Titanium Mesh Exposure in Guided Bone Regeneration Procedures: A Systematic Review and Meta-analysis

Chunning Gu, MDS¹/Lu Xu, MDS¹/Anyuan Shi, MDS¹/Li Guo, MDS¹/Hao Chen, PhD²/Haiyan Qin, PhD¹

**Purpose:** To investigate whether titanium mesh exposure is influenced by the type of titanium mesh, the type of bone graft material, or the associated employment of absorbable membranes. **Materials and Methods:** Electronic literature searches were conducted using four databases: PubMed, EMBASE, Web of Science, and Cochrane. Articles reporting titanium mesh exposure rates were included, and exposure rates in different subgroups were compared to determine whether a factor significantly influenced titanium mesh exposure. The review protocol was registered in the PROSPERO registry (CRD42020210187). **Results:** Twenty and 12 articles were included in the qualitative and quantitative synthesis, respectively. The weighted exposure rates of employing conventional titanium mesh or 3D-customized titanium mesh were 19.9% and 15.2% (P = .34). When employing autogenous bone combined with anorganic bovine bone material as bone graft material, the weighted exposure rate was 21.7%, whereas when using other bone graft material, the exposure rate was 23.5% (P = .74). The weighted exposure rate of using titanium mesh associated with absorbable membranes is 23.9%, while the weighted exposure rate of using titanium mesh without absorbable membranes is 20.2% (P = .36). Meta-regression showed that when analyzing one factor, the other two confounding factors did not influence the result (P = .28). **Conclusion:** It seemed that the type of titanium mesh, the type of bone graft material, or the combined employment of absorbable membranes did not statistically significantly influence the titanium mesh exposure rate in guided bone regeneration. *Int J Oral Maxillofac Implants* 2022;37:e29–e40. doi: 10.11607/jomi.9098

**Keywords:** exposure, guided bone regeneration, influence factor, systematic review, titanium mesh

The first condition that ensures a long-term prognosis and survival rate of oral implants is sufficient bone volume.¹² There are many different methods for bone augmentation, including distraction osteogenesis, guided bone regeneration (GBR), bone block grafting, tent pole technique, etc.²³ The GBR technique is the most widely employed of all ridge augmentation techniques.¹² The principle of the GBR technique is that the membranes applied can prevent faster proliferating epitheliums from affecting bone formation.⁴ Various membranes applied in the GBR procedure can be divided into two groups: absorbable membranes and nonabsorbable membranes. Absorbable membranes can be fabricated by collagen or synthetic polymers, such as polyglycolide (PGA) and polylactide (PLA).⁵ The most common absorbable membrane is the collagen membrane. The nonabsorbable membranes include expanded polytetrafluoroethylene (ePTFE), dense polytetrafluoroethylene (dPTFE), titanium-reinforced PTFE, and titanium mesh.⁵ Titanium mesh is the most widely used nonabsorbable membrane. Because of its rigidity, titanium mesh can maintain the space needed for bone regeneration more steadily than resorbable membranes.⁶ Gutta et al⁷ showed that compared with absorbable membranes and microporous titanium mesh, macroporous titanium mesh led to greater bone formation and regeneration and could prevent soft tissue ingrowth better than nonabsorbable membranes.

However, the employment of titanium mesh has a limitation. That is, the stiffness and the possible sharp edges of titanium mesh may irritate soft tissue and result in titanium mesh exposure, further causing infection and loss of graft materials. Currently, many studies⁵,⁸,⁹ recommend nonabsorbable membranes as the most suitable membranes for vertical bone augmentation or large area bone defects, whereas absorbable membranes are suitable for mild or moderate bone defects. Since titanium mesh is the most widely employed type of nonabsorbable membrane, it is meaningful to ascertain its exposure rate and determine how to reduce the incidence of exposure. The purpose of this article was to identify whether the exposure of titanium mesh is
influenced by the employment of 3D-customized titanium mesh, the type of bone graft material, and the associated employment of absorbable membranes.

**MATERIALS AND METHODS**

**Focused Questions**
This systematic review focused on the following questions:

1. Is the exposure of titanium mesh affected by the employment of 3D-customized titanium mesh?
2. Is the exposure of titanium mesh affected by the type of bone graft material?
3. Is the exposure of titanium mesh affected by the associated employment of absorbable membranes?

This article followed the Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) statement. The review protocol was registered and assigned the identification number CRD420202101877 on the PROSPERO website.

**Inclusion Criteria**

*Patients.* Adult patients with completely or partially edentulous maxillae or mandibles who needed bone grafting to gain bone volume were included.

*Interventions.* The article focused on three related factors. Therefore, there were three groups of interventions and comparisons:

- The employment of 3D-customized titanium mesh in the GBR procedure.
- The combined employment of autogenous bone (AB) and anorganic bovine bone material (BBM) in the GBR procedure.
- The combined employment of absorbable membranes and titanium mesh in the GBR procedure.

*Comparisons.*

- The employment of conventional titanium mesh in the GBR procedure.
- The employment of other bone graft material (ie, hydroxyapatite particles, freeze-dried bone allografts, AB, or BBM alone) in the GBR procedure.
- The exclusive employment of titanium mesh in the GBR procedure.

*Outcomes.* The outcomes were the titanium mesh exposure rate (primary outcome), the exposure time, and vertical or horizontal bone augmentation (secondary outcomes).

*Study design.* The study design was as follows: randomized controlled trials (RCTs), prospective cohort studies, retrospective cohort studies, and case series reports. Case series reports needed to have at least 10 cases.

**Exclusion Criteria**

The exclusion criteria were as follows:

- Studies involving concomitant interventions (ie, simultaneous maxillary sinus floor elevation).
- Studies with nonparticulate bone graft material (ie, block graft).
- Studies reporting on the usage of medications or therapy that could affect the healing of bone (ie, bisphosphonates or radiation therapy).
- Studies involving maxillary or mandibular segmental resection due to tumors.
- The follow-up time after titanium mesh placement was < 6 months.
- Animal trials.
- Studies that were not published in English.

**Information Sources and Search Strategy**

Four electronic databases were searched to meet the eligibility criteria: PubMed, EMBASE, Web of Science, and Cochrane. These databases were searched for articles published up until July 21, 2020, using the following search described below (Table 1).


**Study Selection and Data Extraction**

EndNote X9.0 software was used to manage the literature. The study selection was divided into two phases. In the first phase, two independent reviewers (C.G., L.X.) individually screened the titles and abstracts of all studies to exclude irrelevant articles (A.S.). If there were any disagreements when reading titles or abstracts, the studies were noted and were further scrutinized in the second phase by reading the full text. Electronic forms
were established using Excel (Microsoft) for data extraction. The main extracted items included author, study type, number of patients, titanium mesh and implants, type of titanium mesh, type of bone graft materials, usage of absorbable membrane, titanium mesh exposure rate, exposure time, exposure area, and vertical or horizontal bone augmentation. If the data of an article were used in other articles, only the article with the most patients was included. Finally, the two information tables were cross-checked, and if there was any disagreement, adjudication was performed by the third author (A.S.).

Assessment of the Risk of Bias
The risk of bias of the included RCTs was assessed according to the Cochrane Collaboration tool, which included the following seven criteria: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting bias, and other sources of bias. The risk of bias of cohort studies was assessed by the Newcastle-Ottawa scale (NOS), whereas observational case series were assessed by the Agency for Healthcare Research and Quality (AHRQ) scale. The NOS included three main categories: selection, comparability, and outcome, whereas the AHRQ scale included 11 items. The assessment was also performed by two authors (C.G., L.X.), and disagreements were resolved in consultation with the third author (A.S.).

Data Synthesis and Statistical Analysis
The exposure rate of titanium mesh was the primary outcome, and the contribution of each article was weighted. The risk ratio and relatively weighted exposure rate were calculated using computer software (Comprehensive Meta-Analysis, Version 3, Biostat). First, the overall exposure rate of titanium mesh was demonstrated, considering only the study type (RCTs, cohort studies, and case series). Then, due to the sample size and heterogeneity, the data from case series were synthesized, whereas those from RCTs and cohort studies were not. To identify whether one factor affected the exposure rate of titanium mesh, the data from case series were divided into two subgroups. As there were three related factors, meta-regressions were performed to identify potential mutual influences.

The statistical heterogeneity of each subgroup was assessed using the I² test and chi-square test. A fixed-effects model was chosen for low heterogeneity (I² < 50%) and a random-effects model for high heterogeneity (I² ≥ 50%). Sensitivity analyses were performed to check the sources of heterogeneity. Forest plots were produced to graphically demonstrate the weighted exposure rate and 95% confidence interval (CI). Funnel plots were employed to evaluate publication bias.

RESULTS

Study Selection
The selection process is summarized in Fig 1. A total of 2,895 articles were found by electronic search (1,034 in PubMed, 140 in Cochrane, 1,061 in Embase, and 660 in

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Table 1  Electronic Search Strategy

| 1. (((Alveolar Ridge Augmentation[MeSH Terms]) OR (augmentation)) OR (augmentations)) OR (GBR)) OR (Mandibular Reconstruction[MeSH Terms]) OR (reconstruction)) OR (bone regeneration [MeSH Terms]) OR (bone regeneration) |
| 2. (((Alveolar bone loss[MeSH Terms]) OR (Alveolar bone loss)) OR (bone resorption[MeSH Terms])) OR (bone resorption)) OR (ridge atrophy) OR (bone atrophy) OR (bone defect?) |
| 3. (((titanium mesh)[Title/Abstract]) OR (titanium meshes[Title/Abstract])) OR (titanium grid[Title/Abstract]) OR (titanium grids[Title/Abstract]) OR (microtitanium mesh[Title/Abstract]) OR (microtitanium meshes[Title/Abstract]) |
| 4. (#1) OR (#2) |
| 5. (#3) AND (#4) |

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Fig 1  Flowchart demonstrating the selection process.
The search for gray literature and clinical trials did not result in any extra studies. Only one extra study was found by manual search. After deleting the duplicated literature, 1,877 articles were retained. After screening for titles and abstracts, 41 articles qualified for inclusion. After reading the full text, only 20 articles were included. The reasons for excluding 21 articles are provided in Table 2. Finally, 20 articles were included for qualitative evaluation, and 12 articles were included for quantitative synthesis.

### Study Characteristics

Four RCTs, 12–15 four cohort studies, 16–19 and 12 case series20–31 were included. The characteristics of all included studies are shown briefly in Table 3. Altogether, 404 patients, 443 titanium meshes, and 876 implants were included. In all the studies, the follow-up time varied from 6 to 96 months. Sixteen articles 12–19,23,24,26–31 reported on conventional titanium mesh, whereas customized mesh was used in five articles.17,20–22,25 Conventional commercial titanium meshes were 0.1 26,27 or

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**Table 2** Reasons for Exclusion

<table>
<thead>
<tr>
<th>Not reporting on exposure rate</th>
<th>Inadequate no. of cases</th>
<th>Data used in another article</th>
<th>Using the block graft</th>
<th>Simultaneously elevating the sinus floor</th>
<th>Data missing</th>
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<tbody>
<tr>
<td>Artzi et al (2003)59</td>
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**Table 3** Characteristics of Included Studies

<table>
<thead>
<tr>
<th>Author</th>
<th>Study type</th>
<th>No. of patients</th>
<th>No. of titanium mesh</th>
<th>No. of implants</th>
<th>Titanium mesh type</th>
<th>Grafting material</th>
<th>Absorbable membrane</th>
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<tbody>
<tr>
<td>Funato et al (2013)26</td>
<td>Case series</td>
<td>19</td>
<td>19</td>
<td>None</td>
<td>Conventional AB+BBM (1:1 or 1:4 ratio)</td>
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<tr>
<td>Cucchi et al (2017)14</td>
<td>RCT</td>
<td>20</td>
<td>20</td>
<td>54</td>
<td>Conventional AB+BBM (1:1 ratio)</td>
<td>Yes</td>
<td></td>
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<tr>
<td>Hartmann and Seiler (2020)29</td>
<td>Case series</td>
<td>55</td>
<td>68</td>
<td>98</td>
<td>Customized AB+BBM (1:1 ratio)</td>
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<td>Atef et al (2020)12</td>
<td>RCT</td>
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<td>10</td>
<td>None</td>
<td>Conventional AB+BBM (1:1 ratio)</td>
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<tr>
<td>Pieri et al (2008)28</td>
<td>Case series</td>
<td>16</td>
<td>19</td>
<td>44</td>
<td>Conventional AB+BBM (7:3 ratio)</td>
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<tr>
<td>Corinaldesi et al (2009 a)19</td>
<td>Cohort studies</td>
<td>13</td>
<td>13</td>
<td>20</td>
<td>Conventional AB</td>
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<tr>
<td>Corinaldesi et al (2009 b)19</td>
<td>Cohort studies</td>
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<td>14</td>
<td>36</td>
<td>Conventional AB</td>
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<tr>
<td>Miyamoto et al (2012)18</td>
<td>Cohort studies</td>
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<td>50</td>
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<tr>
<td>Jung et al (2014)25</td>
<td>Case series</td>
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<td>10</td>
<td>12</td>
<td>Customized AB+BBM (1:1 ratio)</td>
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<td>Mounir et al (2019)13</td>
<td>RCT</td>
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<td>8</td>
<td>16</td>
<td>Conventional AB+BBM (1:1 ratio)</td>
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<td></td>
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<tr>
<td>Proussaefs et al (2006)29</td>
<td>Case series</td>
<td>17</td>
<td>17</td>
<td>41</td>
<td>Conventional AB+BBM</td>
<td>No</td>
<td></td>
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<tr>
<td>Poli et al (2014)24</td>
<td>Case series</td>
<td>13</td>
<td>13</td>
<td>20</td>
<td>Conventional AB+BBM (1:1 ratio)</td>
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<tr>
<td>Sagheb et al (2017)22</td>
<td>Case series</td>
<td>17</td>
<td>21</td>
<td>44</td>
<td>Customized AB+BBM; AB</td>
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<tr>
<td>Uehara et al (2015)16</td>
<td>Cohort studies</td>
<td>21</td>
<td>23</td>
<td>64</td>
<td>Conventional AB+HA (1:1 ratio; n = 20); AB (n = 8)</td>
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<tr>
<td>Her et al (2012)27</td>
<td>Case series</td>
<td>26</td>
<td>27</td>
<td>69</td>
<td>Conventional Various materials</td>
<td>No</td>
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<tr>
<td>Sumida et al (2015 a)17</td>
<td>Cohort studies</td>
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<td>13</td>
<td>21</td>
<td>Customized Unclear</td>
<td>No</td>
<td></td>
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<tr>
<td>Sumida et al (2015 b)17</td>
<td>Cohort studies</td>
<td>13</td>
<td>13</td>
<td>18</td>
<td>Conventional Unclear</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>Torres et al (2010)15</td>
<td>RCT</td>
<td>15</td>
<td>15</td>
<td>97</td>
<td>Conventional BBM</td>
<td>No</td>
<td></td>
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<tr>
<td>Zhang et al (2019)21</td>
<td>Case series</td>
<td>12</td>
<td>12</td>
<td>16</td>
<td>Customized BBM</td>
<td>Yes</td>
<td></td>
</tr>
</tbody>
</table>

RCT = randomized controlled trial; AB = autogenous bone; BBM = (anorganic) bovine bone material; XB = xenogeneic bone; HA = hydroxyapatite particle; FDBA = freeze-dried bone allograft.
0.2 mm thick, and they could be prebent or not. Customized titanium meshes were computer-aided, designed, and manufactured for each patient. Their thicknesses were not mentioned in most studies. Of all included articles, the most widely used graft material was the combined employment of AB and anorganic BBM, with a popular ratio of 1:1 or 7:3. In some cases, AB or BBM was used alone or in different proportions. Other graft materials, such as freeze-dried bone allografts (FDBAs) and hydroxyapatite particles (HAs) were also applied in some studies. As absorbable membranes collapse more easily and cannot maintain the space needed for bone regeneration, they were employed in combination with titanium mesh in some cases. In all included studies, seven articles demonstrated the associated employment of titanium membranes and collagen membranes, whereas in 13 studies, titanium mesh was employed alone.

Assessment of the Risk of Bias
The results are shown in Fig 2 and Table 4. For RCTs, two studies were considered to have a low risk of bias, and two had a moderate risk of bias. For the cohort studies, according to their total scores, all were evaluated as having a low risk of bias. Regarding the case series, their total scores were all < 4, indicating that they were all rated as having a high risk of bias.

Exposure Rate of Titanium Mesh
For all included studies, the exposure rate of titanium mesh varied from 5.3% to 69.6%. High heterogeneity occurred due to too many cofounding factors. Therefore, to further investigate the exposure rates under different circumstances, three subgroups, described later, were created based on the study design (Fig 3).

Results in RCTs
The exposure rate of titanium mesh was 30% (95% CI = 18.7% to 44.2%), with a low value of heterogeneity ($I^2 = 5.0\%$, $P = .37$). In the study by Atef et al of all 10 titanium meshes, three were exposed 3 weeks postoperatively, whereas one site was exposed 4 months postoperatively. In the study by Mounir et al, eight titanium meshes were prebent, and one site was exposed. In the study by Cucchi et al, 20 titanium meshes were covered by collagen membranes, and four were exposed. To reduce the exposure rate, Torres et al covered the titanium mesh with platelet-rich plasma (PRP) in 15 patients, whereas the other 15 patients were treated with

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**Table 4 Risk of Bias Assessment of Four Cohort Studies**

<table>
<thead>
<tr>
<th></th>
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</thead>
<tbody>
<tr>
<td>Selection of the nonexposed cohort</td>
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<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Ascertainment of exposure</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Demonstration that outcome of interest was not present at start of study</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Comparability Comparability of cohorts on the basis of the design or analysis</th>
<th>****</th>
<th>**</th>
<th>**</th>
<th>**</th>
</tr>
</thead>
<tbody>
<tr>
<td>Outcome Assessment of outcome</td>
<td></td>
<td></td>
<td>**</td>
<td>**</td>
</tr>
<tr>
<td>Was follow-up long enough for outcomes to occur?</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Adequacy of follow-up of cohorts</td>
<td></td>
<td></td>
<td>**</td>
<td>**</td>
</tr>
<tr>
<td>Total</td>
<td>7/9</td>
<td>7/9</td>
<td>8/9</td>
<td>9/9</td>
</tr>
<tr>
<td>Risk of bias</td>
<td>Low</td>
<td>Low</td>
<td>Low</td>
<td>Low</td>
</tr>
</tbody>
</table>

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titanium mesh alone. For the titanium mesh group, six sites were exposed. In the PRP treatment group, no exposure cases were reported.

Results in Cohort Studies
Sumida et al\textsuperscript{17} recruited 26 patients to compare customized titanium mesh and conventional titanium mesh. In this study, the customized titanium mesh group had one case of exposure, whereas the conventional titanium mesh group had three cases of exposure. In the study by Miyamoto et al\textsuperscript{18}, of 50 conventional titanium meshes, 18 meshes were exposed, regardless of the type of bone defect. In the study by Corinaldesi et al\textsuperscript{19}, the one-stage GBR procedure and two-stage GBR procedure were compared. In the one-stage GBR procedure, of all 13 conventional titanium meshes, three were exposed, whereas in the two-stage GBR procedure, only one site was exposed. The exposure rates of these three articles\textsuperscript{17–19} were acceptable. However, in the study by Uehara et al\textsuperscript{16}, of 23 titanium meshes, 16 meshes were exposed. The exposure rate seems too high.

Results of Case Series Reports
The total exposure rate was 22.5% (95% CI = 17.5% to 28.3%), with a low value of heterogeneity ($I^2 = 17\%$, $P = .28$). This article focused on three variables that could influence the exposure rate of titanium mesh. Therefore, the results were demonstrated from three aspects: the type of titanium mesh, the type of bone graft materials, and the associated employment of absorbable membranes and titanium mesh.

Employment of 3D-customized titanium mesh. Conventional titanium mesh was employed in eight articles, and customized titanium mesh was employed in four articles. The exposure rate of the former was 19.9% (95% CI = 13.8% to 27.9%), whereas the exposure rate of the latter was 25.2% (95% CI = 17.9% to 34.4%; Fig 4). Interestingly, this result was contrary to the aforementioned cohort study.\textsuperscript{17} Values of heterogeneity of the two groups were low ($I^2 = 29.3\%$, $P = .2$; $I^2 = 0\%$, $P = .49$), indicating high credibility. The two exposure rates (19.9%, 25.2%) showed no significant difference ($P = .34$), indicating that the type of titanium mesh did not affect titanium mesh exposure. In addition, meta-regression, which was performed to identify the potential influence of the type of bone graft materials and the combined employment of absorbable membranes on the exposure rate, showed that there was no statistically significant difference ($P = .28$).

Type of bone graft material. Six articles employed AB combined with anorganic BBM as the bone graft material, and six articles employed other graft materials. For the former, the weighted exposure rate of titanium mesh was 21.7% (95% CI = 15.4% to 29.6%), whereas for...
the latter, the weighted exposure rate was 23.5% (95% CI = 16.2% to 32.8%; Fig 5). Values of heterogeneity ($I^2 = 35.5\%, P = .17; I^2 = 7.3\%, P = .37$) of the two groups were low. The two exposure rates (21.7%, 23.5%) showed no significant difference ($P = .74$), indicating that the type of bone graft material did not affect titanium mesh exposure.

With or without absorbable membranes. Five articles reported on the combined employment of absorbable membranes and titanium mesh. The weighted exposure rate was 23.9% (95% CI = 17.5% to 31.8%). The result was similar to the study by Cucchi et al.$^{14}$ Seven articles reported on the exclusive employment of titanium mesh, and the weighted exposure rate was 20.2% (95% CI = 13.3% to 29.5%; Fig 6). For the two groups, the

<table>
<thead>
<tr>
<th>Study name</th>
<th>Group by subgroup within study</th>
<th>Event rate</th>
<th>Lower limit</th>
<th>Upper limit</th>
<th>Z-value</th>
<th>P value</th>
<th>Event rate and 95% CI</th>
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</thead>
<tbody>
<tr>
<td>Funato et al (2013)$^{26}$</td>
<td>AB+BBM</td>
<td>0.105</td>
<td>0.026</td>
<td>0.337</td>
<td>-2.863</td>
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<td>Hartmann and Seiler (2020)$^{20}$</td>
<td>AB+BBM</td>
<td>0.250</td>
<td>0.161</td>
<td>0.366</td>
<td>-3.923</td>
<td>.000</td>
<td></td>
</tr>
<tr>
<td>Maiorana et al (2001)$^{30}$</td>
<td>AB+BBM</td>
<td>0.143</td>
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<td>0.427</td>
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<td>.019</td>
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<tr>
<td>Pieri et al (2008)$^{28}$</td>
<td>AB+BBM</td>
<td>0.053</td>
<td>0.007</td>
<td>0.294</td>
<td>-2.813</td>
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<tr>
<td>Proussaefs et al (2006)$^{29}$</td>
<td>AB+BBM</td>
<td>0.353</td>
<td>0.168</td>
<td>0.596</td>
<td>-1.194</td>
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<tr>
<td>Poli et al (2014)$^{24}$</td>
<td>AB+BBM</td>
<td>0.077</td>
<td>0.011</td>
<td>0.391</td>
<td>-2.367</td>
<td>.017</td>
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<tr>
<td>Gomes et al (2016)$^{23}$</td>
<td>AB+BBM</td>
<td>0.240</td>
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<td>-2.461</td>
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<td>AB+BBM</td>
<td>0.259</td>
<td>0.129</td>
<td>0.453</td>
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<td>AB+BBM</td>
<td>0.053</td>
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<td>Hartmann and Seiler (2020)$^{20}$</td>
<td>Customized</td>
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<td>0.366</td>
<td>-3.923</td>
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<td>Jung et al (2014)$^{25}$</td>
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<td>0.200</td>
<td>0.050</td>
<td>0.541</td>
<td>-1.754</td>
<td>.080</td>
<td></td>
</tr>
<tr>
<td>Sagheb et al (2017)$^{22}$</td>
<td>Customized</td>
<td>0.333</td>
<td>0.168</td>
<td>0.553</td>
<td>-1.497</td>
<td>.134</td>
<td></td>
</tr>
<tr>
<td>Zhang et al (2019)$^{21}$</td>
<td>Customized</td>
<td>0.083</td>
<td>0.012</td>
<td>0.413</td>
<td>-2.296</td>
<td>.022</td>
<td></td>
</tr>
<tr>
<td>Zhang et al (2019)$^{21}$</td>
<td>Other material</td>
<td>0.235</td>
<td>0.162</td>
<td>0.328</td>
<td>-4.988</td>
<td>.000</td>
<td></td>
</tr>
</tbody>
</table>

Fig 4  Forest plot of titanium mesh exposure rate (conventional titanium mesh vs customized titanium mesh).

Fig 5  Forest plot of titanium mesh exposure rate (AB+BBM vs other graft materials).
values of heterogeneity ($I^2 = 4.5\%, P = .38$; $I^2 = 30.5\%, P = .2$) were low. The two exposure rates (23.9%, 20.2%) showed no significant difference ($P = .36$), indicating that employing absorbable membranes simultaneously did not affect titanium mesh exposure.

Secondary Outcomes
Not all included studies reported the exposure time. Eleven studies\textsuperscript{12–15,21,22,26–29,31} reported early exposure, which occurred within 3 months postoperatively. Three articles\textsuperscript{13,21,27} demonstrated the fastest exposure, as early as 2 weeks after the surgery. Six studies\textsuperscript{12,14,16,19,24,29} reported delayed exposure, which meant that the exposure time was more than 3 months postoperatively. The latest exposure time was 6 months postoperatively, which was reported by Cucchi et al.\textsuperscript{14} Infections and soft tissue dehiscence were also reported in some studies,\textsuperscript{16,18} but the complication rate was evidently lower than the titanium mesh exposure rate. Only one study\textsuperscript{20} mentioned the exposure area. However, the study only described the size as either punctual exposure, premolar size, complete exposure, or no exposure and did not provide quantifiable data. Regarding bone augmentation, eight articles\textsuperscript{13,19–22,26,28,30} reported vertical bone augmentation, whereas seven articles\textsuperscript{14,18,21–23,28,29} reported horizontal bone augmentation. Only five articles\textsuperscript{18,21,22,28,29} reported both of these measures. The least vertical bone augmentation was 3.1 mm,\textsuperscript{21} and the most was 8.6 mm.\textsuperscript{26} The least horizontal bone augmentation was 3.6 mm,\textsuperscript{21} whereas the most horizontal bone augmentation was 5.5 mm.\textsuperscript{22}

Publication Bias
The heterogeneity test showed low values of heterogeneity in each subgroup. Sensitivity analysis showed that heterogeneity did not change obviously regardless of whether any single study was removed. The funnel plots of each subgroup were obviously unsymmetrical, indicating the risk of potential publication bias (Appendix Figs 1 to 6; see Appendix in online version of this article at quintpub.com).

DISCUSSION
Data from the present literature showed that the employment of 3D-customized titanium mesh did not influence the titanium mesh exposure rate. Although the exposure rate (25.2%) of customized titanium mesh was slightly higher than that (19.9%) of conventional titanium mesh, there was no significant difference between the two numbers ($P = .34$). This result differed from that of the study by Sumida et al.\textsuperscript{17} In this study, the researchers directly compared the exposure rate of customized and conventional titanium mesh, showing that the exposure rate of customized titanium mesh (23.1%) was significantly lower than that of conventional titanium mesh (7.7%). It was believed by many dentists that customized titanium mesh could effectively reduce the exposure rate in oral implantation.\textsuperscript{17} However, according to the search results, only one study\textsuperscript{17} demonstrated a direct comparison between the two groups. In addition, the sample size of the study was
small. Therefore, it seemed that there was no adequate evidence that could prove that customized titanium mesh had a significantly lower exposure rate. The thickness and pore size of titanium mesh were not provided in most of the included studies, and these measurements were not considered potential factors that influenced the exposure rate. Thinner titanium mesh resulted in less mucosal irritation, which means that the odds of mesh exposure were small. However, thinner titanium mesh also resulted in a worse ability to maintain the space needed for bone regrowth. Balancing the two sides, Bai et al recommended a thickness of 0.4 mm for clinical use.

The data also showed that the type of bone graft material did not influence the exposure rate (21.7% vs 23.5%, P = .74). This result was similar to the study by Lim et al, which showed that the type of graft material did not affect the incidence of soft tissue complications regardless of whether absorbable or nonabsorbable membranes were used. However, the study by Carini et al showed that 100% autologous bone grafts were related to better bone regrowth and less titanium mesh exposure. In their opinion, combined employment with BBM was a suitable compromise for the insufficiency of autologous bone. When only considering clinical effects, autologous bone grafts were the first choice.

Titanium mesh with a large pore size (≥ 2 mm) could lead to better bone formation but also to ingrowth of a greater volume of soft tissue. Therefore, it was recommended by Her et al to cover a resorbable collagen membrane over the titanium mesh to decrease the passage of gingival fibroblasts. The present study showed that employing absorbable membranes simultaneously did not lead to a lower exposure rate of titanium mesh than employing titanium mesh exclusively (23.9%, 20.2%, P = .36). From the literature screened in the present review, it was found that no human trials have directly compared the exposure rate using titanium mesh with or without absorbable membranes. In animal trials, Lim et al overlaid titanium mesh with collagen membranes in five dogs to compare the effect of mucosal healing and buccal bone preservation by employing titanium mesh exclusively. The conclusion was that the combination of two materials did not have better effects. This inference was consistent with the present findings. However, Li et al found that when employing titanium mesh associated with collagen membranes, bone regeneration was better than when using titanium mesh exclusively. Since the sample size of the study by Li et al was much larger than that of Lim et al, the latter conclusion seemed to be more valuable.

In addition to the three factors that were focused on in this review, there are other potential factors affecting the exposure of titanium mesh. Miyamoto et al compared three different kinds of preoperative bone defects and found that complex bone defects had higher possibilities of surgical complications. Because most of the included articles lacked detailed records of these data, further analyses about the relevance between the exposure rate and the type of bone defects could not be provided in this review. Sagheb et al found that midcrestal incisions had a higher exposure rate than modified poncho incisions, and the exposure rate in the maxilla was significantly higher than that in the mandible. It was also found that sex, smoking, periodontal status, disease, gingival type, augmentation materials, and membrane materials had no significant effect on the exposure rate. Hartmann and Seiler found that advanced platelet-rich fibrin (A-PRF), which is a kind of platelet concentrate (PC), led to significantly less titanium mesh exposure; also, Hartmann and Seiler found that other parameters, such as tobacco abuse, diabetes, or flap design, did not influence the exposure rate. Moreover, the researchers found that sex (female) was significantly associated with a lower exposure rate. In the study by Torres et al, PRP, which is another kind of PC, was also demonstrated to significantly reduce the exposure rate of titanium mesh. It seemed that PCs could obviously reduce the exposure rate. Therefore, after reviewing 22 relevant articles, Stähli et al concluded that PRP might have a positive effect on wound healing and bone regeneration in compromised patients. Therefore, in this article, it was impossible to control all these variables, and these variables were the sources of heterogeneity.

Clinical Implications

The exposure of mesh was a common complication when employing titanium mesh in the GBR procedure. Many studies have found that exposure has negative effects on bone regeneration. Uehara et al thought that frequent exposure to titanium mesh might be responsible for the lower implant success rate. The study by Hartmann et al showed that exposure to titanium mesh was associated with loss of grafted material. The studies by Her et al and Maio et al also showed that titanium mesh exposure could lead to graft resorption without influencing implant placement. Moreover, Garcia et al reviewed current articles about the effect of membrane exposure on GBR. The researchers found that the sites without membrane exposure achieved 74% more horizontal bone gain than the sites with exposure, and for peri-implant dehiscence defects, 27% more defect reduction was obtained for the sites without membrane exposure. Therefore, determining the potential factors influencing the exposure rate of titanium mesh is important. Ascertain the influencing factors would contribute to the determination of methods that reduce the exposure rate. The three factors that were focused on in this review were common variables
in clinical practice. Identifying whether the three factors evaluated influence the exposure rate of titanium mesh is clinically significant.

Limitations and Future Directions
Few studies have summarized the exposure rate of titanium mesh so far, and this review took the lead in focusing on this topic. Compared with congeneric studies, which evaluated the overall complication rate of absorbable and nonabsorbable membranes employed in the GBR procedure, the article covered nearly all literature about this topic because there were no excessive restrictions in the search strategy. The two points were the notable strengths of this review. However, there were also several limitations. First, there were only four RCTs included in this article. Most of the included studies were case series. Second, when analyzing the influence of a single factor, although a meta-regression was performed for two confounding factors, other confounding factors, such as the type of bone defect, thickness of titanium mesh, and follow-up period, were not controlled. As a result, the values of heterogeneity of most groups were not reduced to very low levels. Third, meaningful information, such as the exposure area of titanium mesh, quantity of alveolar bone resorption, and type of bone defects, was not recorded in most articles. The lack of these data prevented further analysis. Therefore, to obtain more significant results, more scientifically designed clinical trials are needed. More RCTs are expected to compare potential factors directly. In addition, more meaningful information, such as the missing aforementioned data, is expected to be recorded in detail.

CONCLUSIONS
Based on available literature, it seems that the employment of 3D-customized titanium mesh, the type of bone graft material (AB combined with anorganic BBM vs other graft materials), and the combined employment of absorbable membranes did not statistically significantly influence the exposure rate of titanium mesh in GBR.

ACKNOWLEDGMENTS
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REFERENCES


APPENDIX

Appendix Fig 1  Funnel plot for the subgroup employing conventional titanium meshes.

Appendix Fig 2  Funnel plot for the subgroup employing customized titanium meshes.

Appendix Fig 3  Funnel plot for the subgroup employing AB combined with BBM.

Appendix Fig 4  Funnel plot for the subgroup employing other graft material.

Appendix Fig 5  Funnel plot for the subgroup employing titanium meshes exclusively.

Appendix Fig 6  Funnel plot for the subgroup employing absorbable membranes simultaneously.