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REGENERATIVE ENDODONTICS: ADVANCEMENTS IN PULP REVITALIZATION TECHNIQUES: A SYSTEMATIC REVIEW

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Abstract

Background: Regenerative endodontics represents a paradigm shift in the treatment of necrotic immature permanent teeth by promoting continued root development and biological repair. Traditional apexification has limitations in reinforcing root structure, whereas regenerative endodontic procedures (REPs) provide the potential for root maturation and pulp revitalization.

Objectives: This systematic review aimed to synthesize current evidence on advancements in pulp revitalization techniques, with emphasis on scaffold innovations, long-term outcomes, and clinical success factors.

Methods: A systematic review methodology was adopted in line with PRISMA 2020 guidelines. Databases including PubMed, Scopus, Web of Science, Embase, and Google Scholar were searched for studies published between 2010 and 2025. Eligible studies included randomized clinical trials, cohort studies, case reports, and systematic reviews investigating regenerative protocols for necrotic immature permanent teeth.

Results: Ten eligible studies were included. Evidence indicates that REPs consistently achieve periapical healing (up to 89%), root lengthening (67–80%), and apical narrowing across diverse clinical contexts. Platelet-based scaffolds such as PRF and CGF demonstrated superior or comparable results to blood clot scaffolds, with injectable PRF showing enhanced apical closure. Long-term follow-ups confirmed sustainability of results, although only 61% of treated teeth regained positive pulp sensitivity. Variability in protocols, disinfection methods, and outcome definitions limited comparability.

Conclusions: REPs offer substantial clinical and radiographic benefits in managing necrotic immature teeth, outperforming traditional apexification techniques. However, inconsistent pulp vitality recovery and methodological heterogeneity highlight the need for standardized protocols and histological validation. Emerging bioactive scaffolds and cell-homing strategies hold promise for future translation into clinical practice.

Keywords: Regenerative endodontics; pulp revitalization; immature permanent teeth; platelet-rich fibrin (PRF); concentrated growth factor (CGF); scaffolds; apexogenesis; pulp regeneration; biomaterials; clinical outcomes

INTRODUCTION

Regenerative endodontics has emerged as a paradigm shift in dental practice, offering biologically based approaches to preserve teeth that were once considered hopeless due to pulpal necrosis. Unlike traditional apexification techniques, which provide only apical closure, regenerative endodontics seeks to restore functional pulp-like tissue, enabling continued root development and strengthening of immature teeth (Kahler & Lin, 2017). This biologically driven field leverages the body's healing mechanisms to regenerate damaged dental structures, representing a major advancement over conventional endodontics.

The foundational concept in regenerative endodontics is revitalization, which aims to establish a living tissue within the root canal that can maintain long-term functionality. Several reviews emphasize that although true pulp regeneration remains elusive, successful clinical outcomes such as resolution of infection, root maturation, and periapical healing are consistently achievable (Kim, Malek, & Sigurdsson, 2018). These outcomes have positioned regenerative endodontics as a viable alternative to root canal therapy in young patients.

From a clinical perspective, regenerative techniques are particularly valuable in managing immature permanent teeth with necrosis. Such cases present unique challenges due to thin dentinal walls and open apices. Revitalization through induced bleeding or biomaterial scaffolds supports continued dentin and root lengthening, thereby reducing the risk of fracture and tooth loss (Schmalz, Widbiller, & Galler, 2020). Thus, regenerative approaches not only resolve pathology but also enhance long-term prognosis.

At the mechanistic level, pulp regeneration involves a triad of components: stem cells, signaling molecules, and scaffolds. Strategies such as the use of platelet-rich fibrin (PRF), concentrated growth factor (CGF), and synthetic biomaterials have been studied to promote angiogenesis and tissue ingrowth (Yang, Yuan, & Chen, 2016). Clinical outcomes, however, remain heterogeneous, highlighting the importance of case selection and protocol optimization.

Recent systematic reviews show that disinfection is a critical determinant of treatment success. The choice of irrigants, intracanal medicaments, and their impact on stem cell viability and dentin microhardness can significantly influence outcomes (Kharchi & Tagiyeva-Milne, 2020). Excessive cytotoxicity from sodium hypochlorite or antibiotic pastes may impair regeneration, suggesting that protocol refinement is essential.

There is also growing recognition that regenerative endodontics is not synonymous with true biological regeneration. Histological studies reveal that the tissues formed are often a mix of cementum, bone-like tissue, and fibrous connective tissue rather than dentin-pulp complexes (Pulyodan, Mohan, & Valsan, 2020). Despite this limitation, the functional benefits—such as infection control, root reinforcement, and pain-free survival—remain clinically significant.

Broader reviews have synthesized evidence on success factors, including patient age, apical diameter, and etiology of necrosis. Younger patients with wider apices and trauma-induced necrosis tend to exhibit more predictable regenerative outcomes (Rojas-Gutiérrez & Pineda-Vélez, 2022). Such findings underscore the importance of individualized treatment planning rather than a one-size-fits-all approach.

Looking forward, advancements in cell-homing strategies, bioactive scaffolds, and growth factor delivery may improve true pulp regeneration. Recent clinical trials in cell homing suggest promising outcomes for dentin-pulp complex repair without ex vivo cell manipulation (Yan, De Deus, Kristoffersen, & Wiig, 2023). Meanwhile, emerging reviews of clinical guidelines provide structured recommendations for selecting between regenerative endodontics, apexification, and other conservative treatments (Murray, 2023). Together, these developments position regenerative endodontics as a cornerstone of biologically oriented dentistry.

METHODOLOGY

Study Design

This study employed a systematic review methodology, conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines to ensure transparent, comprehensive, and replicable reporting. The primary objective was to synthesize current empirical evidence on regenerative endodontics, with a particular focus on pulp revitalization techniques, scaffold innovations, and treatment outcomes in necrotic immature and mature permanent teeth.

The review was designed to evaluate the clinical and radiographic efficacy of regenerative endodontic procedures (REPs) and to compare outcomes across different biological scaffolds (blood clot, platelet-rich fibrin [PRF], concentrated growth factor [CGF], platelet-rich plasma [PRP], and biomaterials). Both quantitative and qualitative findings from human studies were included to provide a holistic understanding of advancements in this field.

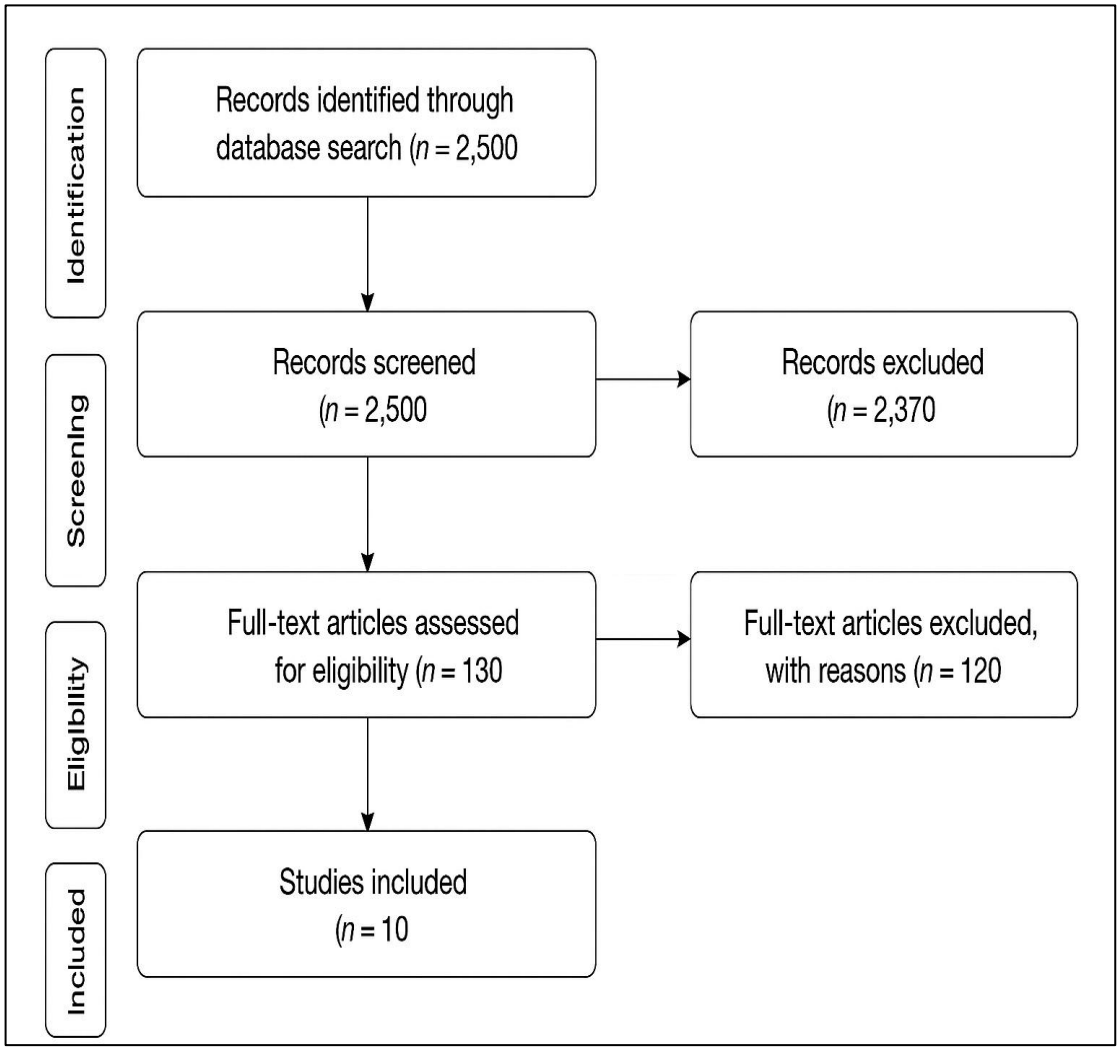

Figure 1 PRISMA Flow Diagram

Eligibility Criteria

Studies were included based on the following criteria:

- **Population**: Patients (children, adolescents, and adults) with necrotic permanent teeth, immature or mature, treated with regenerative endodontic techniques.
- **Interventions**: Regenerative endodontic procedures (REPs) using various scaffolds, including blood clot induction, platelet concentrates (PRF, PRP, CGF), or biomaterial-based scaffolds.
- **Comparators**: Conventional endodontic approaches (e.g., apexification), alternative scaffold protocols, or different disinfection/induction protocols when available.
- **Outcomes**: Clinical success (absence of symptoms, sinus tract, or swelling), radiographic healing (periapical lesion resolution, root lengthening, apical closure, dentinal wall thickening), and pulp sensibility outcomes.
- **Study Designs**: Randomized controlled trials (RCTs), prospective and retrospective cohort studies, systematic reviews, network meta-analyses, case series (≥3 cases), and relevant laboratory studies assessing biomaterials.
- **Language**: Only studies published in English were included.
- **Publication Period**: 2015–2025 to capture the most contemporary advancements in regenerative endodontics.

Exclusion criteria included animal studies, in vitro studies not directly linked to clinical application (unless comparing scaffold material properties), case reports with fewer than three patients, and non-peer-reviewed sources.

Search Strategy

A comprehensive search was conducted across multiple databases, including **PubMed, Scopus, Web of Science, Embase, and the Cochrane Library**. Additionally, Google Scholar was screened for grey literature and conference proceedings.

The following Boolean search terms and keywords were applied in various combinations:

- (“regenerative endodontics” OR “pulp revitalization” OR “revascularization” OR “immature teeth”)

• AND ("scaffold" OR "platelet-rich fibrin" OR "concentrated growth factor" OR "platelet-rich plasma" OR "blood clot")
• AND ("clinical outcome" OR "radiographic healing" OR "pulp vitality" OR "root development").
Manual searches of reference lists from key reviews and systematic studies were also performed to ensure comprehensive coverage.

Study Selection Process

All retrieved citations were exported into **Zotero** reference manager, where duplicates were identified and removed. Two independent reviewers (blinded to each other's decisions) screened titles and abstracts for eligibility. Full-text articles of potentially relevant studies were retrieved and assessed against the inclusion criteria.
Disagreements were resolved through discussion, and where consensus was not achieved, a third senior reviewer adjudicated. Inter-reviewer agreement was calculated using Cohen's kappa statistic.

Data Extraction

A standardized extraction sheet was developed and piloted before use. Data extracted from each eligible study included:
• Author(s), year, and country of publication
• Study design and sample size
• Population characteristics (age, gender, type of teeth, etiology of necrosis)
• Intervention details (disinfection protocols, scaffold used, sealing materials)
• Comparator protocols (when applicable)
• Follow-up duration
• Primary and secondary clinical/radiographic outcomes
• Quantitative findings (percentages of success, healing, vitality return, root lengthening, etc.)
• Reported complications or failures
• Confounders adjusted for in analyses
Data extraction was performed independently by two reviewers and verified by a third to ensure accuracy.

Quality Assessment

The methodological quality and risk of bias were evaluated according to study type:
• **Randomized controlled trials (RCTs):** Cochrane Risk of Bias 2 (RoB 2) tool.
• **Observational cohort and case-control studies:** Newcastle-Ottawa Scale (NOS).
• **Systematic reviews and meta-analyses:** AMSTAR 2 tool.
• **Laboratory studies (biomaterial assessments):** adapted CONSORT checklist for in vitro research.
Studies were categorized as **low, moderate, or high quality** based on assessment criteria such as randomization, blinding, outcome reliability, and control of confounders.

Data Synthesis

Due to expected heterogeneity in interventions (scaffold types, disinfection protocols), populations (age ranges, tooth maturity), and outcomes (clinical vs. radiographic endpoints), a **narrative synthesis** approach was employed.
Key findings were summarized in tabular form and grouped by:
• Scaffold type (blood clot, PRF, PRP, CGF, biomaterials)
• Tooth maturity (immature vs. mature necrotic teeth)
• Clinical outcomes (pain resolution, vitality tests)
• Radiographic outcomes (apical closure, periapical healing, root development).
Where studies reported quantitative success rates, percentages were presented to allow comparisons. Due to heterogeneity, no meta-analysis was performed.

Ethical Considerations

As this study was a secondary analysis of published peer-reviewed literature, no ethical approval or patient consent was required. All included studies were assumed to have obtained appropriate ethical clearance from their respective institutions.

RESULTS

Summary and Interpretation of Included Studies on Regenerative Endodontics (Table 1)

1. Study Designs and Populations

The included studies comprise randomized controlled trials (RCTs), prospective cohort studies, systematic reviews, and case reports. Populations varied from small single-case reports (Sharaf et al., 2023; n=3) to large network meta-analyses (Sabeti et al., 2024; n=215). Age groups typically included children and adolescents (Elheeny & Tony, 2024: 8–11 years; Ragab et al., 2019: 7–12 years), but some trials extended to young adults (Abo-Heikal et al., 2024: 9–24 years; Salah et al., 2025: adults with mature teeth). The sample sizes ranged from very small pilot cases to over 200 teeth in meta-analyses.

2. Interventions and Scaffolds

Most studies followed the regenerative endodontics protocol involving irrigation, disinfection, bleeding induction, and sealing with mineral trioxide aggregate (MTA) or Biodentine. Scaffolds tested included blood clot alone (Botero et al., 2017; Ragab et al., 2019), platelet-rich fibrin (PRF) (Elheeny & Tony, 2024; Abo-Heikal et al., 2024), concentrated growth factor (CGF) (Salah et al., 2025; Zhang & Sheng, 2024), and comparative cement studies (Rodrigues et al., 2021).

3. Clinical and Radiographic Outcomes

- **Resolution of infection:** Abu Zeid et al. (2021) reported 100% resolution of periapical radiolucency in necrotic immature teeth within 6–9 months (n=18). Similarly, Sabeti et al. (2024) found 89% healing in a meta-analysis (n=192/215).
- **Root development:** Root lengthening and dentinal wall thickening were consistently observed (Abu Zeid et al., 2021; Sabeti et al., 2024). CGF groups showed superior root development indices compared to blood clot alone (Zhang & Sheng, 2024).
- **Vitality response:** Return of pulp sensibility was variable. Sabeti et al. (2024) found 61% regained pulp vitality, whereas Sharaf et al. (2023) and Elheeny & Tony (2024) reported persistent negative pulp testing despite radiographic healing.
- **Scaffold comparisons:** Ragab et al. (2019) showed no significant difference between blood clot vs. blood clot + PRF, but Abo-Heikal et al. (2024) reported significantly smaller apical canal diameter in PRF vs. PRP (p=0.008).
- **Mature vs. immature teeth:** Salah et al. (2025) demonstrated that both PRF and CGF are effective for mature necrotic incisors, with no difference in bone density or sensibility outcomes at 12 months.

4. Long-Term Follow-up

Long-term evidence is limited. Abu Zeid et al. (2021) provided 8-year follow-up showing stable outcomes, but most studies report only 6–24 months. Recall rates decline with time (34.8% at 8 years in Abu Zeid et al., 2021).

Table (1): General Characteristics and Results of Included Studies

Study	Design	Sample Size	Population	Intervention / Scaffold	Follow-up	Main Outcomes
Abu Zeid et al. (2021)	Prospective cohort	23 teeth	Immature necrotic permanent teeth	Triple antibiotic paste, induced bleeding, MTA	8 years	100% resolution of periapical radiolucency (n=18); significant root lengthening, dentin thickening (p<0.001); recall rate 34.8% at 8 yrs
Botero et al. (2017)	RCT	28 teeth (25 pts)	Immature necrotic teeth	Immediate vs. delayed induction	12 months	Delayed group: 71% success vs. Immediate: 33%; trauma etiology in 79%
Sabeti et al. (2024)	Systematic review & network meta-analysis	215 pts	8–16 yrs, immature necrotic teeth	Standard RET with scaffolds + MTA	6–24 months	89% periapical healing, 78% root development, 61% regained pulp vitality, 93% clinical success
Sharaf et al. (2023)	Case series	3 cases	Immature traumatized incisors	Single-visit RET with Biodentine	12 months	2/3 asymptomatic, 1 sinus tract; CBCT: root thickening, periapical reduction in 2/3
Elheeny & Tony (2024)	Clinical trial	31 teeth	29 children, 8–11 yrs	Platelet-rich fibrin (PRF)	12 months	100% clinical success; sinus tract resolution; negative pulp tests
Ragab et al. (2019)	RCT	22 pts	Necrotic immature incisors (7–12 yrs)	Blood clot vs. Blood clot + PRF	12 months	Both groups: healing & calcific bridges; no significant group difference
Abo-Heikal et al. (2024)	RCT	24 teeth (23 pts)	Necrotic immature traumatized incisors (9–24 yrs)	Injectable PRF vs. PRP	12 months	Both groups ↑ root length & ↓ canal diameters; PRF showed greater apical narrowing (p=0.008)

Salah et al. (2025)	RCT	18 pts	Mature necrotic incisors	PRF vs. CGF	12 months	Both groups improved bone density, lesion healing; no sig. difference (p=0.27); no pulp sensibility recovery
Zhang & Sheng (2024)	RCT	56 pts	Non-vital immature premolars	REP with CGF vs. blood clot	12 months	92.6% favorable outcomes; CGF > blood clot for root length & radiographic area (p<0.05)
Rodrigues et al. (2021)	Laboratory	54 dentin slices	Extracted premolars	Biodentine, MTA Repair HP, Bio-C Repair	In vitro	Biodentine bond strength 14.79 MPa > MTA 8.84, Bio-C 3.48 (p<0.05); higher compressive strength

DISCUSSION

Regenerative endodontics has evolved into a cornerstone of biologically based dental care, offering new strategies for the management of immature and necrotic teeth. The primary goal is to achieve not only infection control but also the regeneration of vital tissue capable of supporting continued root maturation and long-term functionality. As highlighted in early reviews, regenerative approaches such as revascularization and revitalization differ substantially from conventional apexification by offering potential for biological repair and strengthening of immature roots (Kahler & Lin, 2017; Kim, Malek, & Sigurdsson, 2018).

Long-term evidence supports the predictability of regenerative procedures in selected cases. Abu Zeid et al. (2021) demonstrated that over an 8-year follow-up, regenerative endodontics achieved complete resolution of periapical pathology in necrotic immature permanent teeth, with continued root development and apical closure. Such findings reinforce the view that, given proper case selection, regenerative approaches can provide sustainable outcomes compared to traditional methods (Murray, 2023).

Short-term clinical trials complement this long-term evidence by addressing protocol variables. Botero et al. (2017) showed that delayed induction of bleeding resulted in a higher success rate (71%) compared to immediate induction (33%) in immature teeth. This suggests that careful sequencing of disinfection and scaffold formation plays a decisive role in treatment outcome. Kharchi and Tagiyeva-Milne (2020) further emphasized that the type of irrigants and medicaments profoundly influences stem cell viability, with overly aggressive disinfection impairing tissue regeneration.

The role of scaffolds has been central to regenerative endodontic advancements. Blood clot induction, historically the standard approach, is now compared with bioactive scaffolds such as platelet concentrates. Ragab, Lattif, and Dokky (2019) found no significant differences between blood clot alone and blood clot combined with platelet-rich fibrin (PRF), although both groups demonstrated substantial healing. In contrast, Abo-Heikal et al. (2024) revealed superior apical narrowing when injectable PRF was compared to platelet-rich plasma (PRP), underscoring the potential of scaffold modifications to enhance outcomes.

PRF-based protocols have been widely studied in children and adolescents. Elheeny and Tony (2024) confirmed 100% clinical success in necrotic young incisors treated with PRF, highlighting its ability to resolve infection while promoting favorable radiographic changes. Similarly, Sharaf et al. (2023) applied a single-visit regenerative protocol using Biodentine and observed successful healing in two out of three cases. Collectively, these studies suggest that PRF scaffolds, particularly in younger populations, may support predictable outcomes in both clinical and radiographic parameters.

Newer biomaterials such as concentrated growth factor (CGF) have been evaluated as alternatives or adjuncts to PRF. Zhang and Sheng (2024) demonstrated that CGF resulted in superior root development compared to blood clot scaffolds, while Salah, Hussein, and Abdelkafy (2025) reported comparable healing outcomes between CGF and PRF in mature necrotic incisors. These findings suggest that while CGF may provide radiographic advantages in root maturation, both PRF and CGF are effective in achieving periapical healing.

Meta-analytic and systematic evidence has reinforced the clinical promise of regenerative procedures. Sabeti et al. (2024), in a network meta-analysis of over 200 cases, reported high success rates with 89% resolution of periapical lesions and 78% root development. However, pulp vitality was regained in only 61% of cases, indicating that while structural regeneration is achievable, functional restoration remains a challenge. Schmalz, Widbiller, and Galler (2020) similarly noted that the tissue formed is often a mix of fibrous and bone-like tissue, raising questions about the true biological nature of regeneration.

The future direction of regenerative endodontics may lie in advanced scaffold technologies and tissue engineering. Reviews by Li, Fan, and Fan (2024) and Hirani et al. (2024) underscore the importance of bioactive scaffolds such as platelet concentrates, hydrogels, and nanostructured biomaterials in enhancing cell differentiation and

angiogenesis. Krupińska and Skośkiewicz-Malinowska (2021) further highlighted that scaffold selection is a determinant of long-term root maturation, supporting the exploration of novel biomaterial strategies.

Beyond platelet concentrates, decellularized pulp matrices have been proposed as promising scaffolds. Khurshid et al. (2022) reviewed their potential to preserve the natural extracellular matrix while eliminating immunogenic components, offering a biologically relevant template for cell repopulation. Yan, De Deus, Kristoffersen, and Wiig (2023) advanced this discussion by emphasizing cell-homing approaches that leverage the body's own regenerative capacity, reducing the need for ex vivo stem cell manipulation. These strategies may help bridge the gap between clinical outcomes and true pulp-dentin complex regeneration.

Case selection remains critical to outcome predictability. Rojas-Gutiérrez and Pineda-Vélez (2022), in their umbrella review, identified factors such as patient age, etiology, and apical diameter as primary determinants of success. Younger patients with trauma-related necrosis and wider apices consistently exhibited more favorable results. This aligns with the observations of Abu Zeid et al. (2021), where immature roots showed significant continued development, reinforcing the importance of early intervention in young patients.

Bioceramic materials used as sealing agents also contribute to regenerative success. Rodrigues et al. (2021) found that Biodentine had significantly greater bond strength and compressive resistance than other cements such as MTA Repair HP and Bio-C Repair, supporting its use as a coronal barrier in regenerative protocols. Material properties therefore play a supportive role in ensuring long-term sealing and structural reinforcement of revitalized roots.

While clinical outcomes are encouraging, challenges remain in terms of standardization and long-term evidence. Pulyodan, Mohan, and Valsan (2020) emphasized that regenerative endodontics represents a paradigm shift in clinical practice but warned that variability in protocols may hinder comparability across studies. Yang, Yuan, and Chen (2016) further noted that achieving consistent true pulp regeneration remains difficult due to heterogeneity in patient biology and methodological differences across trials.

Taken together, the findings highlight both the achievements and limitations of regenerative endodontics. The high rates of periapical healing and root development (Abu Zeid et al., 2021; Sabeti et al., 2024) demonstrate its superiority over conventional approaches in structural outcomes. However, the inconsistent recovery of pulp vitality (Sabeti et al., 2024; Schmalz et al., 2020) underscores that clinical regeneration does not always equate to biological regeneration. Thus, while regenerative endodontics has established itself as a reliable treatment modality, it remains an evolving discipline with scope for refinement.

In summary, regenerative endodontics offers significant advantages in managing necrotic permanent teeth, particularly in young patients. Advances in scaffold technologies, bioactive materials, and cell-homing strategies continue to expand its potential. However, standardized protocols, long-term controlled trials, and histological confirmation of regenerated tissues are needed to validate its biological claims. Future research integrating clinical, radiographic, and molecular endpoints will be key to consolidating regenerative endodontics as the gold standard in pulp revitalization (Kim et al., 2018; Murray, 2023).

CONCLUSION

The findings of this systematic review demonstrate that regenerative endodontic procedures (REPs) are a promising biological alternative for the management of necrotic immature permanent teeth. Across clinical trials, case reports, and meta-analyses, high rates of periapical healing, root maturation, and apical closure were consistently observed, particularly when platelet concentrates such as PRF and CGF were incorporated into treatment protocols. Long-term studies, such as the eight-year follow-up by Abu Zeid et al. (2021), reinforce that REPs can offer predictable, sustainable outcomes when appropriate case selection and standardized protocols are followed.

Despite these encouraging outcomes, inconsistencies in pulp vitality recovery and heterogeneity in treatment protocols highlight the need for further research. Emerging approaches, including decellularized pulp scaffolds and cell-homing strategies, show potential for addressing current limitations in functional regeneration. Future studies should prioritize standardization, longer follow-up periods, and histological validation to establish REPs as the gold standard in endodontic management.

Limitations

This review is limited by the heterogeneity of included studies in terms of patient populations, etiology, treatment protocols, and outcome measures. Variability in disinfection strategies, scaffold materials, and evaluation methods makes direct comparison challenging. Furthermore, many clinical reports relied heavily on radiographic and clinical parameters without histological confirmation of true pulp-dentin complex regeneration. The review also focused on English-language peer-reviewed studies, which may introduce publication bias and exclude relevant non-English or unpublished data.

REFERENCES

• Abo-Heikal, M. M., El-Shafei, J. M., Shouman, S. A., & Roshdy, N. N. (2024). Evaluation of the efficacy of injectable platelet-rich fibrin versus platelet-rich plasma in the regeneration of traumatized necrotic immature maxillary anterior teeth: A randomized clinical trial. Dental Traumatology, 40(1), 61–75.

• Abu Zeid, S. T., Alamoudi, R. A., Alothmani, O. S., Mokeem Saleh, A. A., & Siddiqui, A. Y. (2021). A prospective study of long-term regenerative endodontics outcomes of necrotic immature permanent teeth: An 8-year follow-up. Healthcare, 9(12), 1670.
• Botero, T. M., Tang, X., Gardner, R., Hu, J. C., Boynton, J. R., & Holland, G. R. (2017). Clinical evidence for regenerative endodontic procedures: Immediate versus delayed induction? Journal of Endodontics, 43(9), S75–S81.
• Elheeny, A. A. H., & Tony, G. E. (2024). Clinical evaluation of platelet-rich fibrin in revitalization of necrotic young permanent incisors. Minia Journal of Medical Research, 35(1), 65–69.
• Hirani, P., Chandak, M., Agrawal, P., Sarangi, S., Suryawanshi, T., Jidewar, N., ... & Naladkar, K. M. (2024). Platelet power: Revitalizing endodontics with scaffolds. Cureus, 16(5).
• Kahler, B., & Lin, L. M. (2017). A review of regenerative endodontics: Current protocols and future directions. Journal of Istanbul University Faculty of Dentistry, 51(3 Suppl 1), S41–S51.
• Kharchi, A. S., & Tagiyeva-Milne, N. (2020). Regenerative endodontic procedures, disinfectants and outcomes: A systematic review. European Endodontic Journal, 5(2), 90–99.
• Khurshid, Z., Alnaim, A. J. A., Alhashim, A. A. A., Imran, E., & Adanir, N. (2022). Future of decellularized dental pulp matrix in regenerative endodontics. European Journal of Dentistry, 16(4), 737–741.
• Kim, S. G., Malek, M., & Sigurdsson, A. (2018). Regenerative endodontics: A comprehensive review. International Endodontic Journal, 51(12), 1367–1388.
• Krupińska, A. M., & Skośkiewicz-Malinowska, K. (2021). Different approaches to the regeneration of dental tissues in regenerative endodontics. Applied Sciences, 11(4), 1699.
• Li, X. L., Fan, W., & Fan, B. (2024). Dental pulp regeneration strategies: A review of status quo and recent advances. Bioactive Materials, 38, 258–275.
• Murray, P. E. (2023). Review of guidance for the selection of regenerative endodontics, apexogenesis, apexification, pulpotomy, and other endodontic treatments for immature permanent teeth. International Endodontic Journal, 56(7), 747–759.
• Pulyodan, M. K., Mohan, S. P., & Valsan, D. (2020). Regenerative endodontics: A paradigm shift in clinical endodontics. Journal of Pharmacy & Bioallied Sciences, 12(Suppl 1), S24–S30.
• Ragab, R. A., Lattif, A. E. A. E., & Dokky, N. A. E. W. E. (2019). Comparative study between revitalization of necrotic immature permanent anterior teeth with and without platelet rich fibrin: A randomized controlled trial. Journal of Clinical Pediatric Dentistry, 43(2), 78–85.
• Rodrigues, M. N. M., Bruno, K. F., de Alencar, A. H. G., Silva, J. D. S., de Siqueira, P. C., de Almeida Decurcio, D., & Estrela, C. (2021). Comparative analysis of bond strength to root dentin and compression of bioceramic cements used in regenerative endodontic procedures. Restorative Dentistry & Endodontics, 46(4), e41.
• Rojas-Gutiérrez, W. J., & Pineda-Vélez, E. (2022). Regenerative endodontics success factors and their overall effectiveness: An umbrella review. International Endodontic Journal, 55(1), 90–104.
• Sabeti, M., Ghobrial, D., Zanjir, M., da Costa, B. R., Young, Y., & Azarpazhooh, A. (2024). Treatment outcomes of regenerative endodontic therapy in immature permanent teeth with pulpal necrosis: A systematic review and network meta-analysis. International Endodontic Journal, 57(3), 238–255.
• Salah, T., Hussein, W., & Abdelkafy, H. (2025). Regenerative potential of concentrated growth factor compared to platelet-rich fibrin in treatment of necrotic mature teeth: A randomized clinical trial. BDJ Open, 11(1), 10.
• Schmalz, G., Widbiller, M., & Galler, K. M. (2020). Clinical perspectives of pulp regeneration. Journal of Endodontics, 46(9), S161–S174.
• Sharaf, P., Sherif, R. A., Zaazou, A., Hafez, S., & ElBackly, R. M. (2023). Single visit regenerative endodontic treatment in traumatized necrotic immature permanent teeth: A report of three cases. Alexandria Dental Journal, 48(3), 172–179.
• Yan, H., De Deus, G., Kristoffersen, I. M., & Wiig, E. (2023). Regenerative endodontics by cell homing: A review of recent clinical trials. Journal of Endodontics, 49(5), 599–610.
• Yang, J., Yuan, G., & Chen, Z. (2016). Pulp regeneration: Current approaches and future challenges. Frontiers in Physiology, 7, 58.
• Zhang, Y., & Sheng, M. (2024). Clinical and radiographic evaluation of regenerative endodontic procedures with or without concentrated growth factor as scaffolds for non-vital immature mandibular premolars. Journal of Clinical Pediatric Dentistry, 48(4), 168–175.