The Review Of
DIABETIC
STUDIES
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Operative Interventions For The Management Of Persistent Apical Periodontitis

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Abstract
Persistent apical periodontitis sticks around in roughly 10-20% of teeth even after solid root canal work, posing a real challenge in dental practice. This review gathered fresh data through October 2025 from key sources like PubMed, Scopus, and more, analyzing 47 studies—32 randomized trials plus 15 cohort follow-ups—tracking over 4,200 teeth for a minimum of one year. Success rates impressed: 91.5% healing with microsurgery using bioceramic retrofills, 87.2% via intentional replantation, and 93.4% through regenerative approaches in young teeth. Bigger lesions above 5 mm, full-thickness bone loss, and poor crown seals dragged results down. Today's microsurgery with sharp magnification, ultrasonic preps, advanced sealers, and cone-beam guidance beat traditional apicoectomy hands down, boosting outcomes by about 40%. Issues stayed rare under 4%, and over 96% of teeth remained in service past five years. In short, when retreatment without surgery flops or isn't feasible, modern endodontic microsurgery stands as the top choice for predictable, lasting recovery.

Keywords: Operative Interventions**,** Bioceramic Retrofills, Traditional Apicoectomy, Persistent Apical Periodontitis.

1. Introduction

1.1 Background and Clinical Significance

Persistent apical periodontitis (PAP) represents a chronic inflammatory lesion around the apex of a tooth that fails to resolve 12 months or more after adequate nonsurgical root canal treatment. Even with major advances in endodontic techniques, materials, and technology, persistent apical periodontitis still affects 10% to 20% of treated teeth across different populations. It poses a serious clinical challenge and requires careful judgment in choosing the right treatment strategy (Tibúrcio-Machado et al., 2021; Kirkevang et al., 2007).The clinical manifestations of PAP vary considerably, ranging from completely asymptomatic cases discovered during routine radiographic examination to symptomatic presentations with pain, swelling, sinus tract formation, or tenderness to percussion (Siqueira & Rôças, 2008). On X-rays, persistent apical periodontitis shows up as a dark area around the root tip that varies in size and shape, and when it hangs on, it means the tissues around the root haven't healed after the initial root canal treatment.

1.2 Etiopathogenesis of Persistent Apical Periodontitis

The persistence of apical periodontitis following root canal treatment is multifactorial and can be attributed to several key mechanisms (Siqueira & Rôças, 2022):

Intraradicular Infection:
- Persistent bacterial biofilms in anatomically complex areas including isthmuses, lateral canals, apical ramifications, and dentinal tubules
- Enterococcus faecalis and other resistant microorganisms capable of surviving in harsh environments
- Inadequate chemomechanical preparation leaving untreated canal spaces
- Missed canals or undetected anatomical complexities
- Iatrogenic complications including ledges, perforations, or separated instruments

Extraradicular Infection:
- Actinomyces species forming self-sustaining biofilms on the external root surface
- Periapical actinomycosis resistant to intracanal antimicrobial procedures
- Complex microbial communities in periradicular tissues (Siqueira & Rôças, 2022)

Foreign Body Reactions:
- Extruded endodontic filling materials (gutta-percha, sealer)
- Cholesterol crystals and immune complexes
- Endogenous materials (dentin chips, pulp stones)

True Periapical Cysts:
- Epithelial-lined cavities with self-sustaining inflammatory mechanisms
- Reduced vascul from intracanal treatment

Host-Related Factors:
- Impaired immune response
- Genetic predisposition affecting healing capacity
- Systemic conditions influencing periradicular healing

Understanding these etiological factors is essential for selecting appropriate treatment modalities and predicting treatment outcomes.

1.3 Treatment Decision-Making

The management of persistent apical periodontitis follows a hierarchical approach based on established principles (Friedman, 2002, 2005):

First-Line Approach: Nonsurgical retreatment remains the gold standard when feasible, offering the opportunity to address intracanal infection and correct deficiencies in the original treatment (Torabinejad et al., 2009).

Indications for Operative Intervention:
1. Persistent or recurrent disease despite adequate nonsurgical retreatment
2. Inaccessible root canal system (severe calcification, complex anatomy)
3. Presence of well-adapted posts or crowns where removal risks tooth fracture
4. Procedural errors (ledges, perforations, separated instruments) preventing orthograde retreatment
5. Root canal obstruction by foreign materials
6. Extra radicular infection (actinomycosis, foreign body reaction)
7. Suspected vertical root fracture (VRF) requiring verification
8. Patient factors (time constraints, anatomical limitations, previous retreatment failures)

Contraindications:
- Unrestorable tooth structure
- Vertical root fracture (in most cases)
- Advanced periodontal disease with poor prognosis

- Medical conditions contraindic surgical procedures
- Inadequate bone support
- Unfavorable anatomy precluding surgical access

1.4 Evolution of Surgical Endodontics

Traditional apicoectomy techniques employed before the 1990s were associated with relatively poor outcomes, with success rates ranging from 44% to 74% (Setzer et al., 2010). These conventional procedures typically involved:

- Limited or no magnification
- Large bevel angles (≥45°) on the resected root surface
- Bur preparation of root-end cavities
- Amalgam or zinc oxide-eugenol based retrofill materials
- Inadequate hemostasis and visualization

The evolution of endodontic microsurgery (EMS) has transformed surgical endodontics through the integration of several key technological and technical advances (Kim & Kratchman, 2006; Setzer & Kratchman, 2022):

1. **Surgical Operating Microscopes:** Providing high magnification (8-25×) with coaxial illumination and improved ergonomics
2. **Microsurgical Instruments:** Smaller, more precise instruments designed for minimally invasive procedures
3. **Ultrasonic Root-End Preparation:** Allowing precise cavity preparation following canal anatomy
4. **Bioactive Retrofill Materials:** Calcium silicate-based cements (MTA, Biodentine) with superior sealing ability and biocompatibility
5. **Cone Beam Computed Tomography (CBCT):** Enabling three-dimensional assessment and precise surgical planning

These advances have resulted in dramatically improved success rates, with contemporary studies reporting healing rates of 88-96% (Setzer et al., 2010, 2012; von Arx et al., 2012).

1.5 Rationale for This Review

While several narrative reviews and meta-analyses have evaluated surgical endodontic outcomes, there remains a need for a comprehensive systematic review that:

- Synthesizes the most recent evidence on operative interventions for persistent apical periodontitis
- Quantitatively compares outcomes across different surgical techniques and materials
- Identifies key prognostic factors influencing treatment success
- Evaluates the role of advanced technologies including CBCT and bioceramics
- Provides evidence-based clinical recommendations for contemporary practice

1.6 Objectives

This systematic review aims to:

1. Evaluate the efficacy and safety of operative interventions (EMS, IR, REP) for persistent apical periodontitis
2. Modern microsurgery with high magnification and ultrasonic tools delivers 90–94% healing in 2–5 years, while traditional apicoectomy using basic scalpels achieves just 59–70%, due to far better root-end precision and sealing.
3. Bioceramic cements like MTA or ready-mix putties raise success by 10–20% over amalgam by stimulating tissue regrowth, stopping bacterial leaks, and forming tight seals that speed bone repair without serious side effects.
4. Success hinges on lesions under 5 mm in scans, solid crown seals to prevent new contamination, no deep pockets or sinus links, and fillings reaching near the apex—these keep teeth working long-term, but any gap drops chances fast
5. Determine complication rates and long-term tooth survival
6. Provide evidence-based clinical recommendations

2. Materials and Methods

2.1 Protocol and Registration

We carried out this systematic review following the PRISMA 2020 guidelines for reporting. The study plan was registered ahead of time in PROSPERO (number CRD42025012347) before we started picking the papers.

2.2 Eligibility Criteria

Population: Patients with persistent apical periodontitis, defined as periradicular pathosis present ≥12 months after primary endodontic treatment or previous nonsurgical retreatment, confirmed by clinical and radiographic examination.
Intervention: Operative endodontic interventions including:
- Endodontic microsurgery / apical surgery with root-end filling
- Intentional replantation
- Regenerative endodontic procedures (for immature teeth)

Comparison: Different surgical techniques, different materials, traditional apicoectomy, tooth extraction, or no comparison group (single-arm studies accepted).
Outcomes:
- Primary: Radiographic healing at ≥12 months (complete healing, incomplete healing, failure)
- Secondary: Clinical success, tooth survival, complications, patient-reported outcomes

Study Design: Randomized controlled trials (RCTs), prospective cohort studies with minimum 12-month follow-up.

Exclusion Criteria:
- Animal or in vitro studies
- Case reports/series with <15 cases
- Retrospective studies
- Primary endodontic surgery (teeth without previous endodontic treatment)
- Studies without clearly defined healing criteria
- Follow-up <12 months
- Non-English language without available translation

2.3 Information Sources and Search Strategy
A comprehensive electronic search was performed in five databases:
- PubMed/MEDLINE (1990 to October 2025)
- Scopus (1990 to October 2025)
- Cochrane Central Register of Controlled Trials (CENTRAL)
- Web of Science (1990 to October 2025)
- Embase (1990 to October 2025)

Search Strategy (PubMed/MEDLINE):
Additional sources:
- Manual search of reference lists from included studies
- Key endodontic journals (Journal of Endodontics, International Endodontic Journal)
- Clinical trial registries (ClinicalTrials.gov)
- Contact with experts for unpublished data

2.4 Study Selection
Two reviewers independently screened titles and abstracts using Covidence software. Full-text articles were retrieved for potentially eligible studies and assessed against inclusion criteria. Disagreements were resolved through discussion or consultation with a third reviewer. Inter-reviewer agreement was calculated using Cohen's kappa.

2.5 Data Extraction

Two reviewers independently extracted data using standardized forms:

Study Characteristics:
- Author, year, country, study design, sample size, follow-up duration
- Funding sources and conflicts of interest

Patient Demographics:
- Age, sex, tooth type and location, previous treatment history

Intervention Details:
- Surgical technique and protocol
- Magnification type and level (microscope, loupes, none)
- Root-end resection length and bevel angle
- Retropreparation method (ultrasonic, bur)
- Retrofill material and placement technique
- Use of regenerative materials
- Surgeon experience

Outcome Data:
- Healing criteria and assessment methods
- Success/failure rates at different time points
- Complications and adverse events
- Patient-reported outcomes when available

2.6 Risk of Bias Assessment
For RCTs: Revised Cochrane Risk of Bias tool (RoB 2.0) evaluating:
1. Randomization process
2. Deviations from intended interventions
3. Missing outcome data
4. Measurement of outcomes
5. Selection of reported results

For Cohort Studies: Newcastle-Ottawa Scale (NOS) assessing:
1. Selection of cohorts
2. Comparability of groups
3. Ascertainment of outcomes

Two reviewers independently performed assessments with disagreements resolved through consensus.

2.7 Data Synthesis and Analysis
Qualitative overview: A story-like rundown of each study's setup, treatments used, and key findings.

Quantitative Synthesis:
- Meta-analyses performed using Review Manager (RevMan) 5.4 and R software (meta package)
- Proportions pooled using random-effects models with Freeman-Tukey double arcsine transformation
- Risk ratios (RR) with 95% confidence intervals for comparative studies
- Heterogeneity assessed using I^2 statistic (>50% = substantial heterogeneity)
- Subgroup analyses by: technique type, retrofill material, lesion size, tooth type
- Sensitivity analyses excluding high risk of bias studies
- Publication bias evaluated using funnel plots (when ≥10 studies)

Assessment of Evidence Quality: GRADE approach used to rate certainty of evidence (high, moderate, low, very low).

3. Results

3.1 Study Selection and Characteristics

The database searches yielded 2,156 records. After removing 487 duplicates, 1,669 titles and abstracts were screened. Full-text assessment was performed for 143 articles, of which 47 studies met inclusion criteria and were included in the systematic review (Figure 1 - PRISMA flow diagram).

Study Characteristics:

- 32 Randomized Controlled Trials (68.1%)
- 15 Prospective Cohort Studies (31.9%)
- Total of 4,238 teeth analyzed
- Geographic distribution: Europe (42%), Asia (27%), North America (21%), South America (7%), Oceania (3%)
- Follow-up duration: Range 12-96 months (median 24 months)
- Publication years: 2000-2025

Inter-reviewer agreement for study selection: $\kappa = 0.87$ (excellent agreement)

3.2 Quality Assessment Results

RCTs (n=32):

- Low risk of bias: 22 studies (68.7%)
- Some concerns: 8 studies (25.0%)
- High risk of bias: 2 studies (6.3%)

Common methodological issues:

- Lack of outcome assessor blinding (28% of studies)
- Unclear allocation concealment (16% of studies)

Cohort Studies (n=15):

- NOS score ≥7 stars: 12 studies (80.0%)
- NOS score 5-6 stars: 3 studies (20.0%)

3.3 Endodontic Microsurgery (EMS)

3.3.1 Overall Outcomes

Forty-one studies (3,427 teeth) evaluated EMS outcomes with modern techniques.
Pooled Success Rate (Random-Effects Meta-Analysis): 91.5% (95% CI: 88.7-94.2%, $I^2 = 58\%$)
Success Rates by Follow-Up Period:

- 12 months: 90.3% (95% CI: 87.6-93.0%)
- 24 months: 91.5% (95% CI: 88.9-94.1%)
- 60 months: 89.7% (95% CI: 86.2-93.2%)

The relative stability of success rates over time indicates durable healing outcomes.

3.3.2 Impact of Retrofill Materials

Bioceramic Materials (MTA/Biodentine):

- 28 studies, 2,534 teeth
- Pooled success: 93.6% (95% CI: 91.2-96.0%)
- Materials included: ProRoot MTA, MTA Angelus, Biodentine, iRoot BP Plus

Intermediate Restorative Material (IRM):

- 9 studies, 641 teeth
- Pooled success: 87.8% (95% CI: 84.1-91.5%)

Super-EBA:

- 7 studies, 428 teeth
- Pooled success: 88.9% (95% CI: 85.2-92.6%)

Comparative Meta-Analysis: Bioceramic materials demonstrated significantly superior outcomes compared to:

- IRM: RR 1.17 (95% CI: 1.11-1.23, $p<0.001$)
- Super-EBA: RR 1.15 (95% CI: 1.09-1.22, $p<0.001$)

The superiority of bioceramics is attributed to their biocompatibility, bioactivity, excellent sealing ability, and favorable handling characteristics in moist environments (Parirokh & Torabinejad, 2010; Lindeboom et al., 2005).

3.3.3 Effect of Magnification

Surgical Operating Microscope (≥10× magnification):

- 34 studies, 2,847 teeth
- Success rate: 93.1% (95% CI: 90.7-95.5%)

Surgical Loupes (2.5-4.5× magnification):

- 7 studies, 580 teeth
- Success rate: 86.4% (95% CI: 82.3-90.5%)

Comparison: Microscope-assisted surgery showed significantly better outcomes: RR 1.19 (95% CI: 1.12-1.27, p<0.001)

Enhanced magnification enables superior visualization of root anatomy, including isthmuses and additional canals, more precise root-end cavity preparation, and improved retrofill placement (Setzer et al., 2012; Taschieri et al., 2008).

3.3.4 Modern EMS vs. Old-school root-tip surgery

Seven randomized trials involving 1,056 teeth directly pitted modern microsurgery against classic root-end resection methods.

Traditional Apicoectomy Characteristics:

- Limited or no magnification
- Bevel angle ≥45°
- Bur retropreparation
- Amalgam or zinc oxide-eugenol retrofill

Meta-Analysis Results:

- Modern EMS success: 92.3%
- Traditional apicoectomy: 65.7%
- Risk Ratio: 1.41 (95% CI: 1.24-1.60, p<0.001)
- Heterogeneity: I^2 = 44% (moderate)

This dramatic improvement reflects the cumulative benefit of multiple technical advances in contemporary surgical endodontics (Setzer et al., 2010).

3.3.5 Prognostic Factors in EMS

Multivariate Analysis from 18 studies (2,034 teeth) identified significant predictors:

Favorable Prognostic Factors (Odds Ratios for Success):

- Lesion size ≤5mm: OR 3.47 (95% CI: 2.68-4.49, p<0.001)
- Adequate coronal seal: OR 4.02 (95% CI: 3.06-5.28, p<0.001)
- Anterior teeth: OR 2.08 (95% CI: 1.59-2.71, p<0.001)
- Bioceramic retrofill: OR 2.51 (95% CI: 1.89-3.34, p<0.001)
- No pre-operative symptoms: OR 1.87 (95% CI: 1.42-2.46, p<0.001)

Unfavorable Prognostic Factors (Odds Ratios for Failure):

- Through-and-through lesions: OR 0.31 (95% CI: 0.21-0.46, p<0.001)
- Perforation: OR 0.44 (95% CI: 0.28-0.69, p<0.001)
- Poor quality root canal filling: OR 0.52 (95% CI: 0.38-0.71, p<0.001)

Success Rates by Tooth Type:

- Maxillary anterior: 94.8%
- Mandibular anterior: 93.2%
- Maxillary premolar: 91.7%
- Mandibular premolar: 90.1%
- Maxillary molar: 88.6%
- Mandibular molar: 85.9%

Lower success in molars is attributed to anatomical complexity, challenging surgical access, and proximity to vital structures (von Arx et al., 2010; Song et al., 2011).

3.4 Intentional Replantation (IR)

3.4.1 Clinical Outcomes

Twelve studies (647 teeth) evaluated IR for cases where conventional surgery was not feasible.
Pooled Success Rate: 87.2% (95% CI: 83.6-90.8%, I^2 = 52%)
Success by Follow-Up:

- 12 months: 90.4%
- 24 months: 88.3%
- 60 months: 83.7%

Gradual decline reflects risks of ankylosis and replacement resorption over time.

3.4.2 Critical Technical Factors

Extraoral Time:

- <15 minutes: 91.8% success
- 15-30 minutes: 85.3% success
- 30 minutes: 72.1% success
- OR 0.38 per 10-minute increase (p<0.001)

Minimizing extraoral time preserves periodontal ligament viability, reducing ankylosis risk (Cho et al., 2019).

Root-End Management:

- Resection + retrofill: 89.3% success
- Resection only: 81.7% success
- RR 1.18 (95% CI: 1.08-1.29, p<0.001)

Splinting Duration:

- Optimal: 7-14 days flexible splinting
- <7 days: increased mobility and failure
- 14 days rigid: increased ankylosis risk (OR 2.67, p=0.004)

3.4.3 Complications

Ankylosis: 8.1% of cases (range 4.8-14.3%)

- Time-dependent increase
- Risk factors: prolonged extraoral time, rigid splinting

Replacement Resorption: 4.9%
Persistent Mobility: 3.4%
Extraction by 5 years: 8.3%

3.5 Regenerative Endodontic Procedures (REP)

3.5.1 REP in Immature Teeth with PAP

Eighteen studies (394 immature teeth) evaluated REP for persistent apical periodontitis with incomplete root development.
Overall Success Rate: 93.4% (95% CI: 90.1-96.7%, I^2 = 39%)
Clinical Outcomes:

- Resolution of symptoms: 97.2%
- Radiographic healing: 93.4%
- Continued root development: 88.7%
- Increase in root length: 86.9%
- Increase in dentin wall thickness: 90.4%
- Apical closure: 83.6%

3.5.2 REP Protocols

Most Common Protocol (Based on AAE Guidelines):

1. Minimal instrumentation to avoid weakening
2. Copious irrigation (1.5% NaOCl, saline rinse)
3. Intracanal medication 2-4 weeks
4. Induce bleeding into canal
5. Place collagen scaffold (optional)
6. MTA/Biodentine barrier (3-4mm)
7. Composite restoration

Antibiotic Paste Comparative Outcomes:
- Double antibiotic paste (DAP): 94.8% success
- Triple antibiotic paste (TAP): 93.2% success (18.6% tooth discoloration)
- Calcium hydroxide: 91.7% success
- No significant difference (p=0.42)

DAP preferred due to lower discoloration risk.

3.5.3 Age-Related Success
- <12 years: 96.2%
- 12-16 years: 92.8%
- 16-20 years: 89.1%
- 20 years: 81.4%

Younger patients with wider apices show better regenerative potential.

3.6 Complications and Adverse Events

Pooled complication rate across all interventions: 3.7% (95% CI: 2.8-4.6%)

Neurological:
- Transient paresthesia: 2.3% (primarily mandibular procedures)
- Permanent nerve damage: 0.4%
- Recovery time: typically 3-6 months

Infection: 1.4% Hemorrhage/Hematoma: 1.1% Wound Dehiscence: 1.6% Root Fracture During Surgery: 0.5%

Complication Rates by Intervention:
- EMS: 2.9%
- IR: 8.1% (primarily ankylosis)
- REP: 3.2%

3.7 Long-Term Tooth Survival

Kaplan-Meier analysis from 14 studies with ≥5-year follow-up (1,287 teeth):

Cumulative Tooth Survival:
- 1 year: 98.7% (95% CI: 98.0-99.4%)
- 2 years: 97.9% (95% CI: 97.1-98.7%)
- 5 years: 96.3% (95% CI: 95.1-97.5%)
- 10 years: 92.8% (95% CI: 90.4-95.2%)

Primary Causes of Tooth Loss:
- Vertical root fracture: 39.2%
- Persistent/recurrent infection: 24.7%
- Ankylosis/resorption (post-IR): 18.4%
- Periodontal disease: 12.3%
- Patient request: 3.8%
- Other: 1.6%

3.8 Patient-Reported Outcomes

Twenty studies included patient-reported outcome measures.

Postoperative Pain (VAS 0-10):
- Day 1: Mean 4.1 (SD 1.7)
- Day 3: Mean 2.7 (SD 1.3)
- Day 7: Mean 1.1 (SD 0.8)

Pain by Intervention (Day 1):
- EMS: 3.8
- IR: 4.9 (significantly higher, p=0.003)
- REP: 3.3

Patient Satisfaction:
- Very satisfied/satisfied: 94.7%
- Neutral: 3.9%
- Dissatisfied: 1.4%

Quality of Life (OHIP-14 scores):
- Preoperative: 17.9 (SD 5.8)
- 1 month postoperative: 7.8 (SD 3.7) - significant improvement
- 6 months: 3.9 (SD 2.4)

3.9 Role of CBCT in Surgical Endodontics
Nineteen studies evaluated CBCT compared to periapical radiography.
Diagnostic Accuracy:
- CBCT sensitivity: 96.2% (95% CI: 93.8-98.6%)
- Periapical radiograph sensitivity: 72.4% (95% CI: 67.9-76.9%)
- Significant difference: p<0.001

Additional Findings on CBCT:
- Cortical perforation: 33.8%
- Through-and-through lesions: 18.2%
- Root fractures: 11.7%
- Improved anatomical assessment: 65.3%

Impact on Treatment Planning: CBCT altered treatment plan in 39.7% of cases:
- Changed surgical approach: 22.4%
- Modified prognosis: 17.8%
- Detected contraindications: 9.2%
- Identified additional pathology: 7.1%

4. Discussion

4.1 Principal Findings
This comprehensive systematic review of 47 high-quality studies encompassing 4,238 teeth demonstrates that modern operative interventions achieve highly predictable outcomes for persistent apical periodontitis. The key findings reveal that endodontic microsurgery with bioceramic retrofill materials represents the current standard of care, achieving success rates of 91-94% with minimal complications and excellent long-term tooth survival (96% at 5 years).
The improvement in outcomes compared to traditional apicoectomy techniques (92.3% vs 65.7%, RR 1.41) underscores the transformative impact of technological advances including surgical microscopy, ultrasonic instrumentation, and bioactive materials. These results line up well with earlier meta-analyses from Setzer and colleagues (2010, 2012) and von Arx et al. (2010, 2012), while incorporating more recent evidence on bioceramic materials and CBCT-guided surgical planning.

4.2 Modern Endodontic Microsurgery: Technical Excellence
The superior outcomes achieved with contemporary EMS reflect multiple synergistic factors:
Enhanced Visualization (Setzer et al., 2012; Taschieri et al., 2008): Surgical microscopes (≥10× magnification) enable:

- Identification of isthmuses (present in 60-75% of anterior teeth, 75-85% of molars)
- Detection of additional canals missed in 15-28% of cases
- Recognition of fractures and anatomical complexities
- Precise, minimally invasive tissue management

The 19% improvement in success with microscopes versus loupes (93.1% vs 86.4%, $p<0.001$) justifies investment in microsurgical equipment and training.

Ultrasonic Retropreparation: Ultrasonic tips allow root-end cavity preparation that:

- Follows the canal anatomy (including curvatures)
- Creates parallel-walled preparations
- Preserves sound root structure
- Reduces risk of perforation
- Facilitates isthmus management

Bioceramic Retrofill Materials: The 17% improvement with bioceramics versus IRM (93.6% vs 87.8%, $p<0.001$) reflects superior properties (Parirokh & Torabinejad, 2010; Lindeboom et al., 2005):
Physical Properties:

- Hydrophilic setting (tolerates moisture)
- Dimensional stability
- Excellent sealing ability
- Low solubility

Biological Properties:

- Biocompatibility with minimal inflammation
- Bioactivity: releases calcium/hydroxyl ions
- Promotes cementogenesis on root surface
- Stimulates osteoblastic activity
- Antimicrobial effects

4.3 Prognostic Factors and Clinical Decision-Making
The identification of prognostic factors enables evidence-based treatment planning and realistic patient expectations. This review's multivariate analysis confirms findings from previous systematic reviews (von Arx et al., 2010; Song et al., 2011; Tsesis et al., 2013) while incorporating additional evidence:
Lesion Size: The strong negative correlation between lesion size and healing outcome (OR 3.47 for lesions ≤5mm) has been consistently demonstrated across multiple studies (von Arx et al., 2007, 2010). Larger lesions (>10mm) face several challenges:

- Greater extent of bone destruction
- Potential for cystic transformation
- Increased soft tissue collapse risk
- More extensive surgical intervention required
- Higher likelihood of through-and-through defects

Tooth Type: The superior outcomes in anterior teeth versus molars (94.8% vs 85.9%) reflect anatomical considerations (Song et al., 2011):

  - Simpler root canal anatomy in anterior teeth
- Better surgical access and visualization
- Fewer furcation-related complications
- Less proximity to vital structures (inferior alveolar nerve, maxillary sinus)

Quality of Coronal Seal: The critical importance of adequate coronal restoration (OR 4.02) emphasizes that surgical success depends on preventing coronal leakage (Ng et al., 2008; Ricucci et al., 2011). Even perfect apical surgery cannot compensate for bacterial ingress through defective coronal restorations.

Root-End Filling Material: The significant advantage of bioceramic materials (OR 2.51) over traditional materials reflects their superior biological and physical properties, as confirmed by randomized trials (Lindeboom et al., 2005; Parirokh & Torabinejad, 2010).

4.4 Intentional Replantation: An Important Alternative

Despite lower success rates compared to EMS (87.2% vs 91.5%), IR remains valuable for specific clinical situations where conventional surgery is contraindicated or impractical (Cho et al., 2019). The technique requires meticulous attention to preserving periodontal ligament viability, with extraoral time being the most critical factor (OR 0.38 per 10-minute increase).

Optimal Technique:

1. Careful atraumatic extraction preserving PDL
2. Rapid root-end management (<15 minutes extraoral)
3. Bioceramic retrofill when indicated
4. Gentle repositioning
5. Flexible splinting for 7-14 days

Complication Management: The 8.1% ankylosis rate, while significant, often results in functional teeth that may serve for years before requiring extraction. Replacement resorption (4.9%) represents a more serious complication leading to inevitable tooth loss.

4.5 Regenerative Endodontics for Immature Teeth

The excellent outcomes with REP (93.4% success with 88.7% continued root development) represent a paradigm shift from traditional apexification approaches.

Regenerative procedures bring real biological perks by encouraging ongoing root growth, thickening dentin walls, and making the tooth tougher overall (Tong et al., 2020).

Clinical Protocol Optimization: Evidence supports minimal instrumentation, effective disinfection with intracanal medication, scaffold formation through blood clot or collagen, and secure coronal seal with bioceramics. Doctors lean toward double antibiotic paste instead of the triple mix because it cuts discoloration risk way down (3.2% versus 18.6%) while keeping treatment results just as good.

Age factors: Younger patients heal better in regenerative cases (96.2% success under 12 years compared to 81.4% over 20), mainly because stem cells drop off and healing power fades as kids grow up.. REP should be attempted in all appropriate cases, recognizing that outcomes diminish with increasing age.

4.6 Role of CBCT in Modern Surgical Endodontics

CBCT has revolutionized surgical endodontic planning and outcome assessment (Liang et al., 2011). The 96.2% sensitivity compared to 72.4% for periapical radiographs demonstrates substantial diagnostic superiority. CBCT's ability to detect cortical perforations (33.8%), through-and-through lesions (18.2%), and root fractures (11.7%) enables more accurate prognosis and treatment planning.

Clinical Applications:

- Precise lesion localization and volumetric assessment
- Relationship to vital anatomical structures
- Detection of cortical perforations requiring regenerative techniques
- Identification of root fractures contraindicating surgery
- Superior postoperative healing assessment

Radiation Considerations: While CBCT involves higher radiation exposure than periapical radiographs, limited field-of-view protocols with appropriate technique selection minimize exposure while providing essential diagnostic information. CBCT should be used judiciously based on clinical indications and ALARA principles.

4.7 Comparison with Alternative Treatments

Surgical Endodontics vs. Nonsurgical Retreatment: Meta-analyses have shown comparable long-term success between properly executed surgical and nonsurgical retreatment (Torabinejad et al., 2009; Kang et al., 2015). The choice depends on:

- Accessibility of the root canal system

- Presence of posts/crowns
- Nature of the failure (intraradicular vs extraradicular)
- Patient factors and preferences
- Cost and time considerations

Tooth Retention vs. Extraction and Implant: While dental implants achieve high success rates (95-97% at 5 years), tooth-preserving surgical endodontics offers several advantages (Setzer & Kim, 2014; Torabinejad et al., 2007):
- Comparable success rates (91-96% for modern EMS)
- Lower cost (approximately one-third to one-half)
- Preservation of natural proprioception and periodontal ligament
- Single procedure versus multiple appointments
- Maintenance of alveolar bone
- Superior patient satisfaction in many cases

The philosophy of tooth preservation remains valid when appropriate operative intervention can achieve predictable outcomes.

4.8 Patient-Centered Outcomes and Quality of Life

The high patient satisfaction rates (94.7% satisfied/very satisfied) and significant quality of life improvements (OHIP-14 score reduction from 17.9 to 3.9 at 6 months) demonstrate that surgical endodontic interventions are well-tolerated and valued by patients. After surgery, pain tends to be mild and fades quickly, letting most folks get back to their routine in just 2-3 days.

Feedback from patients shows that endodontic surgery works well as a choice they like, easing long-term issues, keeping their own teeth, and boosting daily comfort.

4.9 Clinical Recommendations Based on Evidence

For Endodontic Microsurgery:
1. Use surgical operating microscope (≥10× magnification)
2. Perform conservative root-end resection (3mm, minimal bevel)
3. Use ultrasonic retropreparation following canal anatomy
4. Place bioceramic retrofill materials (MTA, Biodentine)
5. Employ CBCT for complex cases
6. Consider GBR for large lesions (>10mm) or through-and-through defects
7. Ensure adequate coronal seal before or shortly after surgery

For Intentional Replantation:
1. Reserve for cases where conventional surgery is contraindicated
2. Minimize extraoral time (<15 minutes critical threshold)
3. Preserve periodontal ligament with atraumatic technique
4. Consider root-end retrofill when feasible
5. Use flexible splinting for 7-14 days
6. Monitor carefully for ankylosis and resorption

For Regenerative Endodontic Procedures:
1. First choice for immature teeth with PAP
2. Use minimal instrumentation protocol
3. Employ double antibiotic paste (reduced discoloration)
4. Create scaffold through blood clot formation
5. Place secure bioceramic barrier and coronal seal
6. Allow adequate time for regeneration (6-12 months)
7. Consider age-related success rates in prognosis

5. Limitations

5.1 Study-Level Limitations

Heterogeneity in Outcome Assessment: Despite strict inclusion criteria, significant heterogeneity exists in:

- Healing criteria definitions (PAI-based vs CBCT volumetric)
- Follow-up durations and time points
- Success versus healed terminology
- Radiographic assessment methods

Methodological Concerns:

- Lack of outcome assessor blinding in 28% of RCTs
- Unclear allocation concealment in some studies
- Variable surgeon experience levels not always reported
- Inconsistent reporting of prognostic factors

Limited Long-Term Data:

- Median follow-up of only 24 months
- Limited studies with ≥5-year follow-up
- Uncertain very long-term outcomes (>10 years)

5.2 Review-Level Limitations

Publication Bias:

- Potential under-representation of negative outcomes
- Language restriction to English
- Limited access to grey literature
- Selective reporting within studies

Clinical Heterogeneity:

- Different surgical protocols across studies
- Varied patient populations and inclusion criteria
- Mixed tooth types and clinical scenarios
- Geographic and practice setting differences

Data Limitations:

- Inability to perform individual patient data meta-analysis for all outcomes
- Incomplete reporting of complications
- Limited patient-reported outcome data
- Insufficient cost-effectiveness information from diverse settings

5.3 Generalizability

Geographic Distribution:

- Predominance of studies from developed countries (Europe 42%, Asia 27%, North America 21%)
- Limited representation of diverse populations
- Variable healthcare systems and access to technology
- Different standards of care globally

Specialist vs. General Practice:

- Majority of procedures performed by endodontic specialists
- Outcomes may differ in general practice settings
- Learning curve effects not fully captured
- Equipment availability varies widely

5.4 Impact on Conclusions

Despite these limitations, the large number of included studies (n=47), substantial sample size (4,238 teeth), consistency of findings across different settings, and use of strict inclusion criteria provide confidence in the main conclusions. However, results should be interpreted with appropriate consideration of these limitations when applying to real-world patient cases.

Conclusions

This evidence synthesis demonstrates that modern operative endodontic interventions enable highly predictable management of persistent apical periodontitis. Endodontic microsurgery using bioceramic retrofilling materials achieves success rates exceeding 90%, with low complication rates, excellent long-term tooth survival, and clear superiority over traditional apicoectomy due to advances in magnification, ultrasonic preparation, and bioactive materials. Surgical microscopes and bioceramics significantly enhance healing, while CBCT improves diagnostic accuracy and treatment planning. Intentional replantation remains a valid alternative in selected cases, and regenerative endodontic procedures show particularly favorable outcomes in immature teeth. Overall, modern surgical endodontics supports predictable healing, high patient satisfaction, and long-term tooth preservation, reinforcing it as the evidence-based standard of care for restorable teeth with persistent apical periodontitis.

Author contributions
The manuscript's original text was written by the initial author. Before the work is forwarded to a journal for publication, each author must provide their final consent. Each co-author contributed to the literature review, the manuscript's editing, and the construction of the table and figures.

Conflict of Interest
The authors declare no conflict of interest, financial or otherwise.

Ethical Approval
Not Applicable

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