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Original Research

Regenerative strategies in apical surgery with and without biomaterials: a systematic review

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ABSTRACT

Objectives: This systematic review compares the clinical efficacy and radiographic outcomes of membrane-based regeneration, bone grafting, and platelet concentrates in cavities resulting from apicoectomy, assessing healing rates and the quality of newly formed bone.

Methods: Following PRISMA 2020 guidelines, a literature search was performed in PubMed, Cochrane Library, ScienceDirect, Wiley, and Scopus databases for articles published between January 2000 and December 2025. Eligibility criteria were defined using the PICOS framework, and included studies were evaluated based on clinical and radiographic parameters with a minimum follow-up of six months.

Results: Eighteen clinical studies were included. Findings were heterogeneous and predominantly of low to very low certainty. Although some studies suggested potential benefits of regenerative adjuncts in complex defects, such as through-and-through and apicomarginal lesions, a substantial proportion found no statistically significant advantage over conventional apical surgery. Smaller lesions (<3 mm) generally responded favorably to conventional surgery, whereas larger defects may benefit from adjunctive regenerative approaches in selected clinical situations.

Conclusions: Overall, the available evidence suggests a potential benefit of combining physical support (biomaterials) and biological stimulation (platelet-rich fibrin) in regenerative apical surgery. However, findings remain heterogeneous and should be interpreted cautiously. Technique selection should consider defect morphology, lesion characteristics, and available resources. Further standardized and methodologically robust studies are required to strengthen the current evidence base. (Rev Port Estomatol Med Dent Cir Maxilofac. 2026;67(x):1-14)

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Introduction

Apical surgery (apicoectomy) represents an important treatment modality for persistent periapical lesions that do not resolve following conventional or nonsurgical endodontic retreatment. The choice between surgical and nonsurgical approaches depends on multiple clinical factors, including canal accessibility, the presence of intraradicular obstacles, lesion extent, and anatomical conditions. Available evidence suggests periapical healing rates of approximately 82.9% for apical surgery compared with 71.7% for nonsurgical retreatment, although the latter has been associated with higher tooth survival.[1] Apical surgery thus remains a valuable therapeutic alternative in selected cases, particularly when orthograde retreatment is technically limited.

Repair and regeneration represent distinct biological outcomes that should be clearly distinguished in the context of apical surgery: repair involves the restoration of tissue with different structural or functional characteristics, whereas regeneration implies the complete restitution of the original tissue architecture and function.[2]

Apical surgery aims to eliminate the infectious focus and restore the periapical environment through thorough lesion curettage, apical resection, and retrograde filling.[3] The central purpose is to establish optimal conditions for periradicular tissue regeneration by achieving complete infection control. In complex clinical cases, such as extensive, traumatic, or apicomarginal lesions, the effectiveness of surgery may be significantly reduced.[4]

Successful healing depends on sealing of the root apex, dentin modification, wound stabilization, cellular migration, and blood supply. Migration of progenitor cells is crucial for the formation of new cementum, periodontal ligament, and alveolar bone.[2] Healing rates also depend on the integrity of marginal and periapical bone structures. Preserved marginal bone promotes flap readaptation, reducing inflammation and apicomarginal communication.[5] Bone regeneration involves osteoblasts, osteoclasts, cytokines, and growth factors that regulate inflammatory, reparative, and remodeling phases.[6] Regenerative therapies such as platelet-rich fibrin (PRF), bone allografts, and barrier membranes enhance healing by combining osteoinductive and osteoconductive properties.[3] Local factors, such as bacterial biofilm, can delay healing by stimulating resorption.[7] The quality of the blood clot at the apicoectomy site is also considered essential for osteoprogenitor cell activity.[8] Age and sex have shown no significant influence on healing outcomes.[9,10]

Defect morphology is another decisive factor for apical surgery success: through-and-through defects are less predictable for spontaneous regeneration due to a lack of containment, which justifies the use of adjunctive regenerative strategies, such as guided tissue regeneration (GTR).[2] Clinical studies indicate that combining bone grafts with growth factors may enhance regeneration, although interpatient variability may limit predictability. Systemic factors such as diabetes and overall health also influence outcomes.[6,8]

The assessment of bone healing after apical surgery has traditionally relied on two-dimensional periapical radiographs, which use classic literature-based criteria. However, these methods present limitations for evaluating three-dimensional bone regeneration. Cone-beam computed tomography (CBCT) enables more accurate assessment and has led to the development of radiographic indices such as the R index (resection plane), A index (apical area), and C index (cortical plane) (Figure 1). Results indicate the highest complete healing for R (54.1%), followed by A (47.5%), and the lowest for C (21.3%).[11]

GTR isolates bone defects using barrier membranes, allowing slower-proliferating osteogenic cells to repopulate the area.[12–14] Membranes and bone grafts provide structural support, stimulate progenitor cell migration, and prevent epithelial invasion, particularly in apicomarginal and through-and-through lesions.[15,16]

Proper case selection is critical for apical surgery and should consider lesion size, the extent of bone resorption, and the amount of resected root tissue.[17,18] Failures may result from inadequate root canal filling or incorrect case selection, with surgical reintervention being a viable alternative to tooth extraction.[18] Advances in microsurgical techniques combined with regenerative therapies have increased success rates and tooth preservation.[3]

In extensive bony defects or through-and-through lesions, the periosteum alone may be insufficient to achieve complete healing. Chronic lesions, often associated with fistulas, can compromise repair, favoring connective tissue formation rather than bone. In these cases, regenerative strategies are required to maintain space for osteoprogenitor cell growth and prevent infiltration by undesired cells.[2]

A critical step is creating and maintaining a space beneath the membrane used in GTR. When the membrane alone cannot provide this, biomaterials, commonly including freeze-dried

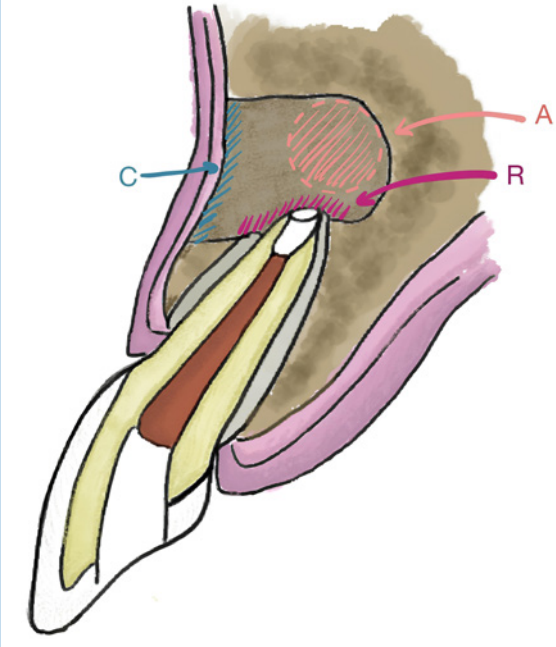

Figure 1. Illustration of bone regeneration. R: resection plane; A: apical area; C: cortical plane. ***Illustration created by the author.***

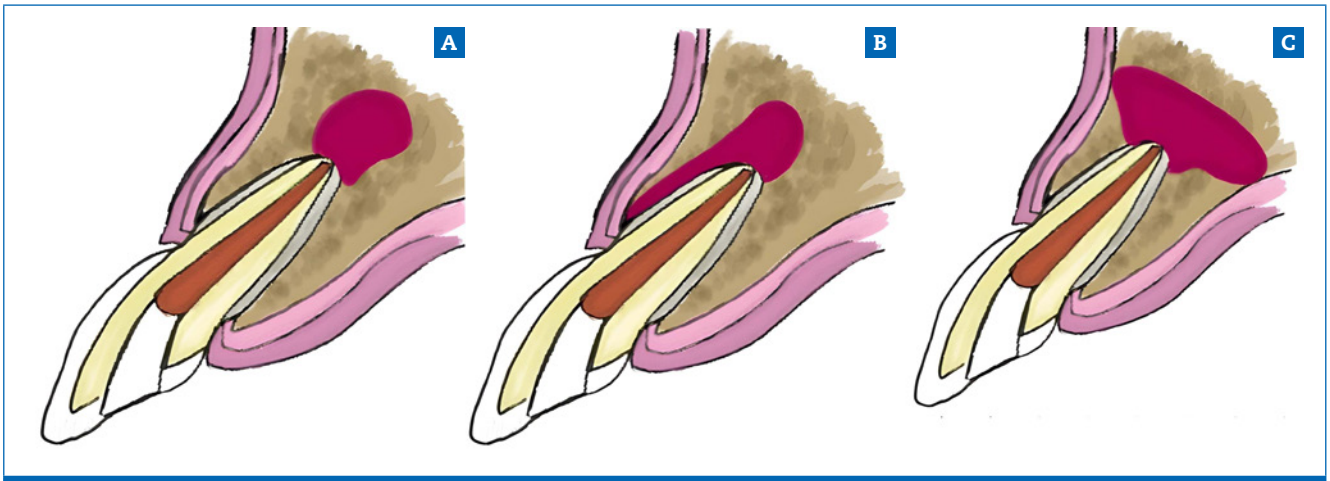

Figure 2. Representation of the lesions. 2A: periapical lesion; 2B: apicomarginal lesion; 2C: through-and-through lesion. *Illustration created by the author.*

demineralized allogeneic bone grafts, hydroxyapatite, autologous bone, and calcium sulfate, serve as space maintainers.[2,12] Ideal grafts should offer osteoconductivity, osteoinductivity, osteogenesis, and good integration with host bone.[19] Autologous grafts meet all these criteria and are the gold standard[20], but have limited availability and require additional surgery. Allogeneic, xenogeneic, and synthetic grafts are widely used alternatives, although they may present lower osteogenic potential due to processing or material properties.[21]

Autologous platelet concentrates, including platelet-rich plasma (PRP), leukocyte- and platelet-rich fibrin (L-PRF), and injectable platelet-rich fibrin (i-PRF), have gained attention due to their autologous nature, ease of preparation, and high growth factor content.[4] PRP acts as a hemostatic and stabilizing agent, promoting clot formation essential for tissue regeneration.[22] L-PRF offers a 3D fibrin matrix for cellular migration and angiogenesis, with sustained growth factor release that supports soft tissue and bone regeneration.[23] i-PRF preserves more viable leukocytes and platelets, enables combination with biomaterials like type I collagen, and allows controlled growth factor delivery, though clinical data remain limited.[24]

Allogeneic grafts provide osteoconductive and occasionally osteoinductive support without requiring a second surgical site, thereby reducing morbidity and the risk of inflammatory reactions.[25] Freeze-dried bone allograft contains bone morphogenetic proteins that stimulate mesenchymal differentiation into osteoblasts, though its slower resorption may delay complete bone replacement. In turn, demineralized freeze-dried bone allograft allows enhanced bone morphogenetic protein release through demineralization.[25] Xenogeneic grafts are abundant but antigenic, and alloplastic grafts, organic or inorganic, may release acidic degradation products that affect osteogenesis; bioactive glass stands out for bone regeneration stimulation.[26] Finally, biomaterials have evolved from autologous grafts to bioengineered approaches incorporating stem cells, combining structural support and biological activity to optimize periapical regeneration.[8]

Periapical lesions are confined to the apex without cortical plate involvement.[13] Apicomarginal lesions are characterized by a complete and localized loss of marginal bone, resulting in communication between the periapical region and the periodontal space. Through-and-through lesions are characterized by destruction of the lingual/palatal cortical plates, associated with simultaneous loss of the buccal cortical plate,[14] as shown in Figure 2. Lesion morphology, including height and depth, directly influences healing outcomes.[27]

Bone healing has traditionally been assessed using two-dimensional radiographs, but CBCT allows more accurate three-dimensional evaluation. Non-resorbable grafts can create radiopaque artifacts, whereas L-PRF demonstrates progressive radiodensity correlating with bone formation.[28] Figure 3 shows a schematic representation of the anatomical dimensions of the periapical lesion and its relationship with adjacent structures. Healing criteria include complete, partial, or failed

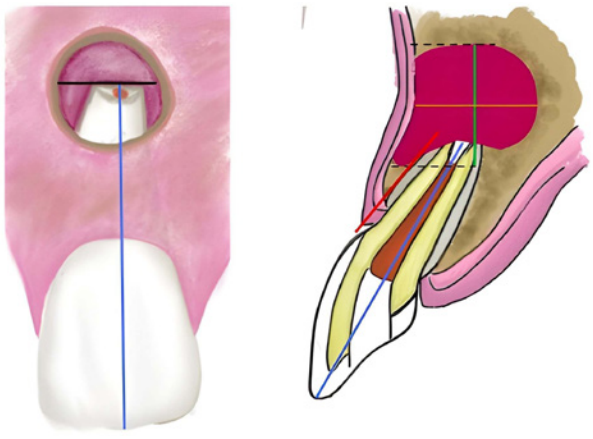

Figure 3. Representation of the anatomical dimensions of the periapical lesion and its relationship with adjacent structures. The color-coded lines indicate the following parameters: black – lesion width; blue – tooth longitudinal axis; red – buccal plate length; green – lesion height; orange – lesion depth. *Illustration created by the author.*

regeneration of the periapical defect, surrounding periodontal ligament, and buccal window.[27]

Previous systematic reviews have evaluated regenerative approaches in endodontic surgery. However, many focused on specific biomaterials or did not stratify outcomes by lesion morphology, imaging modality, or combined regenerative strategies. Furthermore, heterogeneity in study design, biomaterials, and outcome assessment methods has limited the interpretation and comparability of findings across studies.

This systematic review aims to compare the clinical and radiographic outcomes of membrane-based regeneration, bone grafting, and platelet concentrates following apicoectomy, and associated pathology. The study hypothesizes that all three approaches have regenerative potential, although combined regenerative strategies may provide potential benefits in selected clinical situations. The results may contribute to the development of more standardized, evidence-based clinical protocols for the rehabilitation of apical bone defects.

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.[29] It was registered in the International Prospective Register of Systematic Reviews (PROSPERO) under registration number CRD420261292871 on January 29, 2026. Registration occurred after the literature search had already been initiated, in December 2025; this is acknowledged as a late registration with respect to study screening and selection.

The protocol defined clinical success, radiographic success, and periapical tissue healing as the main outcomes of interest, assessed through clinical and radiographic parameters during follow-up periods starting at 6 months. A qualitative narrative synthesis was planned due to the expected heterogeneity among included studies regarding interventions, defect morphology, and outcome assessment methods. Minor protocol amendments were implemented during the review process to improve search comprehensiveness and reporting rigor, including expanding database searches and adding certainty assessments.

Eligibility Criteria

Based on the objectives of this systematic review, the following research question was formulated: "What is the clinical and radiographic efficacy of regenerative techniques applied to apical surgery, considering the type and morphology of periapical lesions?" The research question was structured according to the PICOS framework, which facilitates the systematic definition of eligibility criteria and ensures consistency in study selection and outcome assessment:

- Population (P): patients undergoing apical surgery.
- Intervention (I): regenerative techniques in apical surgery, including membranes, biomaterials, and growth factors.
- Comparison (C): apical surgery performed without regenerative adjuncts (standard apical surgery).
- Outcomes (O): clinical and radiographic success rates, bone regeneration, and periapical tissue healing.
- Study designs (S): randomized clinical studies, randomized controlled trials, and prospective, retrospective, and comparative observational studies.

For the purposes of this review, the term 'guided tissue regeneration' (GTR) is used consistently to refer to membrane-based regenerative interventions, applied alone or in combination with bone graft substrates. Although GTR and 'guided bone regeneration' are used interchangeably in some source studies, all such interventions are referred to as GTR within this manuscript. Platelet concentrates (PRP, PRF, L-PRF, i-PRF) are categorized separately as biological adjuncts and are not incorporated under the GTR designation.

Studies were selected based on the following inclusion criteria:

- Randomized controlled trials and prospective, retrospective, or comparative observational studies.
- Human patients undergoing apicoectomy.
- Evaluation of regenerative techniques in apical surgery, including GTR with membranes and the use of bone grafts, applied alone or in combination.
- Clinical and/or radiographic outcomes (including conventional or advanced radiographic imaging methods) related to bone healing or reduction of periapical lesions.
- Minimum follow-up period of 6 months.
- Publications between January 2000 and December 2025.
- Articles published in any language, with no language restrictions applied.

The following exclusion criteria were applied:

- Narrative or systematic reviews, meta-analyses, and books.
- Case reports or case series with small sample sizes.
- Studies conducted exclusively on animal or in vitro models.
- Research not primarily focused on bone regeneration following apical surgery.
- Lack of a clear description of the regenerative techniques used.
- Articles without quantitative clinical or radiographic outcome data.

Information Sources and Search Strategy

A bibliographic search was conducted in PubMed, Scopus, ScienceDirect, Cochrane Library, and Wiley Library databases, covering publications from January 2000 to December 2025, with no language restrictions. The combination of keywords and MeSH terms was adapted for each database to maximize the identification of relevant studies in accordance with the objectives of this systematic review. The search strategy was adapted for each database due to differences in indexing systems, search field structure, and technical limitations. Conceptual equivalence of the search terms was maintained across all databases by ensuring that core concepts related to apical surgery, regenerative techniques, and periapical heal-

ing outcomes were consistently represented. Controlled vocabulary (MeSH terms where available) and free-text keywords were combined to optimize sensitivity and specificity.

Radiographic terminology was included as a mandatory component of the search strategy to ensure the identification of studies reporting CBCT-based and other imaging-related outcomes relevant to apical surgical procedures and periapical bone healing, which constitutes the primary outcome of this review. This decision reflects the outcome-focused scope of the review rather than a study eligibility filter, as outcome requirements were formally applied at the screening stage. However, because this term was combined with the other search blocks using the Boolean operator AND rather than OR, it is acknowledged that this approach may have functioned as an unintended retrieval filter, potentially excluding clinically relevant studies that report healing or success outcomes without using explicit radiographic terminology in the title, abstract, or keywords. This is considered a major limitation affecting the comprehensiveness of the search and the certainty of the review's conclusions, rather than a minor methodological caveat, and is further discussed in the limitations section.

A manual search of the reference lists of all included studies was performed to identify additional relevant articles through citation tracking (snowballing). The keywords and search strategies applied in each database, as well as the number of records identified, are summarized in Table 1.

Study Selection and Data Extraction

The study selection process was conducted in two phases. In the first phase, two reviewers independently screened the titles and abstracts identified through the bibliographic search. Potentially eligible studies were subsequently assessed in full text to confirm compliance with the inclusion criteria.

Data extraction was performed independently and in duplicate by two reviewers to minimize selection and information bias. Any discrepancies were resolved by consensus and, when necessary, through consultation with a third reviewer. Data extraction prioritized clinical outcomes, including surgical success rates, absence of lesion recurrence, and indicators of adequate healing, as well as radiographic parameters, such as new bone formation in the periapical region and the extent of defect fill. This approach aimed for a critical evaluation of the efficacy and predictability of regenerative interventions associated with apicoectomy. All records were exported to the reference management software (Mendeley®, Elsevier, Amsterdam, Netherlands), where duplicates were automatically removed.

Risk of Bias and Quality Assessment

The methodological quality of the included studies was assessed using validated tools for risk-of-bias evaluation, according to each study's design. Randomized controlled trials (RCTs) were evaluated with the Cochrane Risk of Bias 2.0 (RoB 2.0) tool, which assesses five critical domains of bias: randomization process, deviations from intended interventions, missing outcome data, measurement of outcomes, and selective reporting. Observational studies with intervention, in which participants were not randomly allocated, were evaluated using the Risk Of Bias In Non-randomized Studies of Interventions (ROBINS-I) tool, which allows a systematic assessment of bias by comparing each study with a hypothetical ideal trial (target trial) across seven domains: confounding, participant selection, intervention classification, deviations from intended interventions, missing data, outcome measurement, and selective reporting.

Two reviewers independently performed the methodological assessment. Disagreements were discussed and resolved by consensus, with a third reviewer involved when agreement could not be achieved. Based on the applied criteria, studies were classified as having a low, moderate, or high risk of bias. Studies classified as having a low risk of bias demonstrated adequate methodological design and appropriate control of bias domains. Studies with a moderate risk of bias had methodological limitations, mainly related to a lack of blinding or incomplete reporting of outcome assessment. Studies classified as having a high risk of bias showed significant methodological weaknesses, including the absence of randomization, potential confounding factors, and insufficient reporting of outcome data.

Table 1. Search strategy translated for each database.

Databases	Advanced research	Articles
PubMed	("Apicoectomy"[MeSH] OR periradicular surgery OR endodontic microsurgery) AND ("Bone Regeneration"[MeSH] OR "Guided Bone Regeneration" OR "Bone Healing" OR "guided tissue regeneration") AND ("Radiography, Dental"[Mesh] OR radiograph)	66
Cochrane Library	("Apicoectomy" OR apical surgery OR endodontic microsurgery OR periradicular surgery) AND ("Bone Regeneration" OR "Guided Bone Regeneration" OR "Bone Healing" OR "guided tissue regeneration") AND ("Radiography, Dental" OR radiograph)	45
Science Direct	("Apicoectomy" OR endodontic microsurgery OR periradicular surgery) AND ("Bone Regeneration" OR "Guided Bone Regeneration" OR "Bone Healing" OR "guided tissue regeneration") AND ("Radiography, Dental" OR radiograph)	358
Wiley Library	("Apicoectomy" OR apical surgery OR endodontic microsurgery OR periradicular surgery) AND ("Bone Regeneration" OR "Guided Bone Regeneration" OR "Bone Healing" OR "guided tissue regeneration") AND ("Radiography, Dental" OR radiograph)	299
Scopus	("Apicoectomy" OR apical surgery OR endodontic microsurgery OR periradicular surgery) AND ("Bone Regeneration" OR "Guided Bone Regeneration" OR "Bone Healing" OR "guided tissue regeneration") AND ("Radiography, Dental" OR radiograph)	175

Synthesis Methods

A quantitative meta-analysis was not performed due to clinical and methodological heterogeneity across the included studies, particularly regarding differences in study design, regenerative protocols, and outcome measures. Therefore, a structured narrative synthesis was conducted following the Synthesis Without Meta-analysis (SWiM) reporting framework, considering the direction of effect, consistency of findings across studies, and overall certainty of the evidence, integrating risk of bias and Grading of Recommendations Assessment, Development and Evaluation (GRADE) assessments.

Data analysis was conducted qualitatively through a descriptive synthesis of the main clinical and radiographic findings reported in the included studies. Following the extraction of the relevant data, the studies were categorized by the regenerative technique applied, enabling comparison of different biomaterials and approaches, such as barrier membranes, bone grafts, and combinations of these interventions.

Results

The literature search and study selection process are illustrated in the PRISMA flow diagram (Figure 4). The search conducted in the PubMed, Scopus, Wiley Library, ScienceDirect, and Cochrane Library databases yielded a total of 943 records. After removal of duplicates (n = 160), 783 unique records were screened. Based on title and abstract screening, 679 studies were excluded for not meeting the predefined inclusion criteria. A total of 104 reports were sought for full-text retrieval,

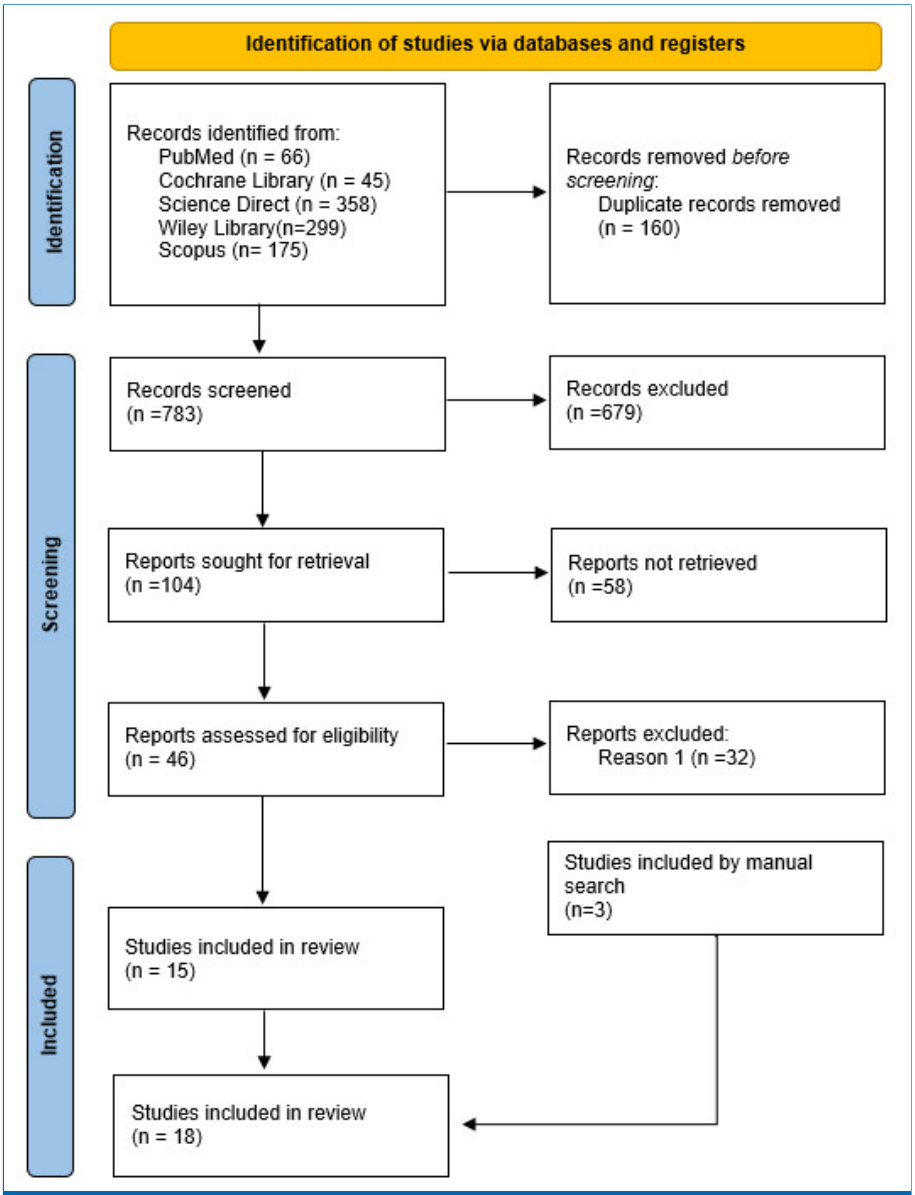

Figure 4. PRISMA flow diagram of the study selection process. Reason 1 for report exclusion (n=31) comprises inadequate intervention (n=17); inadequate study design (n=7); inadequate comparison (n=1); inadequate population (n=6).

but 58 could not be retrieved due to institutional paywalls and access limitations. Although complementary searches were conducted via Google Scholar and ResearchGate to mitigate this, and direct author contact was attempted where institutional access was unavailable, full-text retrieval remained unsuccessful for these records. Given the high proportion of non-retrieved full texts (55.8%), this is acknowledged as a potential source of selection bias, and the direction of this bias is likely conservative, as excluded studies may include both positive and null findings. Conclusions should therefore be interpreted with appropriate caution.

The remaining 46 full-text articles were assessed for eligibility. Upon full-text review, 31 studies were excluded for not meeting the eligibility criteria (Supplementary Table S1). Specifically, 17 studies were excluded for inadequate interventions, 7 for inadequate study designs, 1 for inadequate comparison, and 6 for inadequate population. Fifteen studies met the eligibility criteria and were included in the systematic review. Manual searching of the reference lists of included articles identified 3 additional studies, resulting in a final sample of 18 studies.

The included clinical studies comprised 13 RCTs and 5 non-randomized studies. The regenerative strategies investigated by the 18 studies can be broadly categorized into four intervention groups: (i) barrier membranes with or without bone graft substrates (GTR), used in 44.4% of studies; (ii) platelet concentrates (PRP, L-PRF, or i-PRF) as biological adjuncts, present in 33.3% of studies; (iii) xenogeneic grafts, used in 27.8% of studies; and (iv) alloplastic materials, used in 11.1% of studies. Table 2 summarizes both the methodological characteristics and the clinical and technical variables of each study, including the authors and year of publication, study design, sample size, type and size of the periapical lesion, clinical follow-up period, materials used in GTR approaches, the radiographic assessment method employed, and the healing rate observed at 12 months of follow-up.

Overall, findings across the included studies were mixed. While some studies reported a tendency towards more favorable healing outcomes with regenerative adjuncts, particularly in complex defect morphologies such as through-and-through and apicomarginal lesions, at least 10 of the 18 included studies reported no statistically significant difference between regenerative and conventional approaches. The direction of effect was inconsistent across intervention types, lesion categories, and follow-up periods, reflecting the substantial methodological heterogeneity of the available evidence.

Across the included studies, barrier membranes used in GTR protocols showed a tendency towards more favorable healing outcomes in complex defects, although this trend was not consistently statistically significant. In one RCT, the group treated with a membrane combined with xenogeneic graft material achieved a healing rate approximately 9 percentage points higher than the control group without regenerative adjuncts; however, this difference did not reach statistical significance.[12] Similarly, two RCTs evaluating resorbable collagen membranes in through-and-through lesions reported no significant improvement in total healing rates compared to controls.[13,14] In contrast, an RCT evaluating allograft combined with a collagen membrane in apicomarginal lesions reported significantly higher complete-healing rates in the experimental group (86.6% vs 46.6%).[25] A retrospective comparative study also demonstrated markedly higher complete healing in periapical lesions treated with GTR compared to conventional surgery (85.5% vs 43.9%), and in through-and-through lesions (83.3% vs 0%).[9]

Regarding biological adjuncts, two RCTs assessing L-PRF in apicomarginal lesions observed no statistically significant benefit compared to conventional surgery without regenerative adjuncts, with comparable total healing rates between groups.[28,30] Similarly, trials investigating PRP and i-PRF did not demonstrate statistically significant superiority over controls at 12 months, although some studies noted trends toward reduced failure rates and accelerated early healing.[22,24] Notably, one RCT reported 100% complete healing in both L-PRF and freeze-dried bone allograft groups at 12 months.[3] A 5-year follow-up RCT reported that the PRP-treated group achieved substantially higher complete-healing rates across multiple CBCT-assessed anatomical parameters compared to controls.[31]

Among alloplastic materials, calcium sulfate demonstrated a statistically significant improvement in complete-healing rates in through-and-through lesions when compared to conventional surgery without grafting (77.9% vs 33.3%, $p<0.05$).[2] In contrast, bioactive glass did not demonstrate a statistically significant advantage over the control group in periapical lesions with cavities greater than 5 mm over a 9–48-month follow-up period.[32] With regard to xenogeneic grafts, anorganic bovine bone mineral combined with a collagen membrane achieved a healing rate of 83% at 12 months in a prospective observational study of apicomarginal lesions, although the absence of a control group limits the strength of these conclusions.[33]

Osseous defect size emerged as a key variable influencing healing success. A prospective observational study stratifying outcomes by defect size in the absence of any regenerative adjunct demonstrated that periapical lesions smaller than 5 mm achieved 86.5% complete healing, compared with 77.1% for lesions greater than 5 mm, a difference associated with a 4.7-fold higher failure rate in larger defects.[5,10] A retrospective comparative study found that conventional surgery without GTR yielded complete-healing rates of only 30.6% in periapical lesions of 3–6 mm and 0% in through-and-through lesions, compared with 75.0% and 83.3%, respectively, with GTR.[9]

The radiographic assessment method used influenced the reported healing outcomes. One RCT reported a complete-healing rate of 55.6% using 2D radiography in the experimental group, compared with only 16.7% when assessed by CBCT in the same cohort – a discrepancy of 38.9 percentage points underscoring the risk of overestimation inherent to conventional radiography.[24]

Despite the general trend towards improved healing outcomes, variability was observed across studies in the types of regenerative material used, surgical protocols, and follow-up periods. This heterogeneity resulted in moderate inconsistency in reported outcomes, particularly when comparing studies that used different biomaterials or combined regenerative approaches.

Based on the methodological quality assessment using RoB 2.0 and ROBINS-I, 2 studies were classified as having a

Table 2. Characteristics and periapical healing outcomes of included studies.

Author, year (reference)	Study design	Study sample*	Lesion type	Lesion size (cavity)	Intervention	Comparison	Follow-up	Material used for GTR	Radiographic outcome measure	Healing rate at 12 months (total | partial | failed)#
Randomized Controlled Trials (RCTs)										
Taschieri et al., 2007[12]	RCT	41 patients 59 lesions	PL / TTL	> 9 mm	GTR + xenograft (collagen membrane + Bio-Oss)	No membrane No graft	12 months	Collagen membrane + xenograft (Bio-Oss)	Periapical radiograph (2D)	Exp. (PL, radiolucent): Total, 87.5% | Partial, NR | Failed, NR Exp. (PL, radiopaque): Total, 81.8% | Partial, NR | Failed, NR Control (PL, radiolucent): Total, 75.0% | Partial, NR | Failed, NR Control (PL, radiopaque): Total, 66.7% | Partial, NR | Failed, NR →No significant difference between GTR and control groups.
Garrett et al., 2002[13]	RCT	13 lesions	PL (confined)	3–6 mm	GTR (resorbable membrane)	No membrane	3, 6, 12 months	Resorbable membrane	Periapical radiograph (densitometry)	→Healing rates not reported numerically. →GTR did not improve periapical healing vs. control in confined PL defects.
Parmar et al., 2019[14]	RCT	29 patients 29 lesions	TTL	> 9 mm	GTR (collagen membrane)	No membrane	12 months	Collagen membrane	Periapical radiograph + CBCT	Exp. (GTR): Total, 73% | Partial, NR | Failed, NR Control: Total, 80% | Partial, NR | Failed, NR →GTR with collagen membrane did not enhance healing in TTLs. CBCT offered no advantage over 2D radiography.
Garg et al., 2023[3]	RCT	19 patients 19 lesions	PL	N/A	L-PRF gel + membrane	FDBA	1, 3, 6, 12 months	Autologous biomaterial (L-PRF)	Periapical radiograph	L-PRF: Total, 100% | Partial, 0% | Failed, 0% FDBA: Total, 100% | Partial, 0% | Failed, 0% →Both achieved complete healing at 12 months; L-PRF accelerated early-phase bone formation.
Dhiman et al., 2015[28]	RCT	26 patients 26 lesions	AML	N/A	L-PRF	No GTR	3, 12 months	Autologous biomaterial (L-PRF)	Periapical radiograph	PRF: Total, 53.3% | Partial, 33.3% | Failed, 13.3% Control: Total, 53.3% | Partial, 26.7% | Failed, 20.0% →PRF provided no statistically significant benefit over conventional microsurgery in AMLs.
Pecora et al., 2001[2]	RCT	18 teeth 18 lesions	TTL	> 9 mm	Calcium sulfate graft	No graft	6, 12 months	Alloplastic graft (calcium sulfate)	Periapical radiograph	Exp.: Total, 77.9% | Partial, 22.2% | Failed, 0% Control: Total, 33.3% | Partial, 55.6% | Failed, 11.1% →Calcium sulfate significantly improved complete healing in TTL ($p<0.05$).
Goyal et al., 2011[22]	RCT	25 patients 25 lesions	AML	N/A	PRP alone; PRP + collagen sponge; GTR membrane (3 arms)	GTR membrane (active comparator)	3, 6, 12 months	Autologous biomaterial (PRP); GTR membrane	Periapical radiograph	GTR membrane: Total, 70% | Partial, 10% | Failed, 0% PRP alone: Total, 77.8% | Partial, 11.1% | Failed, 0% PRP + collagen: Total, 83.0% | Partial, 0% | Failed, 0% →PRP ± collagen yielded comparable or superior results to GTR membrane alone.
Marín-Botero et al., 2006[30]	RCT	30 patients 30 lesions	AML	N/A	Resorbable GTR membrane (PGA 910)	Periosteal sliding graft	3, 6, 12 months	Resorbable membrane (PGA 910)	Periapical radiograph	Periosteal graft: Total, 40% | Partial, 47% | Failed, 13% GTR Membrane: Total, 60% | Partial, 27% | Failed, 0% →GTR membrane achieved higher complete healing and eliminated failures.

Author, year (reference)	Study design	Study sample*	Lesion type	Lesion size (cavity)	Intervention	Comparison	Follow-up	Material used for GTR	Radiographic outcome measure	Healing rate at 12 months (total | partial | failed)#
Randomized Controlled Trials (RCTs) (cont.)										
Karan et al., 2020[23]	RCT	40 lesions	PL	3–6 mm	MTA; L-PRF; L-PRF + MTA	No graft (control)	3, 6, 12 months	Autologous biomaterial (L-PRF); MTA	CBCT	→Quantitative healing rates not reported numerically. →High success rates observed with MTA; L-PRF alone did not significantly improve outcomes. →Authors recommend further RCTs to clarify the role of PRF in periapical microsurgery.
Sharma et al., 2025[25]	RCT	30 lesions	AML	N/A	GTR with allograft + collagen membrane	No GTR	12 months	Allograft (DFDBA) + collagen membrane	Periapical radiograph + CBCT	Exp. (GTR): Total, 86.6% | Partial, 13.4% | Failed, 0% Control: Total, 46.6% | Partial, 40.0% | Failed, 0% →GTR with DFDBA + collagen membrane significantly promoted labial bone regeneration in AMLs ($p<0.05$).
Albagle et al., 2023[34]	RCT	58 lesions	PL (4-wall)	3–6 mm	Resorbable collagen-based bone graft	No graft	12 months	Allograft (collagen-based)	Periapical radiograph	Exp.: Total, 87.5% | Partial, 3.1% | Failed, 3.1% Control: Total, 88.4% | Partial, 3.8% | Failed, 3.8% →No significant difference in healing of 4-wall PLs. The higher cortical bone regeneration in the exp. group may hold clinical relevance.
Dhamija et al., 2024[31]	RCT	24 patients 24 lesions	PL	N/A	PRP	No graft	12 months + 62 months	Autologous biomaterial (PRP)	Periapical radiograph + CBCT	Control: Total, 45.5% | Partial, 45.5% | Failed, 0% PRP: Total, 69.2% | Partial, 23.1% | Failed, 0% →PRP showed a trend toward improved complete healing (+23.7%), but did not reach statistical significance.
Arpitha et al., 2023[24]	RCT	38 patients 38 lesions	TTL	N/A	i-PRF + type I collagen	No graft	12 months	Autologous biomaterial (i-PRF + type I collagen)	Periapical radiograph	Control: Total, 56.3% | Partial, 31.3% | Failed, 12.5% Exp. (i-PRF + col.): Total, 55.6% | Partial, 44.4% | Failed, 0% →i-PRF + collagen eliminated failures but did not achieve significant superiority over conventional surgery in TTLs.
Non-Randomized Studies										
Dietrich et al., 2003[33]	Prospective observational	23 patients 23 lesions	AML	N/A	GTR: Bio-Oss + membrane	No control group	12 months	Xenograft (Bio-Oss) + membrane	Periapical radiograph	GTR (single arm): Total, 83% | Partial, 9% | Failed, 9% →GTR with Bio-Oss achieved good periapical and periodontal healing. Absence of a control group limits conclusions.
Alkandari et al., 2024[27]	Retrospective comparative	53 lesions (regenerative: 19; conventional: 34)	PL / TTL	Conventional: < 3 mm; 3–6 mm Regenerative: 3–6 mm; > 9 mm	Regenerative (GTR)	Conventional (no GTR)	12 months	Membrane ± graft (NR)	CBCT	Conventional (PL, < 3 mm): Total, 75.0% | Partial, NR | Failed, NR Conventional (PL, 3-6 mm): Total, 30.6% | Partial, NR | Failed, NR Regenerative (PL, 3-6 mm): Total, 75.0% | Partial, NR | Failed, NR Regenerative (TTL, >9 mm): Total, 100% | Partial, NR | Failed, NR →Regenerative approach markedly superior in larger PLs (2.5x vs. conventional in 3-6 mm) and in TTL. Conventional may suffice for small PLs (<3 mm).

Author, year (reference)	Study design	Study sample*	Lesion type	Lesion size (cavity)	Intervention	Comparison	Follow-up	Material used for GTR	Radiographic outcome measure	Healing rate at 12 months (total | partial | failed)#
Non-Randomized Studies (cont.)										
von Arx et al., 2007[10]	Prospective observational	194 lesions (No lesion: 17; PL <5 mm: 104; PL >5 mm: 70)	PL (stratified by size)	< 5 mm (n=104) > 5 mm (n=70)	Conventional apical surgery (no GTR, no graft)	— (single arm; size-stratified)	12 months	None	Periapical radiograph	No preoperative lesion (n=17): Total, 94.1% | Partial, 5.9% | Failed, 0% PL < 5 mm (n=104): Total, 86.5% | Partial, 9.6% | Failed, 3.9% PL > 5 mm (n=70): Total, 77.1% | Partial, 14.3% | Failed, 8.6% → Lesion size is a significant independent prognostic factor: larger lesions show lower complete healing and higher failure rates, even without GTR. → PLs >5 mm had 9.4% less complete healing and 4.7x more failures than PLs <5 mm. Provides the reference benchmark for the clinical benefit of GTR in large periapical lesions.
Pantchev et al., 2009[32]	Retrospective comparative	186 lesions (Control: 110; PerioGlas: 76)	PL (>5 mm)	> 5 mm	PerioGlas® bone substitute	No bone substitute	9–48 months	Alloplastic graft (PerioGlas®)	Periapical radiograph	Control (no graft): Total, 56.4% | Partial, 41.8% | Failed, 1.8% PerioGlas®: Total, 72.0% | Partial, 22.7% | Failed, NR → PerioGlas® improved complete healing by 15.6% vs. control in PLs >5 mm. The difference was not statistically significant (p>0.05).
Bieszczad et al., 2023[9]	Retrospective comparative	176 lesions (PL: 126; AML: 35; TTL: 15)	PL; AML; TTL	N/A	GTR (membrane ± graft)	No GTR	6–12 months	Membrane ± graft (NR)	CBCT	PL without GTR: Total, 43.9% | Partial, 8.8% | Failed, 1.8% PL with GTR: Total, 85.5% | Partial, 2.9% | Failed, 0% AML without GTR: Total, 33.3% | Partial, 26.7% | Failed, 13.3% AML with GTR: Total, 45.0% | Partial, 15.0% | Failed, 15.0% TTL without GTR: Total, 0% | Partial, 33.3% | Failed, 0% TTL with GTR: Total, 83.3% | Partial, 8.3% | Failed, 0% → GTR markedly improved complete healing in PLs (+41.6%) and TTLs (+83.3%), and eliminated failures in both. Effect on AMLs was modest.

AML – Apicomarginal lesion; CBCT – Cone-beam computed tomography; DFDBA – Demineralized freeze-dried bone allograft; Exp. – Experimental group; FDBA – Freeze-dried bone allograft (mineralized); GTR – Guided tissue regeneration; i-PRF – Injectable platelet-rich fibrin; L-PRF – Leukocyte- and platelet-rich fibrin; PL – Periapical lesion; MTA – Mineral trioxide aggregate; N/A – Not applicable (lesion size not assessed in study); NR – Not reported; PGA – Polyglycolic acid; PRF – Platelet-rich fibrin; PRP – Platelet-rich plasma; RCT – Randomized controlled trial; TTL – Through-and-through lesion. Bio-oss is an anorganic bovine bone mineral (Bio-Oss®, Geistlich Pharma AG, Wolhusen, Switzerland); PerioGlass is a bioactive glass (PerioGlas®, NovaBone Products LLC, Alachua, FL, USA).

* Study samples: these reflect the unit of analysis used by each study (patients, teeth, or lesions). Where available, both are reported to facilitate comparison.

Healing rate categories follow Alkandari et al. (2024): Total = complete resolution of periapical defect; Partial = reduction in defect size without complete fill; Failed = no change or enlargement of defect.

low risk of bias,[28,30] 11 as having a moderate risk of bias,[9,10,12,14,22–24,27,31–33] and 5 as having a high risk of bias,[2,3,13,25,34] which compromises the reliability of their conclusions. Therefore, the overall evidence analyzed in this systematic review can be considered to present a moderate to high methodological risk. The detailed risk of bias assessment is presented in Tables 3 and 4.

Assessment using the GRADE framework indicated an overall certainty of evidence ranging from low to very low due to the moderate to high risk of bias across included studies, heterogeneity in study design and regenerative approaches, and variability in outcome definitions and follow-up periods. Additional downgrading was attributed to imprecision and indirectness (Table 5).

Discussion

A critical appraisal of the total evidence reveals that regenerative adjuncts have not consistently produced superior clinical or radiographic outcomes compared to conventional apical microsurgery across all defect types. This finding is consistent with the overall low-to-very-low certainty of evidence assigned by the GRADE assessment and reflects the substantial methodological heterogeneity across studies in terms of study design, defect morphology, biomaterial selection, surgical protocols, follow-up periods, and outcome definitions. The most plausible interpretation of the available data is that regenerative approaches may offer a tendency towards improved healing in specific, complex defect subsets,

Table 3. Risk of bias assessment (RoB 2.0, Cochrane Collaboration) for randomized controlled trials.

Article	D1	D2	D3	D4	D5	D6	Overall
Taschieri et al., 2007[12]	+	!	+	+	+	+	!
Garrett et al., 2002[13]	+	!	+	-	+	+	-
Parmar et al., 2019[14]	+	!	+	+	+	+	!
Garg et al., 2023[3]	-	-	+	+	+	+	-
Dhiman et al., 2015[28]	+	+	+	+	+	+	+
Pecora et al., 2001[2]	!	-	+	!	+	+	-
Goyal et al., 2011[22]	!	+	+	+	+	+	!
Marín-Botero et al., 2006[30]	+	!	+	+	+	+	+
Karan et al., 2020[23]	+	!	+	!	+	+	!
Sharma et al., 2025[25]	!	-	+	+	+	+	-
Albagle et al., 2023[34]	!	-	+	+	+	+	-
Dhamija et al., 2024[31]	+	!	+	+	+	+	!
Arpitha et al., 2023[24]	+	!	+	+	+	+	!

Domains: D1 – Randomization process; D2 – Allocation concealment; D3 – Deviations from intended interventions; D4 – Missing outcome data; D5 – Outcome measurement; D6 – Selective reporting. Color-coded system: + – low risk; ! – some concerns; - – high risk.

Table 4. Risk of bias assessment (ROBINS-I, Risk of Bias in Non-randomized Studies of Interventions, adapted from Cochrane).

Article	D1	D2	D3	D4	D5	D6	D7	Overall
Dietrich et al., 2003[33]	!	!	+	+	+	!	+	!
Alkandari et al. 2024[27]	!	-	+	+	+	!	+	!
Arx et al., 2007[10]	!	+	+	+	+	!	+	!
Pantchev et al., 2009[32]	!	-	+	+	!	!	+	!
Bieszczad et al., 2023[9]	!	-	+	+	!	!	+	!

Domains: D1 – Confounding; D2 – Participant selection; D3 – Intervention classification; D4 – Deviations from intended interventions; D5 – Missing outcome data; D6 – Outcome measurement; D7 – Selective reporting. Color-coded system: + – low risk; ! – some concerns; - – high risk.

particularly large periapical lesions and through-and-through lesions. However, this benefit is not universal and remains to be confirmed by high-quality RCTs with standardized outcome criteria.

The diversity of regenerative modalities evaluated across the included literature encompassed barrier membranes with or without bone graft substrates (GTR), platelet concentrates as biological adjuncts, xenogeneic grafts, and alloplastic materials. It is important to note that platelet concentrates and bone grafts represent fundamentally distinct regenerative strategies: bone graft materials provide structural support and osteoconductive scaffolding, whereas platelet concentrates function primarily as biological stimulators, enhancing angiogenesis and cellular recruitment through growth factor delivery. These categories should therefore be interpreted separately when evaluating clinical outcomes.

Across the included studies, barrier membranes used in GTR protocols showed a tendency towards more favorable healing outcomes in complex defects, although this trend was not consistently statistically significant. The findings suggest that membranes alone may not confer a clear advantage in through-and-through defects with 3–6-mm cavities.[13,14] In turn, one study revealed a potential benefit of combined GTR approaches in apicomarginal lesions.[25] The results of another study reinforced the relevance of defect morphology in treatment planning.[9]

Studies evaluating platelet concentrates as biological adjuncts yielded mixed results. The results of one RCT suggested that in well-contained periapical lesion defects, L-PRF and freeze-dried bone allograft may achieve equivalent outcomes.[3] Another RCT's findings indicated potential long-term advantages not captured at standard follow-up intervals.[31] Thus, given the limited number of studies with extended follow-up, caution is warranted in generalizing these findings.

Among alloplastic materials, there might be a potential benefit of calcium sulfate in through-and-through defects attributable to its space-maintaining and osteoconductive properties.[2] In contrast, bioactive glass results raise questions about its effectiveness as a sole regenerative adjunct.[32] With regard to xenogeneic grafts, the absence of a control group limited the strength of high healing-rate results.[33]

Lesion morphology emerged as one of the most consistent and clinically relevant prognostic variables across the included studies. Findings suggest that the potential benefit of GTR is likely to be most pronounced in larger or morphologically complex defects.[5,9,10] Taken together, the available evidence suggests that lesions smaller than approximately 3 mm may heal predictably with conventional surgery alone, whereas defects exceeding this threshold, particularly through-and-through lesions and apicomarginal lesions, may benefit from adjunctive GTR strategies in selected clinical situations. However, these thresholds should not be interpreted as universal

Table 5. Summary of the certainty of evidence using the GRADE (Grading of Recommendations Assessment, Development and Evaluation) approach for the main outcomes of the systematic review.

Outcome	Certainty of evidence	Downgrading factors
Clinical success	low	Risk of bias, heterogeneity, imprecision
Radiographic success	low	Risk of bias, heterogeneity, indirectness
Periapical bone regeneration	Very low	High heterogeneity, risk of bias, imprecision, indirectness

clinical rules, as the underlying evidence derives largely from studies with moderate to high risk of bias.

The radiographic assessment method used significantly influenced the reported healing outcomes. Most included studies relied on 2D periapical radiography, which may substantially overestimate complete healing compared to CBCT. The radiopacity of certain graft materials, particularly slowly resorbing xenogeneic grafts, may further confound radiographic interpretation by obscuring the distinction between residual graft and newly formed bone. In this context, CBCT represents a more reliable assessment method and, where feasible, should be combined with histological validation to confirm true tissue quality. Future studies should prioritize CBCT-based outcomes and adopt standardized radiographic indices to improve comparability across studies.

The overall evidence analyzed in this systematic review can be considered to present a moderate to high methodological risk, reinforcing the need for future studies with greater methodological rigor, standardization, and longer follow-up periods.

Several methodological limitations must be considered when interpreting the systematic review's results. The search was conducted across five databases: PubMed, Scopus, ScienceDirect, Cochrane Library, and Wiley Library. EMBASE could not be searched despite multiple attempts to secure access, including institutional requests and a free-trial registration that granted access only to ScienceDirect; this is acknowledged as a limitation that may have prevented identification of additional eligible studies. A complementary search of ClinicalTrials.gov was performed using the terms "apical surgery" and "regeneration," identifying one ongoing trial (NCT06734962) comparing advanced platelet-rich fibrin (A-PRF) with standard apical surgery for periapical bone regeneration; as this trial has not yet reported results, it could not be included in the present synthesis but supports the relevance of this review topic. Moreover, a formal grey literature search was not performed, as this review was restricted to peer-reviewed clinical studies. These combined omissions may have prevented the identification of relevant unpublished or ongoing studies, potentially introducing a degree of publication bias, and represent a residual limitation to consider when interpreting the certainty of the evidence presented in this review.

The inclusion of radiographic terminology as a mandatory ("AND") component of the search strings, while intended to capture imaging-based outcome data, is recognized as a major limitation of this review rather than a minor retrieval caveat. This approach may have excluded clinically relevant studies, particularly those reporting clinical success or symptom resolution without explicit radiographic terminology in the title, abstract, or keywords, and this should be considered when interpreting the comprehensiveness and certainty of the evidence synthesized in this review. A re-run of the search without this term was not feasible within the timeframe of this revision; future updates to this review should consider repeating the search without this restriction to confirm whether additional eligible studies emerge.

Most included studies had small sample sizes and relatively short follow-up periods of 6–12 months, which may be insufficient to capture the long-term biological stability of regenerated tissues. A minimum follow-up of 6 months was adopted as the eligibility threshold to reflect early post-surgical healing assessment, but future research should raise it to at least 12 months to allow adequate maturation of regenerated bone. Additional limitations include patient attrition, lack of blinding, heterogeneity in outcome definitions, and variability in surgical protocols, all of which reduce comparability across studies. Furthermore, the overall evidence base presented a moderate to high methodological risk.

The findings of this review highlight the need for well-designed, adequately powered RCTs with longer follow-up periods (≥12 months), standardized outcome criteria, and the routine use of CBCT-based assessment. Future studies should also ensure consistent reporting of defect morphology, cavity size, and biomaterial category, distinguishing between structural grafts and platelet concentrates, to enable meaningful comparisons across intervention types. Moreover, stratification of outcomes by lesion type (periapical lesions, apicomarginal lesions, through-and-through lesions), defect size, and imaging modality would substantially improve the interpretability and clinical applicability of future evidence.

Conclusions

This review identified the main factors potentially influencing the outcomes of regenerative techniques applied in apical surgery, based on the currently available scientific evidence. In general, combined regenerative approaches involving grafts, membranes, and biological stimulation may provide more favorable outcomes in complex defects, particularly in apicomarginal and through-and-through lesions. However, the evidence remains heterogeneous, and several included studies reported non-significant differences between regenerative and conventional approaches. Small lesions may heal predictably following conventional apical surgery without the need for additional regenerative procedures.

The findings suggest that multifactorial regenerative strategies integrating physical barriers, structural support, and biological stimulation may represent a promising therapeutic approach in selected clinical situations. Nevertheless, treatment selection should be individualized according to lesion morphology, clinical presentation, and available resources. Due to the methodological limitations and heterogeneity of the included studies, further well-designed RCTs with long-term follow-up and standardized outcome assessment are required to strengthen the current evidence base.

Conflict of interest

The authors have no conflicts of interest to declare.

Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this study.

Confidentiality of data. The authors declare that no patient data appear in this article.

Right to privacy and informed consent. The authors declare that no patient data appear in this article.

CRediT authorship contribution statement

Alexandra Simões: Conceptualization; Data curation; Formal analysis; Investigation; Methodology; Visualization; Writing – original draft. **João Pedro Carvalho:** Data curation; Formal analysis; Investigation; Visualization; Writing – review & editing. **Tiago Silva:** Conceptualization; Methodology; Project administration; Resources; Supervision; Writing – review & editing. **António Melo-Ferraz:** Supervision; Validation. **Paulo Miller:** Conceptualization; Methodology; Project administration; Resources; Supervision; Validation; Writing – review & editing.

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Estratégias regenerativas na cirurgia apical com e sem biomateriais: revisão sistemática

RESUMO

Objetivos: Esta revisão sistemática compara a eficácia clínica e os resultados radiográficos da regeneração com base em membrana, enxerto ósseo e concentrados plaquetários em cavidades resultantes de apicectomia, avaliando as taxas de cicatrização e a qualidade do osso neoformado.

Métodos: De acordo com as diretrizes PRISMA 2020, foi realizada uma pesquisa bibliográfica nas bases de dados PubMed, Cochrane Library, ScienceDirect, Wiley e Scopus para artigos publicados entre janeiro de 2000 e dezembro de 2025. Os critérios de elegibilidade foram definidos com base no modelo PICOS, e os estudos incluídos foram avaliados segundo parâmetros clínicos e radiográficos, com um período de acompanhamento mínimo de seis meses.

Resultados: Foram incluídos dezoito estudos clínicos. Os resultados foram heterogéneos e de certeza predominantemente baixa a muito baixa. Embora alguns estudos sugiram potenciais benefícios dos adjuvantes regenerativos em defeitos complexos, como lesões periapicais transfixantes e lesões apicomarginais, uma proporção substancial não encontrou vantagem estatisticamente significativa em relação à cirurgia apical convencional. Lesões pequenas (<3 mm) apresentaram, em geral, boa resposta à cirurgia convencional, enquanto defeitos maiores podem beneficiar de abordagens regenerativas adjuvantes em situações clínicas selecionadas.

Conclusões: Globalmente, a evidência disponível sugere um potencial benefício da combinação de suporte físico (biomateriais) e estimulação biológica (fibrina rica em plaquetas) na cirurgia apical regenerativa. Contudo, os resultados são heterogéneos e devem ser interpretados com cautela. A seleção da técnica deve considerar a morfologia do defeito, as características da lesão e os recursos disponíveis. São necessários mais estudos estandardizados e metodologicamente robustos para reforçar a base de evidência atual. (Rev Port Estomatol Med Dent Cir Maxilofac. 2026;67(x):xxx-xxx)

Palavras-chave:
Apicectomia
Materiais biocompatíveis
Regeneração óssea
Diagnóstico por imagem
Regeneração tecidular guiada
Periodontite periapical
Fibrina rica em plaquetas
Radiografia