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BIOMATERIALS IN GUIDED BONE REGENERATION FOR DENTAL IMPLANTS: A SYSTEMATIC REVIEW OF CLINICAL AND EXPERIMENTAL EVIDENCE

***[1]Gabriel da Silva Costa, [2]Ana Luísa de Castro e Silva, [3]Rafael Arantes Soares Reis, [4]Caroline Weinert Marçal, [5]Dyego Matielo Peres Lemos, [6]Ana Maria Siqueira da Fonseca, [7]Nycolle Ketley Alves Viana, [8]Sabrinna Galletti Neves, [9]Karen Liz Possidonio, [10]Conrado Ribeiro de Oliveira, [11]Jennifer Vera Santos Gumert and [12]Klarice Rafaella Menezes de Oliveira**

[1]Faculdade São Leopoldo Mandic, Rua Sorocaba, 316 – Botafogo, Rio de Janeiro, Brasil; [2]Universidade Salgado de Oliveira, Av. Cora Coralina,Goiânia - Goiás , Brasil; [3]Faculdade de ciências médicas e saúde Suprema - juíz de fora, Minas Gerais, Brasil; [4]Universidade Federal do Espírito Santo, Av. Marechal Campos ,1468Bom Fim -Vitoria, Espírito Santo, Brasil; [5]UFRGS Universidade federal do Rio Grande do Sul, Rua Ramiro Barcelos, 2492 - Porto Alegre, Rio Grande do Sul; [6]Universidade federal do Paraná, Rua XV de Novembro, 1299, Centro, Curitiba – PR, Brasil; [7]Av. Cora Coralina, Goiânia - Goiás Universidade Salgado de Oliveira, Brasil; [8]Faculdade de Imperatriz - Facimp/Wyden, Av. Prudente de Morais, 110 - Jardim Cinco Estrelas - Imperatriz - MA, Brasil; [9]Unimar - Marília São Paulo, Av. Higino Muzi Filho, 1001 - Mirante, Marília - SP, Brasil; [10]Centro Universitario de Lavras – Unilavras, Rua Padre José Poggel, 506 - Padre Dehon, Lavras - MG, Brasil; [11]Universidade Nove de Julho, Rua Vergueiro, 831 - Aclimação, São Paulo - SP, Brasil; [12]Universidade Nilton Lins , Manaus Amazonas Parque das Laranjeiras, Av. Prof. Nilton Lins, 3259 - Flores, Manaus - AM, Brasil

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****Corresponding author:***
Gabriel da Silva Costa

ABSTRACT

Background: Guided bone regeneration (GBR) is a well-established surgical technique in implant dentistry, aiming to promote new bone formation in deficient alveolar ridges. The method relies on barrier membranes and bone graft materials to exclude soft tissue invasion and enhance osteogenesis. ***Objective:*** This systematic review aimed to evaluate the effectiveness of different biomaterials used in GBR associated with dental implant placement, highlighting clinical outcomes and complications. ***Methods:*** A comprehensive literature search was conducted in PubMed, Scopus, Web of Science, and Google Scholar, following PRISMA 2020 guidelines. Studies were selected based on predefined inclusion and exclusion criteria. A total of 26 studies were included, comprising systematic reviews, clinical trials, in vivo animal experiments, and in vitro research. Key variables analyzed included graft type, membrane characteristics, bone gain, and post-operative complications. ***Results:*** Xenografts and allografts, when combined with resorbable collagen membranes, resulted in significant horizontal bone augmentation. Titanium mesh demonstrated superior space maintenance but had higher exposure rates. Bioactive agents such as BMP-2 and magnesium oxide nanoparticles showed promising regenerative effects in early-phase studies. Autogenous bone remained effective but was limited by donor site morbidity. Outcomes were influenced by defect morphology, implant design, and membrane stability. **Conclusion:** GBR remains a predictable approach for alveolar ridge reconstruction in implant dentistry. The choice of biomaterial and membrane should be guided by defect type, patient-specific factors, and clinical expertise. Further high-quality randomized studies are needed to confirm the efficacy of novel biomaterials and refine surgical protocols

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INTRODUCTION

The growing demand for functional and aesthetic dental implant rehabilitation has driven the advancement of guided bone regeneration (GBR) techniques, which aim to reconstruct alveolar defects by using barrier membranes and bone graft materials. GBR has become a predictable approach for horizontal and vertical bone augmentation, particularly in the context of implant placement (Wessing *et al*., 2018; Calciolari *et al*., 2023).

Various biomaterials have been investigated to support bone regeneration, including autogenous bone, allografts, xenografts, and synthetic grafts, often in combination with resorbable or non-resorbable membranes (Mateo-Sidrón Antón *et al*., 2024; Di Stefano *et al*., 2015). The use of titanium mesh has gained attention due to its ability to maintain space and stabilize the graft, although it carries a risk of exposure (Proussaefs *et al*., 2003; Herford *et al*., 2019). Recent advances have also incorporated bioactive elements such as recombinant human bone morphogenetic protein-2 (BMP-2) and magnesium oxide nanoparticles, which have demonstrated enhanced osteoinductive potential in preclinical and early clinical studies (Malaiappan & Harris, 2024; Wu *et al*., 2021). While the effectiveness of GBR is well documented, clinical outcomes are influenced by multiple factors, including defect morphology, biomaterial selection, implant timing, and the presence of membrane exposure (Garcia *et al*., 2018; Quah *et al*., 2024). Additionally, variations in surgical technique and patient-related factors, such as smoking or systemic conditions, may contribute to treatment success or failure (Phillips *et al*., 2019; Monje *et al*., 2023). Given the continuous emergence of new biomaterials and the diversity of clinical protocols, a systematic evaluation of the literature is essential. The present review aims to assess the effectiveness and safety of different biomaterials and membrane types used in guided bone regeneration procedures associated with dental implant therapy, synthesizing evidence from clinical, preclinical, and in vitro studies.

MATERIALS AND METHODS

Protocol and registration: This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA 2020) guidelines. The protocol was not registered in PROSPERO due to the descriptive and narrative nature of part of the included evidence.

Eligibility criteria: Studies were eligible if they met the following criteria:

- Human, animal, or in vitro studies evaluating guided bone regeneration in the context of dental implant therapy
- Studies that investigated bone graft biomaterials (autogenous, xenograft, allograft, synthetic) and/or membranes (resorbable, non-resorbable, titanium mesh)
- Systematic reviews, clinical trials, case series, and experimental studies
- Articles published in English, Portuguese or Spanish from 2000 to 2024

Exclusion criteria

- Narrative reviews without methodological rigor
- Letters, editorials, and expert opinions
- Studies focusing solely on soft tissue grafts without bone augmentation

Information sources and search strategy: A comprehensive electronic search was performed in the following databases: PubMed/MEDLINE, Scopus, Web of Science, and Google Scholar, using a combination of MeSH terms and free-text keywords. The last search was conducted in May 2024.

Keywords included:

- “Guided Bone Regeneration”, “Bone Graft”, “Dental Implants”, “Titanium Mesh”, “Barrier Membranes”, “Osteoconduction”, “Bone Substitutes”, “Collagen Membrane”, “Alveolar Ridge Augmentation”

Study selection and data collection process: Two reviewers independently screened titles and abstracts to identify studies meeting the inclusion criteria. Full-text articles were assessed for eligibility. Disagreements were resolved through discussion. Data were extracted into a standardized table including: author/year, study type, biomaterials used, membrane type, site of intervention, follow-up, outcomes, and complications.

Risk of bias: Due to the heterogeneity of included studies (systematic reviews, clinical trials, in vivo/in vitro models), no universal risk of bias tool was applied. However, methodological quality was assessed based on clarity of objectives, reproducibility of methods, and outcome reporting.

Study selection: A total of 523 records were initially identified through electronic database searches, including PubMed, Scopus, Web of Science, and Google Scholar. After the removal of 102 duplicate entries, 421 studies remained for title and abstract screening. Following this step, 115 articles were selected for full-text review based on relevance to guided bone regeneration and the use of biomaterials in implant dentistry. After applying the predefined inclusion and exclusion criteria, 38 articles were excluded due to insufficient methodological quality, lack of focus on bone grafting techniques, or absence of outcome data. As a result, a total of 26 studies were included in this systematic review for qualitative analysis. A total of 26 studies were included in this systematic review, encompassing a combination of systematic reviews, clinical trials, case series, and preclinical in vivo and in vitro studies. These studies explored the application of various biomaterials and membrane configurations for guided bone regeneration (GBR) associated with dental implant placement. The key findings were organized into thematic categories based on the biomaterial used and their reported clinical or experimental outcomes.

RESULTS

Xenografts and allografts in lateral ridge augmentation: Several studies evaluated the efficacy of xenogeneic and allogeneic bone grafts in lateral bone augmentation procedures. Wessing *et al*. (2018) and Calciolari *et al*. (2023) demonstrated that xenografts, particularly bovine-derived materials, provided consistent horizontal bone gain, especially when combined with resorbable collagen membranes. The network meta-analysis by Calciolari *et al*. reported mean horizontal gains exceeding 3.5 mm, with favorable long-term implant survival rates. However, membrane exposure remained a recurrent complication, particularly with non-crosslinked collagen membranes.

Titanium mesh and space-maintaining devices: The use of titanium mesh in combination with particulate grafts or recombinant growth factors was explored in both clinical and experimental settings (Mateo-Sidrón Antón *et al*., 2024; Di Stefano *et al*., 2015; Herford *et al*., 2019). These studies confirmed the effectiveness of titanium mesh in achieving superior volumetric stability in horizontal and vertical ridge augmentation. Nonetheless, soft tissue dehiscence and mesh exposure were frequently reported in 10–30% of cases, though they did not necessarily compromise the graft integration (Proussaefs *et al*., 2003; Eisig *et al*., 2003).

Growth factors and nanomaterials: Innovative regenerative strategies incorporating biologically active agents such as BMP-2 and magnesium oxide nanoparticles have been evaluated in early-phase studies. Herford *et al*. (2019) reported enhanced bone formation when BMP-2 was applied under titanium mesh. Similarly, Malaiappan & Harris (2024) showed that magnesium oxide nanoparticles significantly improved osteogenic markers in animal and cell studies, highlighting their potential as future adjuncts in GBR protocols.

Autogenous grafts and combined approaches: Autogenous bone remains the gold standard for regenerative procedures due to its osteogenic properties. Starch-Jensen & Becktor (2019) and Proussaefs *et al*. (2003) reported favorable outcomes when autografts were used in combination with titanium mesh or xenografts, resulting in substantial ridge volume increase and good implant stability. However, morbidity related to the donor site and limited graft volume are inherent limitations of this approach.

Influence of implant design and peri-implant bone behavior: Quah *et al*. (2024) demonstrated that implant macrodesign, particularly the presence of machined collars, was associated with greater vertical bone gain when GBR was performed simultaneously. Moreover, studies evaluating buccal bone thickness (Phillips *et al*., 2019) and defect morphology (Monje *et al*., 2023) emphasized the importance of ridge anatomy in predicting regenerative success and minimizing marginal bone loss.

Periodontal regeneration and GBR overlap: Sculean *et al*. (2015) provided evidence that many GBR principles apply to periodontal regeneration as well, particularly in the management of intrabony defects. The use of enamel matrix derivatives (EMD), platelet concentrates (PRF), and graft combinations yielded significant improvements in probing depth and clinical attachment.

DISCUSSION

This systematic review explored the current scientific literature on the use of biomaterials in guided bone regeneration (GBR) associated with dental implant therapy. The findings confirm that GBR remains a predictable and effective technique for horizontal and vertical ridge augmentation, especially when appropriate graft materials and space-maintaining devices are selected based on defect morphology and clinical conditions. The majority of included studies highlighted the clinical reliability of xenografts and allografts as bone substitutes. Their osteoconductive nature and structural stability offer a favorable environment for bone neoformation, particularly when combined with resorbable collagen membranes (Wessing *et al*., 2018; Calciolari *et al*., 2023). Nonetheless, a recurring limitation across studies was membrane exposure, which has been shown to reduce regenerative outcomes and increase the risk of graft contamination (Garcia *et al*., 2018). This reinforces the importance of proper flap design and tension-free primary closure in GBR procedures. The use of titanium mesh demonstrated clear advantages in space maintenance, especially in complex three-dimensional defects. Studies such as those by Di Stefano *et al*. (2015), Herford *et al*. (2019), and Mateo-Sidrón Antón *et al*. (2024) confirmed that titanium mesh provides structural integrity and resists soft tissue collapse. However, its non-resorbable nature predisposes it to higher exposure rates. Interestingly, mesh exposure did not necessarily compromise bone regeneration if early infection was prevented, suggesting that careful clinical monitoring and patient compliance are crucial (Proussaefs *et al*., 2003).

The incorporation of bioactive molecules and nanomaterials into GBR protocols represents a promising frontier in regenerative dentistry. The application of BMP-2 (Herford *et al*., 2019) and magnesium oxide nanoparticles (Malaiappan & Harris, 2024) revealed enhanced osteoinductive activity and accelerated healing in preclinical settings. These materials could potentially reduce healing times and increase the predictability of complex reconstructions, although long-term human data are still limited. Furthermore, anatomical and prosthetic considerations must not be overlooked. Studies by Quah *et al*. (2024) and Phillips *et al*. (2019) emphasized the relevance of implant macrodesign and buccal bone thickness in preserving peri-implant tissues and supporting regenerative outcomes. These findings suggest that a personalized approach—based on defect type, available bone volume, and implant characteristics—is essential for optimal GBR success. An important strength of this review is its inclusion of diverse study designs, which allowed for a comprehensive synthesis of the clinical, surgical, and material science aspects of GBR. However, this heterogeneity also poses limitations. Differences in follow-up duration, patient selection, graft handling protocols, and outcome measures complicate direct comparison and meta-analysis. Moreover, a large portion of the evidence stems from non-randomized trials or experimental models, which may limit the generalizability of results to routine clinical practice.

CONCLUSION

Guided bone regeneration remains a reliable technique for alveolar reconstruction in implant dentistry. The choice of biomaterials—whether xenografts, autografts, synthetic grafts, or titanium meshes—directly influences regenerative outcomes. Emerging bioactive materials show promising potential, but further high-qualityclinicaltrials are needed to validate their routine use.

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