kingdom of Saudi Arabia, Phone: +00966506275782, e-mail: nedal@riyadh.edu.sa

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bone augmentation, such as xenografts, allografts, alloplastic, and composite grafts.⁷ On the other hand, variant barriers have been used as a part of GBR, including polytetrafluoroethylene (PTFE), expanded PTFE (e-PTFE), collagen, freeze-dried fascia lata, freeze-dried dura mater allografts, polyglactin 910, polylactic acid, polyglycolic acid,

polyorthoester, polyurethane, polyhydroxy butyrate, calcium sulfate, and micro titanium mesh.⁹ Bone generation is promoted by adding platelet concentrates which contain plasma rich in growth factors (PRGF) that enhance the healing of hard and soft tissue. Furthermore, PRGF reduces postoperative inflammatory response, swelling, and pain.¹⁰ An important factor for the success of GBR is the ability to maintain a space below the membrane that the newly formed bone will occupy. Different types of membranes, such as reinforced e-PTFE membranes, self-reinforced polyglycolide membranes, and TM, are used to solve the problem of soft tissue collapse, which interferes with bone healing.¹¹ TM has excellent characteristics like a smooth surface, enough hardness to maintain a large amount of space, and elasticity to conform to the alveolar bone. It provides a superior GBR option for dental applications over other membranes.⁸

Titanium mesh is frequently investigated as a barrier for vertical bone augmentation by differently designed studies with variable bone graft materials. There is a need for evaluation and comparison of their results to create an evidence-based summary to help clinicians better understand bone regeneration, soft tissue healing, and the anticipated problems with their proper management. Our study aimed to systematically review the published studies that evaluated the effectiveness and treatment outcomes of the GBR procedure with TM for vertical alveolar bone augmentation.

MATERIALS AND METHODS

This systematic review of the published studies evaluated the clinical outcomes of vertical alveolar bone regeneration by GBR with TM. This review included only full-text articles published in English within 10 years between 2011 and 2021 and the search web was done in December 2021. The University Research Center registered, and the Institutional Review Board approved the study (the approval number "SRP/2021/89/512/479"). The proposal was registered in the international prospective register of systematic reviews (PROSPERO), ID number 262788.

Search Strategies

Articles were searched and revised by two investigators through PubMed (pubmed.ncbi.nlm.nih.gov), SCOPUS (www.scopus.com), Science Direct (www.sciencedirect.com), and Cochrane Library (https://www.cochranelibrary.com) electronic databases. Search terms included medical subject heading (MeSH) terms such as titanium mesh, vertical bone augmentation, alveolar bone, reconstruction, and guided bone regeneration. Additionally, search strings were used, [{"titanium mesh" and "vertical bone augmentation"} or {"titanium mesh" and "alveolar bone"} or {"titanium mesh" and "guided bone regeneration"} or {"vertical bone augmentation" and "guided bone regeneration"} or {"titanium mesh" and reconstruction} or {"guided bone regeneration" and "alveolar bone"}].

Focus Question

What are the clinical outcomes of vertical alveolar bone augmentation by TM? The focus question was addressed using the population, intervention, comparison, and outcomes (PICO) approach. Population (P) included completely or partially edentulous healthy patients with severe/moderate vertical atrophy in the edentulous mandible or maxilla. Intervention (I) incorporated regeneration approaches for vertical bone augmentation to achieve implant stability by GBR with TM. Comparison (C) was made between various approaches using TM and bone graft materials

for vertical alveolar augmentation. Primary outcomes (O) included total bone gain, TM exposure, early TM removal, infection rate, implant failure, and bone graft extrusion. Secondary outcomes were the bone graft type, TM description, and the treatment of wound dehiscence.

Inclusion Criteria

The studies evaluated vertical alveolar bone augmentation by GBR with titanium mesh. The types of studies that were included in this review were RCTs, prospective clinical studies (PS), and retrospective clinical studies (RS) with or without a control group.

Exclusion Criteria

In vitro studies, comments to authors, case series, case reports, and literature reviews were excluded. Moreover, we dropped out studies involving heavy smoker patients (>20 cigarettes/day) with tumors or congenital deformities.

Data Extraction and Analysis

Several parameters were collected and analyzed from the selected articles, including authors, publication year, number of patients, age range, gender, study design, the grafting materials used, bone gain and loss, TM exposure, TM removal, implant insertion, and survival rate, and infection. At least two reviewers performed data extraction and analysis to achieve reliability and avoid data entry errors. The reporting followed Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement. The included studies were assessed for risk of bias using the critical appraisal skills program (CASP) (Table 1). Due to the heterogeneity of the study designs and treatment outcomes, a meta-analysis of the data extracted from the articles included in the present review could not be performed.

Review Results

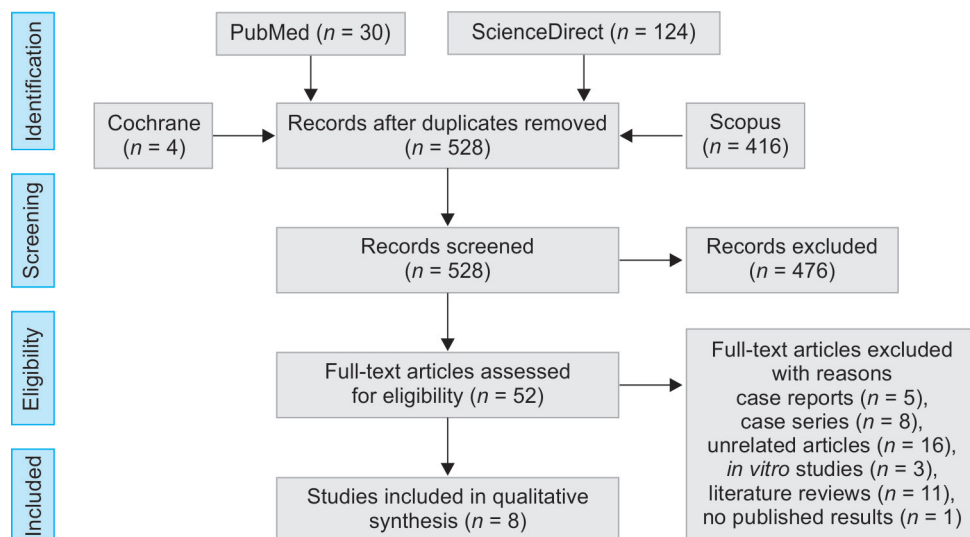
Overall, 574 articles relevant to this topic were retrieved from four databases and were revised by two investigators to apply the exclusion criteria. Around 46 duplicates were excluded, resulting in 528 articles. About 476 articles were excluded because of unrelated titles or abstracts. Around 52 articles were assessed for eligibility, and 44 were excluded 5 case reports, 8 case series, 16 unrelated articles, 3 *in vitro* studies, 11 literature reviews, and one study without published results (Flowchart 1). Only 8 studies fulfilled the quality synthesis's inclusion criteria and were completely agreed upon by the two investigators, with a Cohen's kappa of 100%. The included studies were 3 RCTs, 2 PS, and 3 RS (Table 2).^{11,12,14-18}

The critical appraisal skills program tool is a generic tool for clarifying the strengths and limitations of any qualitative study methodology. The maximum score for the CASP tool is 8 out of 8, which was received by the studies of Cucchi et al.¹³ and Mounir et al.¹⁴ Four studies were varying between "yes" and "can't say" with the low overall level of bias.^{12,15,16,18} The lack of clarity in reporting methods, if they did or did not include that specific element on the CASP checklist, making "can't say" the best answer to describe our uncertainty. On the other hand, Poli et al.,¹¹ got 1 "no" and 1 "can't say" of the CASP checklist tool, while the study of Her et al.¹⁷ got 2 "no" and 1 "can't say".

The studies included males and females, and the patients' ages ranged from 20 to 81 years. The number of patients who received vertical bone augmentation by GBR with TM in RCTs and the prospective studies ranged from 8 to 20.^{12,14,16} The retrospective study by Her et al.¹⁷ had the least number of patients, as only

Table 1: Risk of bias assessment using the critical appraisal skills program (CASP) checklist

CASP question	Her et al., 2012	Poli et al., 2014	Mounir et al., 2017	Cucchi et al., 2017	Ciocca et al., 2018	Mounir et al., 2019	Chiapasco et al., 2021	Li et al., 2021
Was there a clear statement of the aims of the research?	Yes	Yes	Yes	Yes	Can't say	Yes	Yes	Yes
Is a qualitative methodology appropriate?	Yes	Yes	Can't say	Yes	Can't say	Yes	Can't say	Yes
Was the research design appropriate to address the aims of the research?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Was the data collected in a way that addressed the research issue?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Has the relationship between researcher participants been adequately considered?	No	Can't say	Yes	Yes	Can't say	Yes	Yes	Can't say
Have ethical issues been taken into consideration?	Can't say	No	Yes	Yes	Yes	Yes	Yes	Yes
Was the data analysis sufficiently rigorous?	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Is there a clear statement of findings?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

Flowchart 1: PRISMA flowchart

4 got vertical augmentation the other patients had horizontal bone augmentation. Chiapasco et al. included 41 patients in the retrospective studies which was the largest number.¹⁸

Designs and Methods of Vertical Bone Augmentation

The studies included in this review utilized different designs. The studies by Poli et al.,¹¹ Ciocca et al.,¹⁵ Her et al.,¹⁷ and Chiapasco et al.¹⁸ examined the outcomes of vertical bone augmentation by GBR with various forms of TM. Other studies compared GBR utilizing TM with different methods of bone reconstruction. In 2017, Mounir et al.¹² compared intra-alveolar inlay block xenograft with GBR using TM. Cucchi et al.¹³ investigated GBR using TM with dense PTFE (d-PTFE) titanium-reinforced membrane. The study of Li et al.¹⁶ evaluated GBR utilizing 3D-printed TM versus GBR with a resorbable collagen membrane. The studies applied various bone

grafts, including autogenic grafts harvested from intraoral and extraoral sites, xenografts, and allografts. Additional information is provided in Table 2.

Implantation

Four studies performed bone reconstruction on both the mandible and maxilla, two studies on the maxilla alone, while the posterior mandible was the only site of bone grafting for one study.^{11-14,16-18}

Cucchi et al.¹³ and Li et al.¹⁶ inserted the implants simultaneously with the bone augmentation procedure, and the numbers of implants in the two studies were 106 and 65, respectively. The other studies inserted the implants during the stage of TM removal, 5–7 months following bone regeneration, and the numbers ranged from 9 implants to 106 implants.^{17,18}

Table 2: Summarized data of study designs, number of cases, types of titanium mesh, bone grafts, and augmentation sites.

Authors	Study design	Age range and gender	Grafting materials	Methods of bone augmentation		Augmentation site	Number of cases and implants
				GBR TM description:	Other methods		
Her S et al., 2012 (Vertical augmentation)	RS	Mean age: 51 years (34–65) 3 M and 1 F	Xenograft (Bio-Oss) and autogenous bone	–	–	posterior maxilla and mandible	4 patients 9 implants (delayed after a mean of 5.7 months)
Poli et al., 2014	RS	8 M and 5 F	Particulate autogenous bone mixed with deproteinized anorganic bovine bone Bio-Oss®, Geistlich, Wolhusen, Switzerland) in a 1:1 ratio. Number of cases: tuber maxilla: 8 symphysis: 2 ramus: 2 retromolar trigone: 1	TM 0.2 mm-thick (KLS Martin, Tuttlingen, Germany)	–	11 maxillary reconstruction 2 mandibular reconstruction	13 patients 20 implants: 16 in maxilla 4 in mandible (delayed after 6 months)
Mounir et al., 2017	RCT	Mean age: 39 years (25–53) 10 M and 6 F	Particulate xenograft (Tutogen, Neunkirchen am Brand, Germany; particle size 0.25–0.5 nm)	TM applied directly on alveolar bone	Inter alveolar inlay block xenograft fixed with mini-plates	Anterior maxilla	Total: 16 patients TM: 8 patients Inlay block xenograft: 8 patients (40 delayed implants)
Cucchi A et al., 2017	RCT	Mean age: 52 years 13 M and 27 F	Autogenous bone harvested using a bone-scraper (0.5–1.0 gm of bone from external oblique ridge) mixed with allograft bone 1:1 (EnCore, Osteogenics Biomedical, Lubbock, Texas)	TM covered by a cross-linked collagen membrane	Dense PTFE (d-PTFE) titanium-reinforced membrane	Posterior mandible	Total: 39 patients TM: 19 patients (d-PTFE) TM-reinforced: 20 patients 106 implants within the operation of augmentation
Ciocca et al., 2018	PS	Mean age: 50 years (25–68) 3 M and 6 F	Autologous bone chips (harvested from the mandibular ramus or the iliac crest) mixed with anorganic bovine bone (Bio-Oss, Geistlich Pharma) in a 1:1 ratio	CAD design, 3D-printed TM 0.3-mm thickness, and holes 1-mm diameter	–	–	9 patients 26 implants (delayed after 6–8 months)
Mounir et al., 2019	RCT	Mean age: 38 years 6 M and 2 F	Autogenous bone (anterior iliac crest) mixed with xenogenic bone (Bio-Oss, Geistlich Pharma, Switzerland)	Pre-bent TM with 2 mm thickness	Specific milled peek mesh	Maxilla	Total: 16 patients TM: 8 patients 16 implants delayed implant Peek mesh: 8 patients 16 implants delayed implant

Chiapasco et al., 2021	RS	Mean age: 54 years (20–81) 10 M and 31 F	Autogenous bone particles (mandibular ramus and body mixed with deproteinized bovine bone mineral (Bio-Oss®—Geistlich Biomaterials AG), in a 1:1 ratio, and covered with collagen membranes (Bio-Gide®—Geistlich Biomaterials AG).	Customized TM by CAD-CAM technology, 1.4 mm in diameter and 5–13 mm long, with a collagen membrane	–	Maxilla and mandible	41 patients (53 augmentation site) 106 implants (delayed after 7 months)
Li et al. 2021	PS	Mean age: 38 years (25–51) 18 M and 22 F	Autogenous bone mixed with deproteinized bovine bone mineral (Bio-Oss, Wolhusen, Switzerland)	3D-printed TM 0.2 mm thickness	Resorbable membrane group (Bio-gide, Wolhusen, Switzerland)	Maxilla and mandible	60 implants in maxilla 5 implants in mandible within the operation of augmentation Total: 40 patients TM: 20 patients 31 implant sites Resorbable membrane: 20 patients 34 implant sites

F, females; M, males; PS, prospective clinical study; RCT, randomized clinical trials; RS, retrospective study; TM, GBR by titanium mesh

Antibiotics Covering

Augmentin (Amoxicillin and Clavulanate) was the common antibiotic prescribed to the patients.^{11,13,15,18} Amoxicillin was prescribed to the patients in only two studies.^{16,17} The remaining two studies did not mention whether the patients had received antibiotic prescriptions.^{12,14}

Treatment Outcomes

The bone gain was recorded as percentages in the two RCTs of Mounir et al.^{12,14} while the other studies recorded it in millimeters.^{13,15,16,18} Titanium mesh (TM) exposure was reported in all included studies, and the percentages ranged from 7.69 to 66.66%.^{11,15} One failed implant (0.94%) was reported by Chiapasco et al.'s study,¹⁸ however, they did not specify whether it was placed on the mandible or maxilla, posterior or anterior. Further details regarding the treatment outcomes are available in Table 3.

Poli et al.¹¹ determined the amount of peri-implant bone loss by measuring the distance between the implant head and the first apparent bone-implant contact. The mean was 1.743 mm on the mesial and 1.913 mm on the distal sides. In Chiapasco et al.'s¹⁸ study, the mean bone loss was 8.09%.

DISCUSSION

The literature contains different TM types with various thicknesses and multiple bone graft materials that have been utilized for vertical bone augmentation by GBR. This review was conducted for the comparison and discussion of the clinical outcomes of these types regarding attainable bone and the reported complications including TM exposure, infection, and implant failure.

The occlusal function of teeth maintains the alveolar bone structure, while its loss promotes bone resorption.¹⁹ The optimum bone augmentation approach depends on the location, width, and

height of the deficient alveolar bone. Other factors, like the adjacent vital structures, the type of soft tissue available, medical status, and the surgeon's technical skill, can play a role in determining the method of bone augmentation.¹⁷

Various authors have considered using autogenous bone grafts for ridge augmentation as the gold standard due to their osteogenesis, osteoconduction, and osteoinduction properties.²⁰ However, autogenic bone graft harvesting may result in pain, site morbidity, and other complications. Extraoral bone harvesting provides large volumes of bone grafts, allowing over-contouring to address the anticipated resorption. The iliac crest is a frequent extra-oral donor location that offers many benefits, including simple access to and availability of significant quantities of cortical and cancellous bones.²¹ The iliac crest was the extra-oral donor site in two studies in this review.^{14,15} Intraoral harvesting yields only a little amount of bone, which can be compensated for by combining it with allograft or xenograft.²² In the reviewed studies, the intraoral donor sites were maxillary tuberosity, symphysis, retromolar area, ramus, and body of the mandible.^{11,15,18} Allografts are made of fresh/frozen, freeze-dried, or demineralized bones and come from human donors. Because these allografts contain proteins, like bone morphogenetic proteins (BMP), they can function as both osteoconductive and osteoinductive scaffolds.²³ Cucchi et al.¹³ used autogenic and allograft bone as a 50:50 mixture. Xenografts lack the osteogenic properties of autografts but have osteoconductive characteristics. Deproteinized organic bovine bone (DBBM) is a xenogeneic graft material that works as a scaffold, resorbs very slowly, and is replaced by new bone.²⁴ Mounir et al. used two different xenografts in their study particulates in the GBR, TM and inlay block xenografts fixed with mini plates.¹² Six studies in this systematic review used a mixture of autogenic bone grafts from different harvesting sites and xenografts.^{11,14–18}

Table 3: Summarized data of vertical bone augmentation outcomes

Study	Bone gain	Bone loss	Barrier exposure	Treatment of dehiscence	Early mesh removal	Infection (exudates)	Implant failure
Her S et al., 2012 (Vertical augmentation)	–	–	2 (50%) 1 Circular exposure at 2 weeks 1 Circular exposure at 8 weeks	–	No	1 (25%)	No
Poli et al., 2014	–	1.743 ± 0.567 mm on the mesial side and 1.913 ± 0.710 mm on the distal side	1 (7.69%) after 4 months	Chlorhexidine mouthwash rinse for 2 months. Closure of the soft tissue dehiscence occurred after the treatment.	No	No	No
Mounir et al., 2017	TM 20.7% Inlay block xenograft 31.6%	–	TM after 10 days 1 (12.5%)	Daily irrigation using normal saline and finally healed with secondary intention	No	No	No
Cucchi A et al., 2017	TM 4.1 ± 1.0 mm (d-PTFE) TM-reinforced 4.1 ± 1.0 mm	–	TM Early exposure: 1 (5.3%) with infection (0–1 month) Late exposure: 2 (10.5%) 1 with infection (1–3 months) 1 without infection (3–6 months) (d-PTFE) TM-reinforced Early exposure: 1 with infection Late exposure: 1 without infection	–	No	TM Abscess without exposition 1 (5.2%) (d-PTFE) TM-reinforced 1 Abscess without exposition (5%)	No
Ciocca et al., 2018	Mandible: 1.72–4.1 mm (mean: 3.83 mm) Maxilla: 2.14–6.88 mm (mean: 3.95 mm)	–	Early exposure: 6/9 (66.7%) (2 to 4 weeks) Delayed exposure: 3/9 (33.3%) (10–24 weeks)	Use soft toothbrush to apply chlorhexidine digluconate gel 1% (Corsodyl gel, GlaxoSmithKline, Baranzate, Italy)	1 (11.1%) at 3 months after pus discharge	1	No
Mounir et al., 2019	TM 20.9% Peek mesh 31.8%	–	TM 1 (12.5%) 2 weeks postoperatively Peek mesh 1 (12.5%) 2 weeks postoperatively	Daily irrigation using normal saline and finally healed with secondary intention	No	No	No
Chiapasco et al., 2021	4.78 ± 1.88 mm	–8.09%	(11/53) (20.75%) (15–150 days after surgery) Exposure more frequent in maxilla	Healing by secondary intention	1 (2.4%)	No	1 (0.94%)
Li et al. 2021	TM 1.75 mm ± 1.06 mm Resorbable membrane 2.56 mm ± 1.98 mm	–	2 (10%) 1 at the distal mid-vertical incision line 1 at the apex of the alveolar ridge incision small late exposure	The exposed sharp edges of TM were removed and applied topical minocycline hydrochloride	No	No	No

d-PTFE, dense polytetrafluoroethylene; TM, titanium mesh

Guided bone regeneration by resorbable membranes effectively treats specific types of horizontal bone insufficiency. However, to accomplish vertical bone augmentation, the barrier should be space-preserving to minimize soft tissue collapse toward the defect, which might result in graft compression or displacement, and hence failure to obtain the desired results.²⁵ Guided bone regeneration for vertical defects can be accomplished using either a non-resorbable PTFE titanium-reinforced membrane or a TM that may be covered by a resorbable membrane.^{26,27}

The traditional TM method involves trimming and bending the mesh directly on the defective alveolar bone. It is a time-consuming technique that requires the surgeon to have clinical abilities and experience, and the final shape may not be optimal.²⁸ This type of TM was used in four studies, which found that the classical TM's ability to adapt to the curves of the bone was not problematic.^{11-13,17} Moreover, it is simple to handle, bend, contour, and fit any bony deformity. On the other hand, the TM can be shaped and adapted preoperatively on a model, such as a stereolithographic model (STL) model, built from computed tomography (CT) data to form a 3D graft matrix, as utilized in the study of Mounir et al.¹⁴ This technique minimizes the operating time and is highly predictive of achieving the target bone volume.²⁹ Three studies used computer-aided design (CAD), and 3D-printed TM.^{15,16,18} With this type of TM, the procedure is simplified, the operation time is much shorter than with a standard TM, and the quantity of retaining screws is reduced which should be placed away from the proposed future implant sites.^{15,18,30}

Although TM must be sufficiently stiff to support the flap, it must also have a smooth surface and a minimum thickness to prevent mechanical trauma to the soft tissue, which could lead to dehiscence and mesh exposure.¹¹ The average TM thickness ranges from 0.1 to 0.6 mm.²⁸ This review recorded different thicknesses of TM. The minimum was 0.1 mm in the study by Poli et al.,¹¹ followed by 0.2 by Her et al.¹⁷ and 0.3 mm by Ciocca et al.¹⁵ On the other hand, Mounir et al.¹⁴ used 2 mm pre-bent TM which was the thickest in this review.

Considerable debate has emerged about the relationship between bone formation and the size of titanium mesh pores. According to theory, the titanium mesh pores are crucial for creating a blood supply and enabling metabolic activities in the grafts at the defect site. Due to the increased blood flow to the grafted area, large pores (more than 2 mm) can encourage greater bone repair.³¹ However, such a diameter may encourage more soft tissue to grow over the newly produced bone.¹⁷ In the reviewed studies, the minimum mentioned pore diameter was 1 mm in the study of Ciocca et al.,¹⁵ while pore diameters in the study of Chiapasco et al.¹⁸ and Her et al.¹⁷ were 1.4 mm and 1.7 mm, respectively.

Three studies in this review covered TM by a cross-linked collagen membrane to reduce the flow of gingival fibroblasts through the pores and into the grafted defect.^{13,14,18,27} However, a retrospective cohort study that compared the exposure rate of TMs covered by absorbable collagen membranes to a group without covering did not reveal any statistically significant difference between the two methods. Even without exposure, thick fibrous tissue was still discovered underneath the TM.³²

Inadequate adaptation explains soft tissue dehiscence and exposure of the classical TM due to any sharp or rough edges that cause mechanical trauma and may occur away from the incision lines.²⁸ All studies in this systematic review reported exposures

using classical or CAD-3D-printed TM. A reliable comparison between the two approaches cannot be established since only a few cases were reported in some studies, besides differences in the studies' designs. The percentages of exposure in the classical TM ranged from 7.69 to 27%, while the 3D-printed TM exposure ranged from 10 to 66.7% in Ciocca et al.'s study.^{11,15-17}

Titanium mesh pores allow blood to flow freely to the underlying tissues therefore, it might not need to be removed immediately if exposed. Small pores could obstruct the integral vascularization process; hence their size could be a significant concern. Differently, as non-resorbable membranes like titanium-reinforced PTFE membranes obstruct proper vascular supply, they can result in post-operative mucosal dehiscence that does not heal spontaneously, and these membranes must be removed.³³ Furthermore, a high danger of infection might cause all or part of the initial bone gain to be lost.³⁴

The possible outcomes of TM exposures are contamination of the graft material, infection, and partial or complete loss of the initial bone augmentation.²⁸ Time of exposure affects bone gain. The loss of the grafted material is limited if the exposure occurs from 4 to 6 weeks later because the graft is sufficiently maintained by the newly developing bone.³⁵ The included studies showed differences in the frequency and timing of TM exposure detection. Early exposures within the four post-operative weeks were reported in the studies of Mounir et al.,^{12,14} Cucchi et al.,¹³ Her et al.,¹⁷ and Ciocca et al.¹⁵ Other studies recorded exposures after 4 weeks of operation, e.g., Poli et al.,¹¹ Cucchi et al.,¹³ Ciocca et al.,¹⁵ Her et al.,¹⁷ and Chiapasco et al.¹⁸

A higher incidence of exposure occurred in the maxilla in the study of Chiapasco et al.,¹⁸ consistent with other studies.^{36,37} This was explained by the very limited flap release on palatal mucosa that can be performed completely on the buccal flap, which results in tissue thinning and decreased blood flow. In contrast, mandibular releasing incisions can be evenly distributed on both the buccal and lingual sides.¹⁸ Li et al.¹⁶ reported late small TM exposures in 2 out of 20 cases (10%), one at the distal mid-vertical incision line and the other at the apex of the alveolar ridge incision. They highlighted that the low percentages of TM exposure were due to using 0.2 mm TM, which allowed for less discomfort on soft tissues in addition to maintaining space and a degree of plasticity required for adjustments of TM during the operation. Furthermore, the digital design creates the TM in accordance with bone form without over-grafting, which puts more tension on the soft tissues.

Care should be taken with the exposed TM during bone healing to prevent infection. The wound healing management in the reviewed trials relied on daily irrigation with normal saline, chlorhexidine rinse, and topical application of chlorhexidine gel.^{11,12,14} One study reported the healing of wounds by secondary intention.¹⁵

The sequences of TM exposure on bone regeneration varied between the included studies. According to the studies by Poli et al.,¹¹ Mounir et al.,¹⁴ and Li et al.,¹⁶ the exposed sites had good bone quality, and implants could be successfully placed into the newly developed bone. Her et al.¹⁷ reported a slightly insufficient volume of bone on re-entry at circular flap dehiscence locations; however, it did not affect the successful regeneration results of the treatment. Alternatively, Cucchi et al.¹³ pointed out that TM exposure during the first four postoperative weeks led to either full failure of the treatment or inadequate bone regeneration, whereas late exposure did not affect bone regeneration. Chiapasco et al.¹⁸

observed a positive association between TM exposures and bone resorption in the regenerated areas, and the difference compared to non-exposed sites was statistically significant.

In the two RCTs, Mounir et al.^{12,14} determined the percentage of bone gain by comparing the bone height six months after surgery to the preoperative alveolar bone. The reported percentages were 20.7 and 20.9% in the two studies. The other reviewed studies recorded bone gain by millimeters and ranged from 2.56 mm in Li et al.¹⁶ to 4.78 mm in Chiapasco et al.¹⁸ These results are comparable to the mean bone gain of 3.61, 3.90, 4.85, and 5.2 mm reported in Zhang et al.,³⁸ Li et al.,³⁹ Malik et al.,⁶ and De Santis et al.,⁴⁰ respectively. On the other hand, Funato et al.⁴¹ performed a retrospective study of vertical alveolar bone augmentation using pre-adapted TM, bone graft mixed with recombinant human platelet derived growth factor BB and covered by collagen membrane. They reported a bone gain of 8.6 mm, which was greater than the trials in our review.

TM exposure during the GBR procedure's healing phase for vertical bone augmentation is a noticeable complication in the literature, although only a few cases required early removal.^{6,38-42} The case series of Malik et al.⁶ reported four TM exposures in twenty patients who were treated by GBR and allograft; however, one case required early removal. Funato et al.'s⁴¹ study recorded two TM exposures out of 19 GBR cases, and only one case required early removal. In the same way, only a few cases in this systematic review necessitated early TM removal. Chiapasco et al.¹⁸ removed one of the 11 exposed TM, which was associated with implant failure.¹⁸ In the study by Ciocca et al.,¹⁵ 1 out of 6 exposed TM that was associated with infection and was removed 3 months after surgery. The infection may occur regardless of the presence of exposed TM, as reported by Cucchi et al.,¹³ who found a 5% incidence of infection out of 20 GBR with TM cases. At the same time, Her et al.¹⁷ reported 1 infection case out of four vertical augmentation cases.

In this systematic review, implant failure was reported only in Chiapasco et al.'s study,¹⁸ in which one out of 106 performed implants (0.94%) failed to osseointegrate and was removed before loading. They considered the absence of pain, immobility, and no radiolucency as indicators of implant survival, and the rate was 100% for the loaded implants. Graft extrusion was not recorded in any case in this review. It is a rare complication in the literature, and only one case was reported (5%) in the cases series of Malik et al.^{6,38-42}

This systematic review had some limitations due to differences in the study's designs, the types of TM and bone grafts they used, and the parameters used to quantify bone gain and loss, complicating the comparisons across studies.

CONCLUSION

The clinical outcome of GBR with TM, whether classical or 3D-printed, is a reliable and efficient vertical alveolar bone reconstruction without significant bone resorption. The most frequent adverse outcome following vertical bone augmentation with GBR was TM exposure, which was reported in all reviewed studies. Exposures of both the classical TM and the 3D-printed TM were reported; however, the time of exposure affected the unfavorable sequences on bone generation or infection. Daily irrigation with normal saline, Chlorohexidine rinse, or its topical application was required for the management of TM exposure. The exposed TMs were indicated to be removed only in a few cases. Bone graft extrusion was not reported, and implant failure was very rare.

Clinical Significance

This systematic review revealed that GBR with TM is a good choice for vertical alveolar bone reconstruction. Through this procedure, the bone height can be restored to meet the needs for both cosmetic and functional dental implant restorations. However, meticulous follow-up is recommended for the detection of TM exposure, which is common, to be managed effectively.

Data Availability

The collected data supporting this systematic review are from previously reported studies and datasets, which have been cited.

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