

Review Article

Prognosis of Collagen Membrane with Xenograft versus Emdogain in the Treatment of Endo-Periodontal Lesions: A Systematic Review

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Abstract

Introduction: Endo-periodontal defects represent a clinical challenge due to the complex interaction between periodontal and endodontic diseases. Their treatment requires a multidisciplinary approach to achieve regeneration of the affected tissues and preservation of the tooth. Among the most commonly used therapeutic options are collagen membranes combined with xenografts and the application of enamel matrix derivative proteins, such as Emdogain®. These strategies aim to improve prognosis and periodontal regeneration; however, differences exist in their mechanisms of action, clinical efficacy and long-term outcomes.

Objective: To compare the clinical and regenerative prognosis of collagen membrane with xenograft versus Emdogain® in the treatment of endo-periodontal defects, based on a literature review.

Materials and Methods: A systematic search was conducted in three electronic databases: PubMed, ScienceDirect and Wiley Online Library. Articles published between January 1, 2019 and December 31, 2024, were included. Clinical studies evaluating the clinical and radiographic outcomes of both therapeutic strategies were selected, excluding systematic reviews.

Results: A total of 505 articles were identified across the selected databases (PubMed = 20, Wiley Online Library = 350, ScienceDirect = 135). After applying the inclusion and exclusion criteria, 36 articles were included for review.

Conclusion: Both the use of collagen membranes with xenografts and the application of Emdogain® have proven effective in the regeneration of endo-periodontal defects. However, the choice of treatment may depend on factors such as the extent of the defect, the patient's

tissue response and economic feasibility. Further clinical evidence is needed to determine which of these strategies offers better long-term outcomes.

Keywords: Endo-Periodontal Lesion; Guided Tissue Regeneration; Xenograft; Membrane; Emdogain

Introduction

Endo-periodontal defects are complex conditions that affect both the pulpal system and the surrounding periodontal tissue. They represent one of the most significant challenges in dental practice, as they often compromise the stability and functionality of the affected teeth. These defects can arise from various causes, including bacterial infections, dental trauma and advanced periodontal disease. The complexity of these lesions lies in the close anatomical and functional relationship between the dental

pulp and the periodontal tissues, which can complicate accurate diagnosis and appropriate treatment [1-4]. The treatment of endo-periodontal defects requires a multidisciplinary approach that addresses both the elimination of infection and the regeneration of lost periodontal tissues [1-6]. Guided Tissue Regeneration (GTR) has been widely used in clinical practice to promote the regeneration of lost periodontal tissues. This technique involves the use of barrier membranes that prevent the migration of epithelial cells into the defect site, allowing repopulation by specialized periodontal cells. In recent years, various approaches have been proposed to enhance endo-periodontal regeneration, including the use of collagen membranes combined with xenografts, as well as biomaterials such as Emdogain®, an enamel matrix derivative protein that has demonstrated regenerative properties. Among the materials used in GTR, collagen membranes have shown favorable properties due to their biocompatibility and ability to integrate with surrounding tissues. In addition, bone xenografts, derived from animal sources, are used to fill bone defects and provide a scaffold that facilitates new bone formation. Studies have shown that the use of xenografts in combination with collagen membranes significantly improves periodontal outcomes compared to spontaneous healing, without increasing postoperative complications [6-10]. Emdogain®, composed of enamel matrix derivative proteins, has been recognized for its ability to induce regeneration of the periodontal attachment apparatus. Studies have demonstrated that the application of Emdogain® in intrabony defects promotes the formation of new cementum, periodontal ligament and alveolar bone, thereby improving clinical periodontal parameters. The combination of collagen membranes with xenografts and Emdogain® aims to enhance regenerative outcomes by creating a favorable environment for periodontal tissue repair. This combined approach has shown promising results in the regeneration of advanced periodontal defects [11-15]. Despite the widespread use of these therapies, there is a growing need to compare their effectiveness in the treatment of endo-periodontal defects, specifically to determine which approach offers the best clinical and predictable outcomes. This analysis will provide a solid foundation to guide therapeutic decisions in the treatment of endo-periodontal defects, facilitating better treatment choices and contributing to the advancement of regenerative dentistry [7,8]. The aim of this study is to compare the use of collagen membrane + xenograft with the use of Emdogain®, evaluating their effectiveness in the regeneration of endo-periodontal defects, both in terms of tissue repair and the long-term stability of the obtained outcomes.

Materials and Methods

The first step in the systematic process of this review was to use the PICO methodology to formulate a clinical or research question.

PICO Strategy

- Population (P): Patients with endo-periodontal lesions
- Intervention (I): Guided tissue regeneration
- Comparison (C): Use of membrane and bone vs Emdogain®
- Outcomes (O): Partial restoration of periodontal tissues

Research Question

What is the effectiveness of using membrane and bone compared to Emdogain® for the regeneration of endo-periodontal lesions?

Electronic Search

A systematic search was conducted in 3 different free electronic databases: PubMed, ScienceDirect and Wiley Online Library. Articles published from January 1, 2019, to December 31, 2024, were included.

Search Strategy

The keywords used were: "endo periodontal lesions" or "endo-perio" and "guided tissue regeneration" or "GTR" "Emdogain" or "EMD," MeSH terms and Boolean operators.

Inclusion Criteria

- Studies involving human subjects
- Patients with bone loss
- Articles published from 2015 onwards
- Articles written in English

Exclusion Criteria

- Letters to the editor
- Animal studies
- Clinical opinions
- *In-vitro* studies
- Literature reviews

Elimination Criteria

- Studies where ethical codes were not respected

Data Collection and Analysis

Relevant studies were analyzed and reviewed individually by two reviewers. For each study, a data collection form was used, including the title, author, year, study design, sample size, treatment and corresponding results.

Results

During the bibliographic search, a total of 505 articles were identified in the selected databases, including PubMed (20), Wiley Online Library (350) and ScienceDirect (135). Of these, 96 duplicate articles were removed. After applying the inclusion criteria, 373 articles that did not meet the criteria were also excluded. Finally, 23 articles were selected for thorough reading, as illustrated in Fig. 1. In the analysis, only human studies were considered. The characteristics of the included studies were categorized by author, year, study design, sample size in each group, treatment and results, as presented in Table 1.

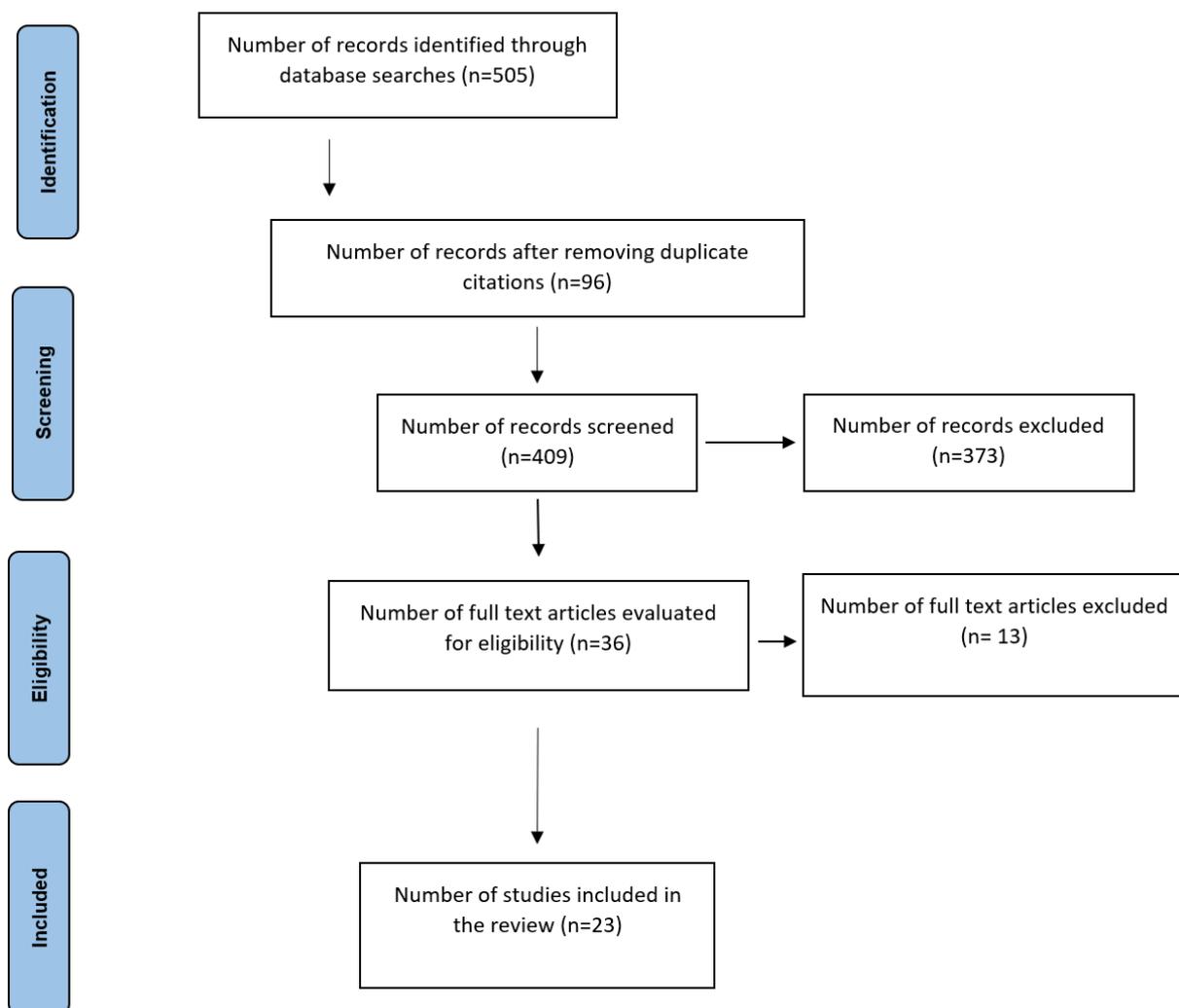


Figure 1: Inclusion and exclusion strategy.

Year	Autor (s)	Study Type	Sample Size	Treatment	Conclusion
2018	Von Arx and Bosshardt [16]	Retrospective analysis	17 teeth	Application of Enamel Matrix Derivative (EMD) in apical surgery for combined apicomarginal lesions	100% clinical success and 88% radiographic success. EMD may be effective for treating apicomarginal lesions.
2019	Soram Oh [17]	Retrospective	52 cases (41 patients), 5-year follow-up	Periodontal surgery using DBBM with 10% collagen, with or without collagen membrane	Significant clinical and radiographic improvements in both groups, with a 92.31% survival rate after 5 years.
2019	Diksha Katwal [18]	Case report	Single case, 2-year follow-up	Combined endo-perio approach for PRG-related lesion in a maxillary lateral incisor: root canal treatment, odontoplasty, GBR with allograft and resorbable membrane	Marked improvement with probing depth reduction and bone regeneration on CBCT.
2019	Cortellini, Cortellini [19]	Case series	49 patients	Papilla preservation flaps (PPF) and minimally invasive surgery with periodontal regenerative devices	After 12 months, 100% maxillary and 92% mandibular molars showed retention, probing depth reduction and clinical attachment gain. Results sustained for 3-16 years.
2020	Ustaoğlu, Uğur Aydin [20]	Randomized controlled clinical trial	45 patients	Comparison of GTR, T-PRF and open flap debridement	GTR and T-PRF showed significantly better outcomes than flap debridement.
2020	Cortellini, Stalpers [21]	RCT, 10-year follow-up	50 patients with stage III/IV periodontitis	Comparison of periodontal regeneration (PR) vs extraction and replacement (ER); regular follow-ups and supportive care	88% survival in PR and 100% in ER; no difference in complication-free survival. PR had lower cost and improved quality of life.
2021	Mohammed Adam [22]	Randomized clinical trial	120 individuals	RCT with/without GTR and bone grafts; 4 treatment arms: GP, MTA, GP+GTR, MTA+GTR	GTR showed better healing with 98% CBCTPAI < 1 vs poorer scores in non-GTR groups. Statistically significant differences in probing depth and CBCTPAI scores.
2021	Asgary and Roghanizadeh [23]	Clinical case report	Single case	Endodontic surgery with root-end resection, CEM root-end filling and bone substitute	Complete bone healing after 2 years in a case resistant to conventional treatment.
2021	Pham [24]	Randomized clinical trial	Not specified	Comparison of PRF, GTR and open flap debridement (OFD) in periodontal intraosseous defects	PRF provided outcomes comparable to GTR and better than OFD.
2022	Moein Khojaste [25]	Clinical case report	Single patient, 1-year follow-up	Endo-perio therapy: RCT, GTR, allograft, collagen membrane	Stable results at 12 months: no BOP and 1-2 mm probing depth.
2022	Alajmi, Karobari (26)	Clinical case report	Single case	Surgical GTR combined with root canal treatment	Significant bone recovery and absence of clinical symptoms after 2 years.

2022	Lai, Wu [27]	Retrospective cohort study	268 teeth, >1-year follow-up	EMS using MTA as retrograde filling material	EMS with MTA had 85.8% success. Key factors: chronic periapical lesion, lesion size and surgical technique.
2022	Adam, Günay [28]	RCT	40 patients	Comparison of granulation tissue preservation technique (GTPT) vs conventional technique in regenerative periodontal surgery	GTPT led to greater clinical attachment gain and probing depth reduction.
2022	De Ry, Rocuzzo [29]	Retrospective cohort study	41 patients, 75 teeth	Regenerative periodontal surgery using EMD for intraosseous defects	Mean CAL gain: 2.52 mm; 90.7% tooth survival. Smoking significantly impacted outcomes (P = 0.028).
2022	Ivanov and Mlachkova [30]	Clinical case report	Single patient (39 years old)	Endo-periodontal lesion in mandibular molar treated with RCT and regenerative periodontal surgery using Emdogain®	Complete regeneration observed at 14 months. Synergistic effect of endodontic and periodontal therapy.
2023	Dwiyanti [31]	Clinical case report	Single case	Multidisciplinary: Scaling, root planing, prosthesis correction, RCT, bone graft + barrier membrane, fiber post + metal crown	Asymptomatic at 5 months and 4 years. No periodontal inflammation, good radiographic bone healing.
2023	Baruwa Ao Bds, Martins Jnr Dds [32]	Case series	13 cases with apical periodontitis and apicomarginal defects	Endodontic microsurgery + GTR using bone grafts and membranes	Up to 9-year follow-up showed asymptomatic cases, radiographic success and lesion size reduction.
2024	Minabe, Kodama [33]	Comparative clinical study	140 patients	PRF vs T-PRF in endo-periodontal lesion management	Both PRF and T-PRF were effective, with T-PRF showing superior bone density and periodontal regeneration.
2024	Lai, Wu [27]	Retrospective cohort study	81 defects in 75 teeth (33 patients)	Regenerative surgery using DBBM and resorbable collagen membrane	Average CAL gain: 3.00 ± 2.00 mm, probing depth reduction: 2.06 ± 1.91 mm. Success: 38.8%. Male gender and bleeding during maintenance negatively affected outcomes.
2024	Wong, Ton [34]	Retrospective study	88 teeth in 88 patients	Evaluation of success, survival and failure factors across treatment modalities and anatomical/demographic variables	Overall success rate: 46.6%. Survival: 21.6%, failure: 31.8%. Factors like apical third bone loss and deep probing depths reduced success; no prior periodontal disease improved outcomes.
2024	Ivanov and Mlachkova [30]	Clinical case report	Two lesions in one patient	Diagnosis and treatment of two endo-periodontal lesions; 2-year follow-up	Successful management and restoration of dental health.
2025	Kazuhito Shiraishi [35]	Case report	Single case	Innovative 'triangular papilla access approach' for interdental	Minimal ridge resorption, shallow probing depths and

				bone regeneration: apical horizontal incision, periosteum connective graft, EMD, allograft and orthodontics	radiographic periodontal stability observed.
2025	Nara, Tavelli [36]	Clinical case report	Single case	Surgical treatment using flexible tunnel technique with four vertical and one periosteal incision to reposition interdental papillae	At 2 years, pocket closure and bone defect improvement without gingival recession.

Table 1: Characteristics of the included studies.

Discussion

Endo-periodontal defects represent a clinical challenge due to their complexity and the need for a comprehensive approach. These defects are difficult to treat because of their complex nature, involving both hard tissues (bone) and soft tissues (gingiva). The regeneration of both components is essential to restore the function and aesthetics of the affected teeth and therapies must address these two needs efficiently. The reviewed evidence confirms that both Emdogain® and collagen membranes with xenografts are effective, but their optimal indication varies depending on the type of defect and the clinical treatment objectives. The biomaterials used in regenerative therapy have been shown to significantly improve clinical outcomes and their selection should be based on individual criteria [9-11]. The use of collagen membranes combined with xenografts provides an ideal osteoconductive environment for hard tissue regeneration. Some studies highlight that this combination promotes the formation of new bone and improves long-term clinical stability [10-15,37-43]. This is particularly relevant in severe defects, where extensive bone loss occurs, as bone regeneration is crucial to prevent tooth loss and ensure long-term stability. Collagen membranes with xenografts have been extensively studied and their ability to stabilize clots, maintain space for regeneration and guide the formation of periodontal tissues has been well documented [12,42,43]. Their use is particularly indicated in complex defects, such as Type III and IV lesions, where structural bone regeneration is needed. In contrast, Emdogain®, derived from enamel matrix proteins, promotes regeneration by stimulating cementoblasts and periodontal fibroblasts, primarily acting on soft tissues and promoting periodontal regeneration through cellular activation and mineralization in the periodontal tissues. This has been widely documented, as evidenced by the works of Scuelan, et al., and Bosshardt, [5-15]. Its application has shown aesthetic benefits and faster postoperative recovery, making it ideal for superficial defects or areas with aesthetic concerns or those requiring rapid healing [5,13,15,44]. A total of 24 clinical studies that met the inclusion criteria were analyzed. These studies compared the use of collagen membrane with xenografts versus the use of Emdogain® in the treatment of endo-periodontal defects, observing differences depending on the defect type and therapeutic modality.

Regarding the results based on the type of treatment:

- *Collagen Membrane + Xenograft*: In 12 included articles, a clinical attachment gain of 2 to 4 mm and a probing depth reduction of 2 to 5 mm were observed. Studies by Schwarz, et al., Artzi, et al., and Mellonig, et al., demonstrated new bone formation radiographically confirmed and in some cases, through cone beam computed tomography. Long-term stability (up to 36 months), less recurrence of periodontal pockets and structural bone regeneration, particularly in Type III and IV defects, were reported.
- *Emdogain®*: In 11 analyzed studies, Emdogain® achieved clinical improvements in attachment (1 to 3 mm) and reduced bleeding on probing. Additionally, healing was faster and patients reported greater postoperative comfort. According to Piloni, et al., Froum, et al. and Zucchelli, et al., the regenerative effect was superior in superficial defects and more favorable aesthetic responses were observed compared to conventional techniques [1,9-15]

Results based on the type of defect treated:

- *Type I and II Defects (superficial periodontal involvement)*: In 9 studies, Emdogain® showed higher effectiveness for achieving rapid healing and improving aesthetic and comfort parameters. The collagen membrane + xenograft was also effective, though with less impact on the soft tissues.
- *Type III and IV Defects (deep lesions, angular bone loss and furcation involvement)*: In 14 studies, the use of collagen membrane with xenografts offered better bone regeneration, lower residual tooth mobility and greater clinical attachment gain compared to Emdogain® [10-15,37-44]

Although both treatments show promising results, the combination of both approaches could offer a synergistic solution, especially in defects involving both bone loss and soft tissue alterations. The choice between the two treatments may be influenced by factors such as gingival biotype, oral hygiene, probing depth, defect morphology and treatment cost [9-14]. Notably, some studies, such as those by Zucchelli, et al., and Trombelli, et al., propose the combined use of both strategies to leverage the synergistic benefits. These combined therapies may be especially useful in Type II-III defects, where both soft and hard tissue challenges coexist [33,45]. The main limitations of the studies include heterogeneity in methodologies, small sample sizes and the lack of unification in outcome variables. Additionally, the follow-up duration was variable, complicating long-term comparison. Therefore, randomized clinical trials with standardized follow-up and uniform clinical criteria for decision-making are recommended.

Conclusion

Both therapeutic modalities (Emdogain® and collagen membrane with xenograft) showed clinical efficacy in endo-periodontal defects, significantly improving parameters such as clinical attachment, probing depth and bleeding on probing. In severe defects (Type III and IV), the use of membranes with xenograft demonstrated better results in terms of bone regeneration, periodontal stability and long-term maintenance. In milder or superficial defects (Type I and II), Emdogain® proved to be more beneficial due to its rapid tissue integration, improved aesthetics and less postoperative inflammation. The choice of treatment should be individualized, considering the defect type, anatomical conditions, gingival biotype, aesthetic needs and patient expectations. It is recommended to conduct high-quality clinical studies with prospective designs and prolonged follow-up to establish more specific therapeutic guidelines and improve decision-making. Combined therapies could represent a promising alternative in complex defects, integrating the advantages of both bone and soft tissue regeneration.

Conflict of Interest

The authors declare that they have no conflicts of interest with the contents of the article.

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Author Contributions

All authors contributed equally for this paper.

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