

Titanium Mesh Exposure: A Case Report of Retrieved Underlying Soft Tissue and a Review of Literature

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Background and objectives: In this study, we aimed to report histopathological evaluation of the underlying tissues in a case of premature Titanium mesh exposure and assess the rate of Titanium mesh (Ti-mesh) exposure in the literature and its effect on treatment outcomes when used as a barrier membrane in jaw-bone reconstruction.

Materials and methods: We reviewed articles that used Ti-mesh with/without grafting materials to reconstruct atrophic ridges both vertically and/or horizontally. Considering our inclusion criteria, 51 studies were included. All relevant RCTs, retrospective studies (cohorts and case-controls) and case-series were included but case-reports and review articles were excluded. Data regarding premature exposure rate, removal rate, associated bone loss, and implant survival rate were extracted. Later, a report of an early Ti-mesh exposure in anterior maxillary horizontal augmentation with autogenous bone graft and deproteinized bovine bone mineral in a 50-year-old female is presented with a histological study of the underlying soft tissue at the time of mesh removal.

Results: A total of 51 studies were included in the review. Among the 41 studies reporting exposure, 18 reported removal of membranes, of which 3 caused significant bone loss. In the obtained biopsy from the reported case, a connective tissue infiltrated with sporadic inflammatory cells covered with keratinized stratified squamous epithelium was observed.

Conclusion: Our results indicate the loss of outcomes (both bone loss and implant failure) may not be associated with Ti-mesh exposure, which could, along with the rate of exposure, help the clinician assess the relative risk of its application.

Keywords: Alveolar ridge augmentation, Guided bone regeneration, Bone graft, Titanium mesh, Exposure.

1. Introduction

Rehabilitation of jaw bones is a major interest in oral and maxillofacial practice (1). Edentulous patients may require vertical and/or horizontal bone augmentation to allow for proper implant placement (2). Guided Bone Regeneration (GBR) is an established treatment method to occlude the invasion of competing non-osteogenic tissues using resorbable and non-resorbable barrier membranes (3). Titanium mesh is a biocompatible, non-resorbable barrier membrane with adequate mechanical properties (4,5).

The main clinical problem is the possibility of membrane exposure, which can increase the risk of secondary infection (6). In a systematic review on horizontal ridge augmentation in the

anterior maxilla, Kuchler et al. reported that the most frequent postsurgical complication included soft tissue dehiscence with exposure of the grafts (7). While in natural teeth, a 1–2 mm recession may not necessarily result in unsatisfactory esthetics, even in the esthetic zone, a minimal amount of titanium exposure can undermine the overall implant treatment success (8,9). Soft tissue dehiscence and membrane exposure in anterior maxillary augmentation causes the resorption of graft material and is considered the most serious esthetic complication according to studies (10-12). In the posterior mandible, the lack of bone volume and keratinized tissue has been correlated with titanium mesh exposure, which can, in turn, cause soft tissue recession, plaque accumulation, and require additional surgeries (13- 15). As a clinical advantage, titanium mesh can be trimmed and adapted to the bone defect to form the desired three-dimensional

outline. Porous titanium mesh maintains its structural integrity during implantation and can act as a cage for the bone substitutes underneath (16). Due to its superior mechanical capacity, it can withhold tissue collapse or displacement of graft during the healing period. Because the existing pores ensure adequate vascular supply to the underlying tissues, it is possible to retain the membrane until new bone formation is achieved (6). There are studies available that evaluate the tissue beneath titanium mesh at the time of removal. However, to the extent of our knowledge, there are no reports of a biopsy taken from the underlying tissue in case of premature exposure when new bone has not yet been formed. Thus, in this study, we report an exposed case where a biopsy was obtained after premature removal of the membrane to investigate the nature of the underlying tissues. As titanium mesh exposure is the most common complication of GBR procedures (4), we also conducted a review to assess the rate of exposure of the Ti-mesh and its effect on treatment outcomes, namely bone gain and implant survival.

2. Materials and methods

2.1. Search strategy and study selection

An electronic search was performed based on PRISMA flow diagram in following databases: PubMed, MEDLINE, EMBASE, Google Scholar, and ScienceDirect. The keywords used to search these bibliographic databases are explained in Figure 1. The search was limited to English articles published until November 2023. In addition, a hand search of the related journals was also conducted. Reference lists of retrieved reviews were also screened.

The electronic and hand search resulted in 1649 articles. All titles and abstracts were retrieved and assessed as to their relevance to our question. We reported only the studies that involved more than five patients followed for at least 6 months.

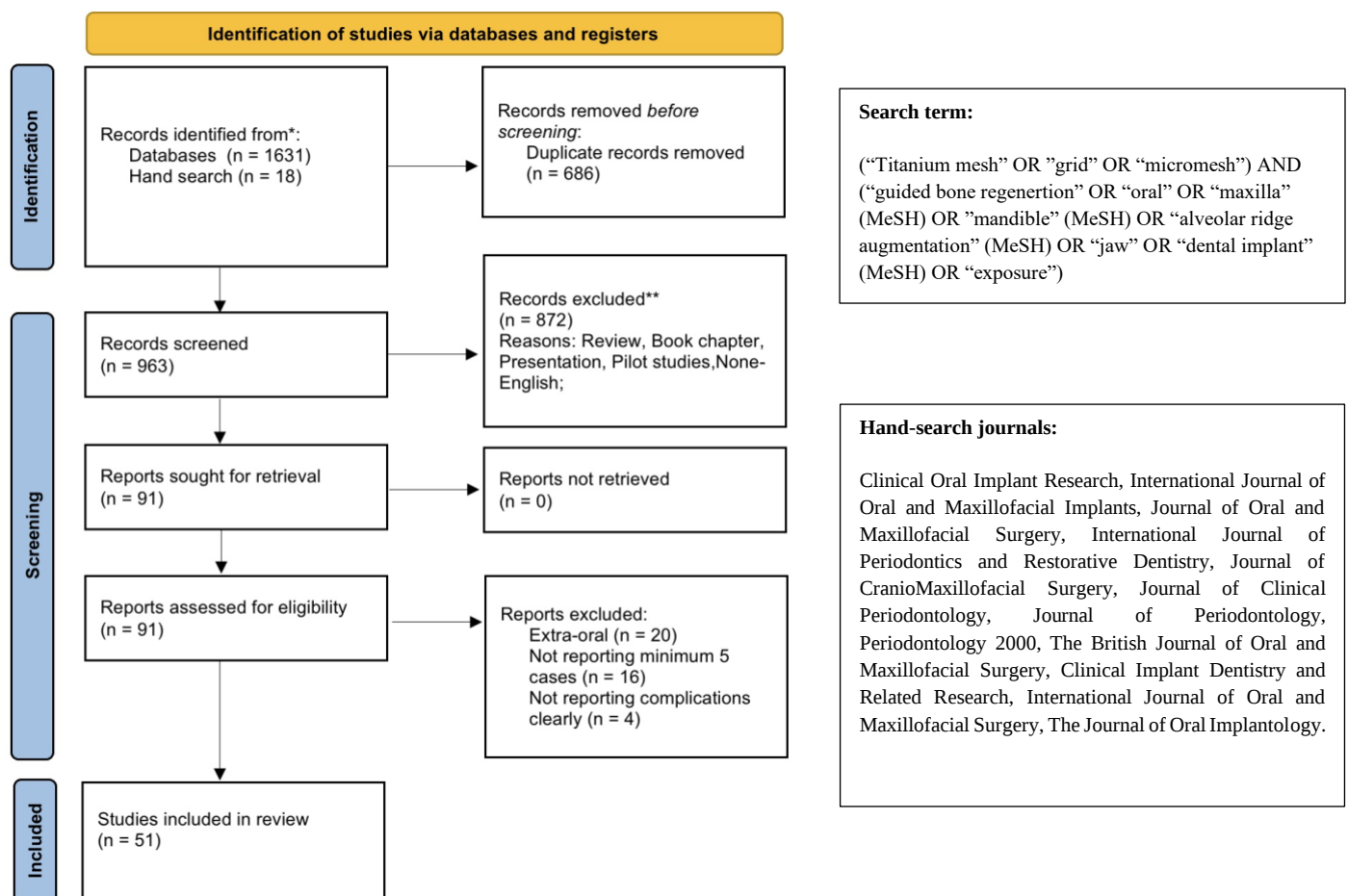


Figure 1. Search strategy and PRISMA flow diagram: The keywords used to search the bibliographic databases and the related journals that were hand searched. A flowchart identifying screened records in each step and explaining reasons for excluded articles.

Studies harvesting autogenous bone from extra-oral sites were also excluded to increase the homogeneity of studies. After examining the full texts, papers reporting bone augmentation in the oral zone (vertical, horizontal, or both) using titanium mesh or grid alone or in combination with other grafting materials with or without implant placement were selected. All relevant RCTs, retrospective studies (cohorts and case-controls), and case series were included, but case reports and review articles were excluded. A flowchart identifying screened records in each step and explaining reasons for excluded articles is shown in Figure 1.

2.2. Data extraction

Two reviewers screened the articles independently, and disagreement was resolved by discussion. Identification information was blocked out in order to avoid bias. Data regarding the type of study and location of the defect (maxilla or mandible) and type of reconstruction (vertical or horizontal), number of treated patients, grafting materials used, and the follow-up duration were extracted. The primary outcomes of the study were 1) exposure rate, 2) mesh removal rate, 3) associated bone loss, and 4) implant survival rate. Descriptive statistics were performed, and data were reported as mean $\pm$ SD.

3. Results

3.1. Report of a case

A 50-year-old female patient suffering from anterior maxillary bone width deficiency was treated with a combination of autogenous bone graft (ABG) and deproteinized bovine bone material (DBBM) (BioOss, Geistlich, Germany) and protected with the titanium mesh (Jeilmed, Seoul, South Korea). Four weeks following surgery, partial exposure of the titanium mesh in the labial side of the augmented site occurred (Figure 2). There was no pus drainage from the exposed area. An intense oral hygiene regimen was instructed to the patient. It was planned to remove the mesh during re-entry surgery 6 months later. During mesh removal, an incisional biopsy (4mm square sample) was taken from the soft tissue beneath and sent for histopathological evaluations. Bone volume was enough to tolerate the burden of dental implants, although the underlying bone showed partial resorption in the exposed area.

3.2. Review results

Among all studies, 30 case series (22,24,29,31,34-37,39,41,43,45,48-51,54,58-60,62-71), 13 retrospective studies (16,20,27,28,32,33,38,42,44,47,52,57,61), and 8 randomized controlled clinical trials (15,25,30,40,46,53,55,56) were included (n=51). Studies involved between 5 to 65 patients. The



Figure 2. A Site of exposure: partial exposure of the titanium mesh in the labial side of the augmented site

atrophic ridges required either vertical (n=15) (15,22,24,25,34,40,43,44,51,55,57,60,61,65,70), or horizontal (n=5) (37,42,45,53,71) bone augmentation or both (n=28) (16,20,27,29-33,36,38,41,46-50,52,54,56,58,59,62-64,66-69). The most frequently applied grafting materials were ABG used in 27 studies (16,20,22,24,25,28,29,31,32,33,36,37,41,47,49-51,53,55,58,59,62,64,66,67,70,71). The exposure rate ranged between zero and 100% (35), as ten studies reported zero occurrence of exposures (39,44,45,54,55,59,63,66,69,71). Among the 41 studies reporting exposure, 18 reported removal of membranes (15,16,24,25,29,33,34,42,43,47,51,60,61,68,70). The effect of exposure on bone loss was seen in 3 studies where the ideal amount of bone gain was not achieved (20,34,56). Regardless of the exposure, a high survival rate of implants, ranging between 86.7% and 100%, was reported in the studies, where 34 studies reported 100% (15,16,22,27-32,35-38,40,41,43-45,48-50,54,55-57-60,62,64-67,70), and 4 studies reported higher than 90% (42,47,68,71) survival rates for the placed implants. Detailed characteristics and the outcomes of the selected articles are demonstrated in Table 1.

3.3. Histologic results

Histological analysis of the retrieved specimen beneath the exposed mesh showed complete epithelial migration. There was a thick connective tissue (3900 μ m) underneath the squamous epithelium with sporadic infiltration of inflammatory cells (Figure 3). Vascular buds and bone substitute remnants were specimen, superior to the augmented site, islands of new bone

Table 1. Evaluation of Ti-Mesh exposure rate and its effect on bone loss and implant survival.

Author (year)	Study type/ Defect type	Number of patients (sites)	Grafting material	Mesh exposure s (%)	Follow-up time	Mesh removal	Associated Bone loss	Implant survival (%)	Ref
1.Nan et al. (2023)	Retro/ Reconstruction in maxilla & mandible	59 (61)	ABG + I-PRF + BioOss ® + 3D TiMesh + BioGide ®	32.8%	30 months	None	-	100%	28
2.Simion et al. (2023)	CS/VRA & HRA in maxilla & mandible	9 (11)	ABG + BioOss ® + BioGide ®	9.9%	13 months	18.18%	-	100%	29
3.Lim et al. (2022)	RCT/ VRA & HRA in maxilla & mandible	16	ABBM + BioOss ® + A-Oss ®	18.75	20 months	None	-	100%	30
4.Wang et al. (2021)	CS/ VRA & HRA in maxilla	18	ABG + CGF + BioOss ® + BioGide ®	5.5%	27 months	None	0.72 mm in 1st year	100%	31
5.Chiapasco et al. (2021)	Retro/ VRA & HRA in maxilla & mandible	41 (53)	ABG + BioOss ® + BioGide ® + Customized TiMesh	20.75%	13 months	None	Less than 1.5 mm	100%	32
6.Malik et al. (2020)	CS/VRA in mandible	20	Alloplastic Novabone putty + TiMesh	20%	6 months	5%	Only 1 mm bone loss in removed case	NE	34
7.El chaar et al. (2019)	Retro/ VRA & HRA in mandible & maxilla	40	MSDBA + Customized TiMesh on stone model or 3D printed model	50%	18 months	10%	NE	100%	27
8.Ghanaati et al. (2019)	CS/ 3D Reconstruction in mandible	7 (13)	Liquid and solid PRF + BioOss ® + Customized TiMesh + Mucograft ® + latex/ t-PTFE	100%	12 months	None	None	100%	35

9.Hartmann et al. (2019)	Retro/ VRA & HRA in maxilla & mandible + sinus floor augmentation	65 (70)	ABG+ Bio-Oss ® + A-PRF+ I-PRF + BioGide ® + customized TiMesh	37.1	6 months	8.6%	partial loss (32.9%) complete loss (7.1%)	NE (significantly associated with exposure)	33
10.Khojasteh et al. (2019)	CS/ VRA & HRA in mandible	14	CeraBone ® + buccal fat pad derived stem cells + ABG + TiMesh	14.2%	6 months	None	None	100%	36
11.Tallarico et al. (2019)	CS/HRA	7 (10)	ABG +BioOss ® + ultra-fine TiMesh	14.2%	20.85 ± 42.84 months	None	None	100%	37
12.Zhang et al. (2018)	Retro/VRA & HRA in esthetic zone	12 (16)	BioOss ® + L-shaped TiMesh + BioGide ®	6.25%	13-41 months	None	None	100%	38
13.Cucchi et al. (2017)	RCT/ VRA in mandible	39 (106)	Dense t-PTFE + Osseoguard ®	21.1%	9 months	2 in d-PTFE and 3 in TiMesh	None	100%	15
14.Lv et al. (2017)	CS/ Reconstruction in maxilla	6 (6)	-	None	14.4 ± 6.5 months	-	-	-	39
15.Mouniret al. (2017)	RCT/ VRA in maxilla	16 (40)	Onlay Tutogen ® + inlay block xenograft	50%	6 months	None	None	100%	40
16.Saghebet al. (2017)	CS/ VRA & HRA in maxilla & mandible	17 (21)	ABG + BioOss ®	33%	12 ± 6 months	None	None	100%	41
17.Gomeset al. (2016)	Retro/ HRA in maxilla and mandible	25 (40)	BioOss ®	24%	12 months	8%	Partial loss (1), complete loss (1)	97.5 %	42

18.Chan et al. (2015)	CS/ VRA in mandible	5	Particulate Allograft (enCore®)	40%	9 months	40%	-	100%	43
19.Misch et al. (2015)	Retro / VRA in maxilla & mandible	15 (40)	rhBMP-2 in ACS carrier and MinerOss®	None	6 months	-	-	100%	44
20.Ribeiro et al. (2015)	CS/ HRA in maxilla	5 (10)	rhBMP-2	None	55 months	-	-	100%	45
21.Sumida et al. (2015)	RCT/ VRA & HRA in mandible	26 (39)	Customized Or Commercial TiMesh	15.38%	NE	None	-	NE	46
22.Uehara et al. (2015)	Retro / VRA & HRA in maxilla & mandible	23 (64)	ABG + HA	70%	40 months	26%	None	98.4 %	47
23.Butura et al. (2014)	CS/ VRA & HRA in mandible & maxilla	7 (14)	rhBMP-2 + BioOss	28%	36 months	None	-	100%	48
24.Jung et al. (2014)	CS/ VRA & HRA in maxilla & mandible	10 (12)	ABG + SureOss®	30%	12 months	None	-	100%	49
25.Lizio et al. (2014)	Retro/VRA & HRA in maxilla & mandible	12 (15)	ABG + BioOss®	80%	14 months	None	16.3% bone loss for every cm ² of mesh exposed	NE	20
26.Poli et al. (2014)	CS/ VRA & HRA in maxilla & mandible	13 (20)	ABG + BioOss®	7.69%	88 months	None	-	100%	50

27. Funato et al. (2013)	CS/ VRA in maxilla & mandible	19 (19)	ABG + BioOss ® + (rhPDGF-BB) + Ossix ®	10.52%	6 months	5.2%	-	-	51
28. Butura et al. (2012)	Retro / VRA & HRA in maxilla & mandible	7 (14)	rhBMP-2 + BioOss ®	9.09%	6 months	NE	None	NE	52
29. Her et al. (2012)	Retro /VRA & HRA in maxilla & mandible	27 (69)	Puros ® + BioOss ® + ABG + Regenafil ®	26%	24 months	None	compromised	100%	16
30. Khamees et al. (2012)	RCT/ HRA in maxilla	13 (16)	ABG + DBBM	25%	6 months	25%	-	NE	53
31. Misch et al. (2011)	CS/ VRA & HRA in mandible	5 (10)	rhBMP-2 + acellular collagen sponge	None	6 months	-	-	100%	54
32. Merli et al. (2010)	RCT/VRA in mandible	22 (22)	ABG + BioGide ® + Expanded t-PTFE	None	36 months	-	-	100%	55
33. Torres et al. (2010)	RCT/ VRA & HRA in maxilla & mandible	30 (97)	DBBM + PRP	20%	30 months	None	little or no bone augmentation in exposed cases	100%	56
34. corinaldesi et al. (2009)	CS/ VRA in maxilla & mandible	24 (56)	ABG	14.8%	17 months	16.6%	Defects not completely repaired	100%	22
35. Canullo et al. (2008)	Retro / VRA in maxilla & mandible	10 (24)	BioOss ® + Expanded t-PTFE	10%	44 months	NE	NE	100%	57
36. Pieri et al. (2008)	CS/ VRA & HRA in maxilla & mandible	16 (40)	ABG + BioOss ®	5.3%	24 months	6.25%	50% of desired amount	100%	58

37. Corinaldesi et al. (2007)	CS/ VRA & HRA in maxilla & mandible	12 (35)	ABG + BioOss ®	None	21 months	-	-	100%	59
38. Rocuzzo et al. (2007)	RCT/ VRA in maxilla & mandible	23	ABG	17.39%	4.6 ± 0.7 months	4.3%	-	-	25
39. Strietzel et al. (2007)	Cs/ VRA in maxilla & mandible	14	OStim® HA	50%	31 months	7.1%	-	100%	60
40. Molly et al. (2006)	Retro/ VRA in maxilla	29 (141)	Hip graft Or TiMesh	6.89%	6-14 years	6.6%	compromised and no implant placed	86.7 %	61
41. Proussae fs et al. (2006)	CS/ VRA & HRA in maxilla & mandible	17 (41)	ABG + BioOss ®	11.76%	12 months	NE	-	100%	62
42. Chen, 2005	CS/ Reconstruction in maxilla	8	Pedicled buccal fat pad	None	24 months	-	-	-	63
43. Rocuzzo, 2004	CS/ VRA & HRA in maxilla & mandible	18 (37)	ABG	22.22%	4.6 months	NE	-	100%	64
44. Artzi et al. (2003)	CS/ VRA in maxilla & mandible	10 (20)	DBBM	20%	33 months	-	-	100%	65
45. Degidi et al. (2003)	CS/ VRA & HRA in maxilla & mandible	18 (50)	ABG + BioGide ® + Polyurethane membrane	None	7 years	-	-	100%	66
46. Proussae fs et al. (2003)	CS/ VRA & HRA in maxilla & mandible	7 (23)	ABG + BioOss ®	57.14%	12 months	-	-	100%	67

47. Van Steenberghe et al. (2003)	CS/ VRA & HRA in maxilla	10 (39)	-	50%	6.5 years	40%	No implant inserted and no bone gain in two cases	92.3 %	68
48. Assenza et al. (2001)	CS/VRA & HRA in maxilla & mandible	18	Expanded PTFE membrane	None	6 months	-	-	NE	69
49. Von Arx et al. (1999)	CS/ VRA in maxilla	15 (20)	ABG	5%	6.6 months	6.6%	Total bone graft loss	100%	70
50. Malchio di et al. (1998)	CS/ HRA in maxilla	25 (120)	ABG	None	8 months	-	-	97.5 %	71
51. Von Arx et al. (1996)	CS/ VRA in maxilla & mandible	19 (28)	ABG	50%	4.7 months	5%	Compromised, no implant inserted	-	24

ABG: Autogenous bone graft, ABBM: Anorganic bovine bone materials, ACS: Absorbable collagen sponge, A-PRF: Advanced platelet-rich fibrin, BioGide: BioGide collagen membrane, BioOss: BioOss bovine bone mineral, DBBM: Deproteinized bovine bone material, CeraBone: Cerabone bovine bone mineral, CGF: Concentrated growth factor, CS: Case series, HA: Hydroxy apatite, HRA: Horizontal ridge augmentation, I-PRF: Injectable platelet-rich fibrin, MinerOss: MinerOss particulate mineralized bone allograft, Mucograft: Mucograft collagen membrane, MSDBA: Mineralized solvent dehydrated bone allograft, NE: Not evaluable, OsseoGuard: OsseoGuard crosslinked collagen membrane, Ossix: Ossix collagen membrane, PRF: Platelet rich fibrin, PRP: Platelet rich plasma, Retro: Retrospective clinical study, RCT: Randomized controlled clinical trial, Reganfil: Reganfil demineralized bone matrix, rh-BMP2: Recombinant human bone morphogenetic protein, rh-PDGF-BB: Recombinant human platelet derived growth factor BB, Puros: Puros mineralized cancellous bone allograft, SureOss: SureOss freeze-dried bone allograft, TiMesh: Titanium mesh, t-PTFE: Titanium reinforced poly-tetra-fluoro-ethylene, Tutogen: Tutogen particulate xenograft bone material, VRA: Vertical ridge augmentation,

evident within the connective tissue. In the deepest part of the with an active osteoblastic rim could be detected.

4. Discussion

This study reviewed reports of titanium mesh exposure in bone augmentation procedures to help the clinician clearly understand this complication's risk and its consequences. According to the results, exposures rate ranged from zero (n=10) to 100%. Comparing the obtained results to those of the systematic review by Rasio dal Polo et al., who reported a mean exposure rate of 16.1%, a pattern of increase in complication rates can be observed (4). In another review on vertical bone augmentation using both resorbable and non-resorbable barrier membranes, Milinkovic et al. reported an exposure rate of 13.1% when placing implants simultaneously with the grafts (18). The rate of exposure, as calculated in our review, is close to a review by Ricci et al., indicating that titanium grid exposure occurred in 22.78% of patients of the studies (19).

In the reviewed articles, 18 studies reported removal of the exposed meshes (n = 41), among which 3 observed a significant resultant bone loss. The mean bone gain was evaluated in either linear or volumetric measures in different studies, and therefore, our review reports the bone loss associated with titanium mesh to make comparison possible. Lizio et al. argued that 16.3% bone volume loss occurs for every cm² of mesh exposed (20). The time point at which these measurements were made, as well as follow-up times, must be similar among studies to compare results. We excluded the studies with a follow-up time of less than 6 months, considering it the minimum amount of time required to truly evaluate the augmented bone. However, the mesh removal and follow-up times were inconsistent in the studies, which made the comparison unattainable.

It has been shown that premature membrane exposure and consequent bone loss are correlated, but this does not necessarily impede implant placement (21). For example, in a study by Corinaldesi et al., a premature exposure rate of 14.8% was observed in four of the 27 micro meshes and were removed, but implants were left in place as they were stable, and thus, a survival rate of 100% and a success rate of 96.4% was achieved (22). In this study, the effect of membrane exposure on long-term implant survival was assessed. It's important to note that a better parameter about implants is implant success rather than survival. This is because an implant could still survive despite signs of radiolucency, inflammation, and bone loss (23). In most of the studies, however, no reports of success could be found. Thus, the survival rates were compared in this review. Excluding those studies that did not include implants in their treatment plan or did not report clinical results regarding their survival (n=11) (20,24,25,33,34,46,51,52,53,63,69), of the studies involving exposures (n=32) (15,16,22,27-32,35-38,40-43,47-50,53,56-58,60-62,64,65,67,68,70), 29 had a survival rate of 100% (15,16,22,27-32,35-38,40,41,43,46,48-50,56-58,60,62,64,65,67,

70) Meanwhile, of the studies without exposures (n=8) (44,45,54,55,59,66,69,71), 6 had a survival rate of 100% (44,45,54,55,59,66). It is suggested that researchers adopt proper success criteria evaluating the "long-term primary outcome of an implant-prosthetic complex as a whole" so that confident deductions can be made (23).

Exposure is the most common complication with titanium mesh, and its prevention and management are important. It's been previously indicated that management and mobilization of flaps are the keys to minimizing exposures, as most exposures occur due to the low flexibility of meshes and poor suturing techniques (18,19). Concerning management, most exposures are not removed but preferably treated with topical chlorhexidine 0.2% or saline oral rinses to avoid infection and bone loss. Her et al. suggested that mesh removal was unnecessary as early exposure (within 2 weeks post-operatively) was closed a few weeks after trimming 2mm of the exposed margins, and late exposures (occurring 2 to 8 weeks after the surgery) were treated by drainage, saline irrigation, the antibiotic regimen, and subsequent bone addition to compensate for the lost bone at re-entry (16). Another issue is purulent exposure and associated inflammation, which jeopardizes graft and implant success. In a study by Von Arx et al., the authors mentioned that inflammation is rarely observed in cases of mesh exposures (24). However, this is not the case with other types of membranes (25). In the histology of the tissue beneath the exposed membrane, sporadic infiltration of inflammatory cells was observed.

In the retrieved specimen, the connective tissue and the bone beneath the exposed membrane were covered completely by a keratinized stratified squamous epithelium. This epithelial migration beneath the exposed titanium mesh membrane may act as protection for the underlying bone (26). This ectodermal healing process involving the bridging of epithelial cells might explain the higher survival rate of the augmented bone achieved with titanium mesh.

It was concluded that titanium mesh is a valid non-resorbable barrier membrane in both vertical and horizontal bone augmentation procedures.

5. Limitations

Due to the heterogeneity of influencing factors, such as graft material, recipient site, and methodology, no definite conclusions could be drawn. No meta-analysis was found in the literature, and only a few systematic reviews were found regarding the exposure rate of titanium mesh membrane, the latest conducted in 2014 (4). Only five studies (15,27,28,32,33) had a sample size greater than 30 (n=59, n=41, n=40, n=65, n=39, respectively), which shows the inadequacy of large-scale randomized studies.

6. Conclusion

In conclusion, our outcomes suggest that the titanium mesh exposure rate is low, and its variable rate among studies could mean that this complication is more dependent on operator skills than on material characteristics. Thus, it's possible to assert, within the scope of this study, that titanium mesh can be used in both vertical and horizontal reconstruction of edentulous ridges with the proper prevention and management of exposures. Nonetheless, long-term randomized controlled clinical trials are favored with specific treatment protocol and outcome evaluation criteria involving an adequate sample size that allows a clear comparison of success and complication rates between titanium mesh and other membranes.

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Authors' contribution

Bijan Akhavan Azari: Conceptualization, Project administration. Hannaneh Safiaghdam: Methodology, Writing - Original draft. Niussha Gharehdaghi: Investigation, Writing - Review & editing. Arash Khojasteh: Validation, Supervision.

Conflict of Interest

None.

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