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Main clinical outcomes of biomaterials in dental implants: a systematic review

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Abstract

Introduction: Over the past 30 years, the number of dental implant procedures has grown significantly worldwide, reaching approximately 1 million per year. In Brazil, implantology has evolved very rapidly in recent decades, with high success rates. Various materials can be used as bone grafts, each with different properties, such as those related to neovascularization. Guided bone regeneration promotes the formation of new bone tissue. When grafting procedures are necessary, the focus is often on the type of biomaterial to be used and the success and predictability of the results. **Objective:** This study aimed to conduct a concise systematic review of bone regeneration processes using biomaterials and the main molecular and cellular constituents for implantology. **Methods:** The research was conducted from January to February 2026 in the Scopus, PubMed, Science Direct, and SciELO databases, using older scientific articles considered gold standard references up to 2026. The quality of the studies was based on the GRADE instrument, and the risk of bias was assessed using the Cochrane instrument. **Results and Conclusion:** 158 studies were found and submitted to eligibility analysis. The final sample presented 22 eligible studies, which were described in the systematic review. Most studies showed homogeneity in their results, with X^2 = 68.8% > 50%. Due to bone regeneration and biological barriers in graft surgeries, there has been technological growth in these materials, as they are seen as potential tools for treating bone loss. The greater potential of guided bone regeneration was associated with graft material due to the higher degree of vital bone and the lower percentage of residual graft particles. All bone substitute materials studied resulted in efficient bone formation for dental implants and alveolar ridge preservation procedures.

Keywords: Bone regeneration. Biomaterials. Biological membranes. Dental implants.

Introduction

Over the past 30 years, the number of dental implant procedures has shown significant growth worldwide, reaching approximately one million dental implants per year [1,2]. In Brazil, in recent decades, there has been a very rapid evolution in implantology with high success rates [3]. The development of biomaterials for use in dental clinics in recent years has represented a powerful therapeutic tool in the correction of bone defects [3]. However, despite the proven benefits, their use requires careful clinical and ethical considerations from the professional, especially in the analysis of the risks and benefits that each biomaterial may present [4].

In this sense, various materials can be used as bone grafts, each with different properties, for example, regarding neovascularization, materials such as hydroxyapatite and calcium phosphate showed the highest rates of expression of vascular endocrine growth factors (VEGF) and microvascular density; while polymer grafts showed the lowest rates [5-8]. In the search for a solution for large bone defects, studies based on guided tissue regeneration therapy or guided bone regeneration have begun. These studies promote the use of filling materials and epithelial barriers that assist in treatment as an accessory to bone grafting techniques. Thus, they favor greater predictability in

alveolar and peri-implant reconstructions and present a good prognosis [4].

In this aspect, the main problem lies with non-absorbable membranes, as they require a second surgical procedure, promote infections if there is any type of exposure, have a firm consistency, which makes it difficult to adapt to the bone defect, and thus impair blood irrigation, which can cause dehiscence and tissue necrosis [5-7]. The membranes can be non-absorbable, such as expanded polytetrafluoroethylene (ePTF), non-expanded polytetrafluoroethylene (PTF), calcium phosphate, titanium mesh or sheet; or absorbable materials, such as collagen, polylactic acid and polyglactin, fibrin and elastin monomers, and Vicryl membrane [6].

Furthermore, guided bone regeneration (GBR) promotes the formation of new bone tissue and prevents gingival tissue from invading into the space between the bone and the implant [5,6]. Covaniet al [9], in a 10-year prospective study comparing patients who received the GBR technique with patients who did not, indicated the possibility of gingival recession in the group that did not receive the technique when compared to the group that did [4]. In this context, filling materials can be hydroxyapatite, lyophilized and ground demineralized medullary bone, or autogenous bone, which is considered the gold standard, among others. Along with filling materials, it is often necessary to use resources to isolate the implant by using biological membranes, which are epithelial barriers that guide tissue regeneration, function as a mechanical barrier separating periodontal tissues from the bone surface or implant, thus promoting bone neoformation, containment of the filling material, and graft stability [6,8].

In this context, when a tooth is lost in the posterior region of the maxilla, natural resorption of the alveolar process occurs, and at the same time, pneumatization of the maxillary sinus will occur. It will increase its volume towards the site where the roots were located, and this will often make it difficult or impossible to restore implants in that location. For this reason, the maxillary sinus floor elevation procedure should be performed, or short implants when possible [5].

In this sense, when grafting procedures are necessary, the focus is often on the type of biomaterial to be used, and the success and predictability of the results do not depend solely on the biomaterial. It is also necessary to consider the type of defect to be treated and its morphology. Morphology will have an impact mainly because defects have different vascularization capacity, different capacity for recruitment of osteogenic cells, and different capacity for natural graft stabilization; therefore, the characteristics of the biomaterials that we should use, but also the characteristics of the bone bed and defect for treatment must be considered [6,7].

As a corollary to this, several surgical techniques can be used to reconstruct the atrophic alveolar ridge, isolated techniques or associated with autogenous, allogeneic, xenogeneic, and alloplastic biomaterials. Autogenous bone graft is the only one capable of presenting three important biological properties (osteogenesis, osteoinduction, and osteoconduction), guaranteeing a self-regenerative potential. As a disadvantage of autogenous bone graft, the need for a second surgical access in the donor area stands out, resulting in longer surgical time, morbidity, and consequently greater patient resistance to the proposed treatment [8].

Allogeneic, xenogeneic, and alloplastic bone grafts are an alternative for the treatment of bone deficiencies of the jaws, as they avoid the need for a second surgical approach. But due to the need for processing to eliminate antigenic components, these grafts are exclusively osteoconductive with less bone formation potential compared to autogenous bone grafts. To increase the bone formation potential of these grafts, combinations have been proposed to obtain better regenerative conditions through volume preservation (osteoconduction) and induction of cell migration and differentiation (osteoinduction) [8-10].

The most widely used xenograft in guided bone regeneration procedures is deproteinized bovine bone mineral, commercially known as Bio-Oss®, which is the most researched product in regenerative dentistry worldwide. It is a bone of bovine origin processed to produce natural bone mineral without organic elements [11]. After thermal and chemical treatments, the inorganic phase of bovine bone consists mainly of hydroxyapatite (HA), which maintains the porous architecture. The excellent osteoconductive properties of Bio-Oss® lead to predictable and efficient bone regeneration; Bio-Oss® particles become an integral part of the newly formed bone structure and retain their volume in the long term [11,12].

Due to its 'great' similarity to human bone, 'Bio-Oss®' is 'incorporated' into the 'natural' process of 'shaping' and 'remodeling'. The highly porous structure of Bio-Oss® provides ample space for the formation of blood vessels (angiogenesis) and the deposition of newly formed bone (osteogenesis) [11]. The 'microstructure' of the 'surface' of Bio-Oss® supports the 'excellent growth' of osteoblasts, which are 'responsible' for the formation of 'bone'. In this way, 'Bio-Oss®' particles become an integral part of the structure of the new bone being formed, and the 'low rate' of conversion into suitable (remodeled) bone of

Bio-Oss® stabilizes the structure and allows the graft volume to be maintained in the long term. These biofunctional processes make Bio-Oss® unique [12,13].

In addition, platelet concentrates have been proposed as regenerative materials in tissue regeneration procedures. Among the platelet concentrates proposed in the literature, PRP (platelet-rich plasma) and FRP (fibrin-rich plasma) stand out, acting as autogenous platelet aggregates with osteoinductive properties. Due to their low morbidity and potential regenerative effects, these biomaterials have been indicated for use in combination with other biomaterials or even alone. FRP is a second-generation concentrate, meaning no anticoagulant is used in its production. After collection, the patient's blood is subjected to a specific centrifugation force, separating the formed elements according to their density. The red blood cells are then discarded, and the resulting platelet concentrate is used for regenerative purposes. Leukocytes and platelets synthesize and release a variety of cytokines and growth factors that act in chemotaxis, angiogenesis, cell differentiation, and inhibition [7-9].

Therefore, the present study carried out a concise systematic review of bone regeneration processes using biomaterials and the main molecular and cellular constituents for implant dentistry.

METHODS

Study Design

This study followed an international model for systematic review and meta-analysis, following the PRISMA (preferred reporting items for systematic reviews and meta-analysis) guidelines [27].

Instruments and Professionals for Study Eligibility

Studies were selected that rigorously presented the results of the search process in Table 1 and that demonstrated scientific quality according to the GRADE classification, and that did not present a significant risk of bias, i.e., that could compromise the safety of the results, according to the Cochrane instrument.

Study Quality, Eligibility Criteria, and Risk of Bias

According to GRADE recommendations [28], the quality of scientific evidence in the studies addressed was classified as high, moderate, low, or very low, according to the risk of evidence bias, sample size, clarity of comparisons, precision, and consistency in the effects of the analyses. High quality of evidence was attributed through four criteria: 1) Randomized or prospective controlled clinical trials; 2) Retrospective clinical trials or case series; 3) Sample size greater than 15 participants; 4) Studies with statistically well-developed results; 5) Studies published in indexed journals with a significant impact factor; 6) Descriptive validity (identification of studies showing the surgical technique), interpretative validity (identification of the advantages and disadvantages of biomaterials), theoretical validity (credibility of the methods), and pragmatic validity (application of the use of each type of biomaterial). Articles that did not report the technique employed were excluded.

Data Sources, Search Strategy, and Study Time

The search strategies for this study were based on the descriptors (DeCS / MeSH Terms): Bone regeneration. Biomaterials. Biological membranes. Dental implants. Search filters designated as clinical studies were used. The research was conducted from January to February 2026 in the Scopus, PubMed, OVID, Science Direct, LILACS, and EBSCO databases, using gold-standard reference scientific articles up to 2026. In addition, a combination of keywords with the Boolean operators "OR", AND, and "NOT" were used to target scientific articles of interest. Titles and abstracts were examined under all conditions. Table 1 presents an example of the search structure in PubMed. The same search strategy was used in the other databases.

Table 1. Example of the search structure in PubMed; the same search strategy was used in the other databases.

PubMed	*Bone regeneration* ***OR*** *Biomaterials*
	AND
PubMed	*Biological membranes* ***OR*** *Dental implants*
	AND
PubMed	*Prospective Clinical studies* ***OR*** *Retrospective Clinical studies* ***OR*** *Randomized clinical trials* ***OR*** *Clinical case series*
	NOT
PubMed	*Review studies* ***OR*** *Editorials* ***OR*** *Short communications* ***OR*** *Case Report*

Source: Own authorship.

Summary of Literary Findings

158 articles were found. Initially, duplicate articles were excluded. After this process, the abstracts were evaluated and a further exclusion was carried out, removing articles that did not include the theme of this article, resulting in 84 articles. A total of 22 articles were evaluated in full and included in this study (Figure 1). Considering the Cochrane tool for risk of bias, the overall evaluation resulted in 13 studies with a high risk of bias and 25 studies that did not meet the GRADE criteria. According to the GRADE instrument, the 22 studies that comprised the systematic review showed homogeneity in their results, with X^2 = 68.8% >50%.

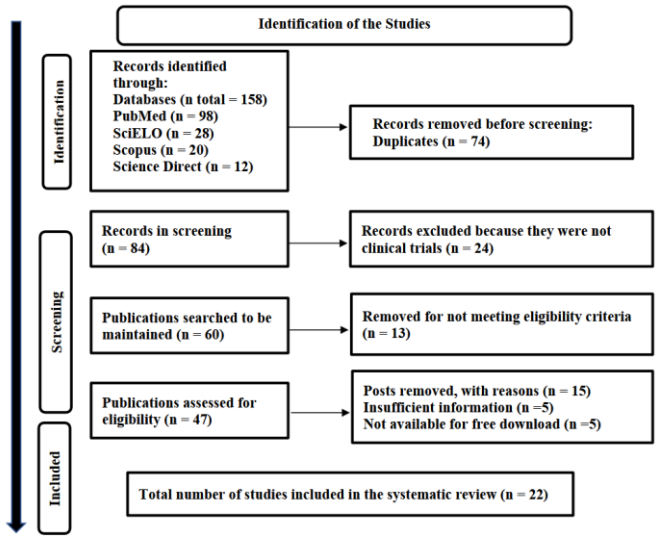

Figure 1. Flowchart showing the article selection process. Source: Own authorship.

Main Clinical Findings

The authors Zampara et al. 2022 [14] clinically evaluated the guided bone regeneration (GBR) potential of allograft, xenograft, and alloplastic materials in combination with resorbable membranes in extraction sockets. Qualitative and quantitative assessments of this prospective study were performed using histological and histomorphometric analyses. Three experimental groups and one control group for comparison (n = 8) received an allograft (lyophilized human cancellous bone, Deutsches Institut für Zell und Gewebeersatz, Berlin, Germany), xenograft (BioOss, Geistlich Pharma AG, Wolhusen, Switzerland), or alloplast (biphasic calcium sulfate, Bondbone, MIS Implants Technologies Ltd., Charlotte, NC). The negative control group did not receive regenerative material. Tissue samples were then evaluated qualitatively and quantitatively based on the percentage of new vital bone, graft particle content, soft tissue, and bone marrow over time. All 3 study groups presented adequate bone volume for the successful placement of a dental implant. The xenograft group yielded significantly less vital bone compared to the allograft and alloplast groups. When comparing the percentage of residual graft particles, significantly higher amounts were associated with the xenograft group in contrast to the allograft and alloplast groups. Similarly, a significantly increased percentage of soft tissue was observed in the xenograft group compared to all other groups. No significant differences were observed in the percentage of residual graft particles between the allograft and alloplast groups. No significant differences were detected in the percentage of vital bone between the allograft, alloplast, and control groups. When evaluating the percentage of bone marrow, the only significant difference detected was between the xenograft and alloplast materials. Overall, no complications (i.e., fever, malaise, purulence, or fistula) were observed throughout the clinical trial among all patients. The greatest GBR potential was associated with the graft material due to the higher degree of vital bone and the lower percentage of residual graft particles. All bone substitute materials studied resulted in bone apposition for efficient use in alveolar ridge preservation procedures.

Furthermore, a randomized clinical trial conducted by the authors Galindo-Moreno et al. 2022 [15] compared the efficacy of two xenografts for maxillary sinus floor augmentation in terms of clinical, radiographic, histological, and molecular outcomes. A total of 10 consecutive patients requiring bilateral maxillary sinus floor augmentation in two stages were included. Each patient received both biomaterials (porcine bone mineral and inorganic bovine bone), which were randomly assigned to bilateral sinus augmentation. Autogenous maxillary bone scraped from the sinus access window was mixed with each xenograft in a 20:80 ratio. After a 6-month healing period, bone biopsies were collected with a trephine during implant placement in the regenerated area. The resulting anatomical characteristics were similar between the two groups. After six months of graft consolidation, graft resorption rates were similar between the two biomaterials. Histological, histomorphometric, and immunohistochemical results showed no statistically significant differences between the groups. Therefore, inorganic bovine bone and porcine bone mineral combined with autogenous maxillary cortical bone showed similar biological and radiological characteristics in terms of biomaterial resorption, osteoconduction, and osteogenesis when used for maxillary sinus floor augmentation.

In addition, the authors Meschi et al. 2021 [16], through a multicenter controlled clinical trial, evaluated the impact of platelet-rich fibrin and leukocytes (PRFL) in regenerative endodontic procedures (REPs) of immature permanent teeth in terms of periapical bone repair (PBR) and subsequent development (RD). Healthy patients aged 6-25 years with an inflamed or necrotic immature permanent tooth were included and divided into the test group (= REP + PRFL) and control group (= REP-PRFL). After receiving REP ± PRFL, patients were recalled after 3, 6, 12, 24, and 36 months. At each recall session, the teeth were evaluated clinically and radiographically (by means of a periapical radiograph [PR]). A cone beam computed tomography (CBCT) was performed preoperatively and 2 and 3 years after surgery. Pulp hemorrhage (PH) and root canal reduction (RD) were evaluated quantitatively and qualitatively. Twenty-nine teeth with necrotic pulp were included, of which 23 (9 tests and 14 controls)

were analyzed. Three teeth in the test group showed a reaction in the first year after pulp resection (PR). With the exception of 2, all teeth analyzed survived up to 3 years after PR, and in cases of failure, apexification preserved them. Complete PH was achieved in 91.3% and 87% of cases based on the qualitative and quantitative evaluation of pulp resection, respectively, with no significant difference between the groups in relation to baseline. The quantitative change in pulp resection in root canal reduction (RD) at the last recall session in relation to baseline was not significant (all p-values > 0.05) in either group. The qualitative evaluation of the type of healing from PH was not uniform. In the test group, 55.6% of the teeth did not present RD or apical closure. Only 50% of the 14 teeth evaluated with CBCT presented complete PH. Regarding volumetric measurements in root resorption (RD) 3 years after permanent root resorption (REP) for change from baseline in root hard tissue volume, mean root hard tissue thickness, and apical area, the control group performed significantly better in favor of RD than the test group (p= 0.03, 0.003, and 0.05, respectively). For volumetric change 3 years after REP from baseline in root length and maximum root hard tissue thickness, no significant difference (p=0.72 and 0.4, respectively) was found between the groups. The correlation between the PR and CBCT variables evaluating RD was weak (root elongation) to very weak (root thickening). Therefore, REP-PRFL appears to be a viable treatment option to achieve PBR and assist in the RD of necrotic immature permanent teeth.

Bone Regenerative Dentistry

The microscopic bone structure consists of osteoprogenitor cells, supporting cells (osteoblasts and osteocytes), remodeling cells – osteoclasts – and a non-mineralized extracellular matrix called osteoid, composed of type I collagen and non-collagenous proteins such as osteonectin, osteocalcin, bone morphogenetic protein (BMP), glycosaminoglycans (GAGs), and bone sialoproteins [14,15,17]. Osteoprogenitor cells are small, spindle-shaped cells found on all non-resorbable bone surfaces, derived from primitive mesenchymal cells, and form a population of precursor cells that can differentiate into more specialized cells such as osteoblasts and osteocytes [18].

The regeneration of composite tissues such as periodontal tissue has also been demonstrated, proving that adipose mesenchymal stem cells associated with platelet-rich plasma can regenerate alveolar bone, cementum, and periodontal ligament eight weeks after implantation [19,20,21]. Clinically, there is a combined study of bone grafting with fibrin glue, a biodegradable biomaterial, and adipose mesenchymal stem cells for the reconstruction of a large bone defect in the skull of a seven-year-old child who was a victim of trauma [19].

Osteoblasts are derived from undifferentiated mesenchymal stem cells and are responsible for the production of the bone matrix, which is rich in collagen (mainly type I) and essential for subsequent mineralization, through the adhesion of calcium hydroxyapatite crystals, magnesium, potassium, sodium, and carbonate ions to collagen fibrils [22]. Osteoblasts are also rich in alkaline phosphatase, which has a high value during periods of bone formation. The process of new bone formation mediated by osteoblasts is called osteogenesis [21]. It is known that osteoblasts bind directly to collagen through integrin-RDG (Arginine-Glycine-Aspartate) interaction sites.

The osteoinduction process is influenced by several factors and consists of the induction of mesenchymal stem cells from adipose tissue into osteoprogenitor cells [18,23]. Osteogenic differentiation requires the presence of inducers, which include β-glycerophosphate, ascorbic acid, and dexamethasone. In the presence of these substances, mesenchymal cells acquire the morphology and membrane components of osteoblasts and begin to express alkaline phosphatase, depositing extracellular matrix rich in calcium and certain proteins, such as osteopontin and osteocalcin [23].

Organic phosphates, such as β-glycerophosphate, promote osteogenesis through their function in mineralization and modulation of osteoblast activity [18]. Thus, free phosphates can induce mRNA and protein expression, exemplified by the osteopontin protein. If organic phosphate, for example β-glycerophosphate, is present, the formation of a mineral content, hydroxyapatite, occurs, which is formed between the collagen fibers. Other compounds, such as phosphated ascorbic acid, are also used in osteogenic induction, involving the increase in alkaline phosphatase activity and promoting the production of osteocalcin and osteopontin [23-25].

BMP function as growth factors with a specific role in the proliferation and differentiation of adipose tissue mesenchymal stem cells [26,27]. BMP-4 is involved in the early stages of osteogenesis, and it has been shown that the differentiation of human mesenchymal stem cells into the osteogenic lineage requires the presence of BMP-4 in the first days of culture and that these cells, after 21 days, express specific proteins of the osteogenic lineage such as osteonectin, osteocalcin, and osteopontin. There are three fundamental parameters in bone tissue engineering that will determine the capacity for osteoinduction: the presence of soluble osteoinductive signals, the viability of

undifferentiated mesenchymal stem cells to respond, the ability to differentiate into bone-forming cells, and the production of adequate extracellular matrix [27].

Tissue engineering offers numerous advantages that meet the needs of the injured tissue or organ for the regeneration process [26,28]. For this, it is necessary to understand chemical, physical, and biological processes, both biological material and the host's biological niche [29]. The cross-referencing of compatible information between microenvironments enables cell recognition and signaling cascades for neovascularization [30]. Another advantage is minimally invasive surgical intervention, that is, it allows the use of faster surgical techniques that cause less risk to the patient [31].

Thus, tissue engineering is a tool that enables, through an appropriate biological niche, the construction and regeneration of any tissues and organs [24,32]. For this purpose, xenografts, autografts, and allografts are used, with and without the use of cells [29,30]. According to the National Institute for Health Consensus Development Conference in 1982, biomaterials are beneficial organic compounds, or combinations thereof, that can be used for a period of time, completely or partially, as part of a system that treats, augments, or replaces any tissue, organ, or function of the human body [24,32,33]. The great challenge is understanding that the science of biomaterials is multidisciplinary and its application requires adjustments to its processing, sterilization, and structural modifications to favor interaction with the tissue of interest.

Bioengineering and cell therapy work together for Regenerative Medicine, favoring and improving biological conditions to accelerate tissue repair and regeneration, thus naturally maintaining tissue homeostasis [34]. This condition is maintained because the required cellular elements, proliferation and cell differentiation factors, and supramolecular structures that guarantee the functional stereochemical organization of the generated tissues and their systemic integration are provided [24,33].

Guided bone regeneration is the technique that uses osteopromotion as a biological principle. It is indicated for bone regeneration in fresh sockets, bone defects with remaining bone walls, to promote bone neoformation around implants installed immediately after tooth extraction, and to correct bone loss (peri-implant) that occurred after osseointegration [35].

Conclusion

It was concluded that, due to bone regeneration and biological barriers in grafting surgeries, there has been technological growth in these materials, as they are seen as potential tools for treating bone loss. The greatest potential of guided bone regeneration was associated with graft material due to the higher degree of vital bone and the lower percentage of residual graft particles. All bone substitute materials studied resulted in efficient bone formation for dental implants and alveolar ridge preservation procedures.

CRediT

Author contributions: **Conceptualization-** All authors**; Investigation-** All authors; **Methodology-** All authors; **Project administration-** All authors; **Supervision -** Janaina Cardoso Moreira; **Writing - original draft-** All authors; **Writing-review & editing-** All authors.

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Informed Consent

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No additional data are available.

Conflict of Interest

The authors declare no conflict of interest.

Similarity Check

It was applied by Ithenticate@.

Application of Artificial Intelligence (AI)

Not applicable.

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It was performed.

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