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Review

Decoding Post-Endodontic Pain: Mapping Patient, Procedural, and Operator Determinants of Early Pain and Flare-Ups: A Scoping Review

Somayeh Majidi[1], Sholeh Ghabraei[2], Hadi Assadian[3] *

[1] Postgraduate Student, Department of Endodontics, School of Dentistry, Tehran University of Medical Sciences, Tehran, Iran
[2] Associate Professor, Department of Endodontics, School of Dentistry, Tehran University of Medical Sciences, Tehran, Iran
[3] Assistant Professor, Department of Endodontics, School of Dentistry, Tehran University of Medical Sciences, Tehran, Iran

*** Corresponding Author:** Hadi Assadian, **Email:** hd.asdn@scident.ir
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Abstract

Background and Aim: Post-endodontic pain (PEP) is a frequent consequence of root canal treatment that impacts patient satisfaction and clinical choices. While many in vivo studies have examined factors influencing PEP—such as tooth characteristics, treatment techniques, materials, and operator variables—the findings are inconsistent and methodologically diverse. This has led to fragmented evidence, prompting a scoping review to consolidate current knowledge and highlight gaps for future research and clinical improvement.

Methods: A comprehensive electronic search of PubMed/MEDLINE, Scopus, Web of Science, Cochrane CENTRAL, and Embase was conducted for studies published between January 2015 and June 2025, in accordance with PRISMA-ScR and JBI guidelines. The search strategy combined controlled vocabulary (e.g., MeSH terms) and free-text keywords, including: *"postoperative pain," "post-endodontic pain," "root canal treatment," "instrumentation," "obturation," "sealer," "single visit," "multiple visit," "retreatment," and "irrigation activation."* Eligible evidence sources included human in-vivo randomized clinical trials, observational studies, and relevant systematic reviews evaluating postoperative pain after non-surgical primary root canal treatment or retreatment. Backward and forward citation tracking and manual searches of leading endodontic journals were also performed.

Results: Of 4,800 screened records, 120 studies met inclusion criteria. PEP was most strongly linked to preoperative pain, symptomatic irreversible pulpitis, molar anatomy, and retreatment complexity. Procedural variables (instrumentation type, visit number, obturation, irrigation activation) showed no consistent clinically meaningful differences when properly executed. Bioceramic sealers yielded slightly lower early pain scores than epoxy-resin sealers, but differences disappeared within 48–72 hours. Higher NaOCl concentrations improved antimicrobial efficacy without reliably reducing pain. Operator expertise and procedural precision significantly modified outcomes. Pain assessment methods varied widely, with VAS and NRS most common but inconsistently reported.

Conclusion: PEP is driven mainly by preoperative inflammation, anatomy, and procedural quality, not just instrument or material choice. This scoping review maps biological, technical, and operator factors from the past decade of in-vivo evidence, showing that many debated variables have only minor, temporary effects under modern standards. Future research should standardize pain assessment at 6, 24, 48, and 72 hours, consistently report analgesic use and extrusion events, and conduct well-powered multicenter RCTs controlling for diagnosis, tooth type, and operator skill.

Key Words: Post-Endodontic Pain; Postoperative Pain; Root Canal Treatment; Endodontic Instrumentation; Irrigation Protocols; Obturation Techniques; Endodontic Sealers; Pain Assessment

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Introduction

Post-endodontic pain (PEP) is defined as pain or discomfort experienced following root canal treatment and remains one of the most common postoperative complaints in endodontic practice (1–3). Reported prevalence ranges from approximately 25% to 40%, with presentations varying from mild, self-limiting discomfort to severe

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pain that may impair daily activities and negatively influence patients' perceptions of treatment success (1,2,4). Pain may occur immediately after treatment or develop within 24–72 hours and can be localized to the treated tooth or radiate to adjacent anatomical regions, complicating postoperative diagnosis and clinical decision-making (1–3).

Postoperative pain represents a multidimensional phenomenon influenced by biological, procedural, operator-related, and patient-related variables (5). Psychological factors, particularly dental anxiety and pain anticipation, have been associated with increased postoperative pain perception and analgesic consumption following endodontic treatment (5). Anxiety-related stress responses may modulate central nociceptive processing and amplify perceived pain intensity (1,6,7). These psychological influences interact with peripheral inflammatory mechanisms, as stress-mediated mast cell activation contributes to the release of inflammatory mediators that reinforce nociceptive signaling (1,6,7).

From a biological perspective, PEP primarily arises from inflammatory responses within periapical tissues triggered by mechanical, chemical, and microbial stimuli during root canal procedures (4,8). Mechanical instrumentation, apical extrusion of debris, and chemical irritation from irrigants such as sodium hypochlorite may induce tissue injury and initiate inflammatory cascades (1,4,8). Residual microorganisms and necrotic debris can perpetuate inflammation through activation of innate immune pathways, including toll-like receptor–mediated signaling, leading to sustained cytokine release (4,9). Key mediators—including prostaglandins synthesized via cyclooxygenase-2 pathways, cytokines such as interleukin-1β and tumor necrosis factor-α, and neuropeptides such as substance P and calcitonin gene-related peptide—contribute to nociceptor sensitization and amplification of trigeminal pain signaling (8,10,11). Peripheral and central sensitization mechanisms may further explain variability in postoperative pain experiences among individuals (9,10).

Clinical and preoperative factors have also been associated with postoperative pain outcomes. Pre-existing periapical pathology, symptomatic irreversible pulpitis, and preoperative pain have consistently been linked to increased risk of postoperative pain (4,7,12). Anatomical complexity, retreatment procedures, and systemic conditions affecting immune response may further influence inflammatory resolution and pain perception (1,4). However, reported associations vary across studies, partly due to differences in patient selection, diagnostic criteria, and outcome measurement (1,4).

PEP has been categorized into acute, chronic (persistent), and referred pain, each involving distinct pathophysiological considerations (1,13,14). Acute pain typically occurs within 0–72 hours after treatment, whereas persistent pain may extend beyond normal healing timelines and has been reported in a minority of cases (1,13,14). Referred pain, attributed to convergence of trigeminal afferents, may mimic non-odontogenic conditions and presents diagnostic challenges (11,13–16). Although these classifications are described in the literature, their reported prevalence, diagnostic thresholds, and follow-up methodologies differ considerably across studies.

Despite substantial research on PEP, the literature remains methodologically heterogeneous and dispersed across multiple domains. Randomized clinical trials and observational studies have examined the influence of pulpal and periapical status, instrumentation kinematics, irrigation protocols, obturation techniques, sealer selection, operator experience, and psychological variables on postoperative pain outcomes (1,2,4,17). However, findings are frequently inconsistent, and variations in study design, pain assessment tools (e.g., VAS vs. NRS), follow-up intervals, and reporting of confounding variables—such as analgesic consumption and procedural complications—limit comparability (1,4). Existing systematic reviews have often focused on isolated variables (e.g., obturation technique or sealer type), without integrating biological, procedural, and operator-related determinants within a unified conceptual framework.

Scoping reviews are designed to map key concepts within a broad and heterogeneous field, examine how existing research is structured and reported, and identify areas where evidence remains limited or inconsistent. Given the wide range of contributing variables and the absence of a comprehensive synthesis of how PEP has been investigated, a scoping review methodology is particularly

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appropriate. This approach allows integration of biological, clinical, procedural, and operator-related determinants while capturing the diversity of in vivo study designs, outcome measures, and reporting strategies. By systematically charting the available evidence, this review examines how postoperative pain has been defined, measured, and analyzed across studies, including variation in pain assessment tools, follow-up intervals, case selection, and intervention protocols. It also enables the identification of potential knowledge gaps, such as lack of standardized outcome reporting, insufficient diagnostic stratification, limited high-quality randomized evidence in certain procedural domains, and inadequate control of confounding variables such as operator experience and treatment complexity. Accordingly, this scoping review aims to map and synthesize contemporary in vivo clinical evidence on PEP following nonsurgical root canal treatment and retreatment, while providing an overview of current research practices and areas requiring further investigation.

Methods and Materials

1. Review Design and Protocol

This scoping review was conducted and reported in accordance with the PRISMA Extension for Scoping Reviews (PRISMA-ScR) and the Joanna Briggs Institute (JBI) methodological framework. A review protocol was developed a priori to define objectives, eligibility criteria, and data charting methods. The protocol was not formally registered.

2. Search Strategy

A comprehensive electronic search was conducted in PubMed/MEDLINE, Scopus, Web of Science, Cochrane CENTRAL, and Embase to identify relevant in vivo human studies published between January 1, 2015, and June 15, 2025.

The search strategy combined controlled vocabulary terms (e.g., MeSH terms in PubMed) and free-text keywords using Boolean operators. Search terms were structured around three main concepts:
(1) postoperative or post-endodontic pain,
(2) root canal treatment, and
(3) procedural, biological, and operator-related variables.

Search strategies were adapted for each database. The full electronic search strategy for PubMed is provided in Supplementary Material 1.

To enhance comprehensiveness, backward and forward citation tracking of included studies was performed. Manual searches of key endodontic journals and articles published ahead of print were also conducted. All searches were completed on June 15, 2025.

3. Eligibility Criteria

3.1. Inclusion Criteria

Studies were included if they met the following criteria:

- In vivo human clinical studies
- Patients undergoing nonsurgical endodontic treatment (primary treatment or retreatment)
- Reported postoperative pain using validated assessment tools (e.g., VAS, NRS, or equivalent)
- Assessed postoperative pain at any defined postoperative time point (including early [e.g., 4–6 hours], short-term [24–72 hours], or extended follow-up [≥1 week])
- Evaluated one or more factors associated with postoperative pain, including procedural, biological, or operator-related variables

No minimum follow-up duration was required, provided that postoperative pain was assessed at least once after treatment.

3.2. Exclusion Criteria

Studies were excluded if they met any of the following criteria:

- In vitro, ex vivo, or animal studies
- Case reports or case series with fewer than 10 patients
- Editorials, commentaries, letters, conference abstracts without full text
- Surgical endodontic procedures
- Studies not related to nonsurgical root canal treatment
- Studies without extractable postoperative pain outcomes or using non-validated pain measures
- Studies conducted exclusively in pediatric populations or primary dentition
- Non-English language publications

4. Study Selection

All identified records were imported into reference management software, and duplicates were removed.

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Two independent reviewers screened titles and abstracts for eligibility. Full texts of potentially relevant studies were subsequently assessed independently by the same reviewers. Disagreements were resolved through discussion, and when necessary, consultation with a third reviewer.

The study selection process was documented using a PRISMA flow diagram.

5. Data Charting

Data were extracted using a standardized charting form developed a priori and pilot-tested on a subset of included studies.

The following variables were collected:

- Study characteristics (design, country)
- Sample size and patient characteristics
- Preoperative diagnosis
- Procedural variables (instrumentation, irrigation, obturation, sealer type)
- Operator-related variables
- Pain assessment tools and follow-up intervals
- Analgesic protocols
- Key postoperative pain outcomes

Data extraction was performed by one reviewer and independently verified by a second reviewer to ensure accuracy and completeness.

Consistent with scoping review methodology, formal risk-of-bias assessment was not used as an exclusion criterion; however, methodological limitations of included studies were recorded narratively to contextualize findings.

6. Synthesis of Results

Given the anticipated heterogeneity in study designs, interventions, outcome measures, and follow-up intervals, a quantitative meta-analysis was not performed.

Findings were synthesized descriptively and mapped across predefined conceptual domains to:

- characterize how evidence is structured and reported,
- identify areas of convergence and inconsistency, and

highlight gaps in the existing literature.

Results

1. Mapping of Evidence Across Domains

The included studies reported PEP (PEP) outcomes across four principal domains:

1. Patient-related factors
2. Procedure-related factors
3. Practitioner-related factors
4. Pain assessment methods

The distribution of evidence was uneven. Most studies focused on patient- and procedure-related variables. Practitioner-related characteristics were evaluated less frequently. Pain assessment methods varied substantially across studies.

Across the mapped literature, the reported incidence of PEP ranged from approximately 25% to 60% within the first 24–72 hours following treatment.

Preoperative pain was repeatedly identified as a significant predictor of postoperative pain, with reported odds ratios of approximately 3.2 in multivariable analyses. Dental anxiety was associated with increased postoperative pain, with reported effect sizes ranging from 1.5 to 2.0 across studies. Several investigations used structural or multivariate models to evaluate direct and indirect associations between psychological variables and postoperative pain; however, statistical approaches and adjustment strategies varied (1,18–20).

The following subsections present descriptive findings across each mapped domain.

2. Patient-Related Factors

Patient-related factors evaluated in the included studies comprised demographic variables, preoperative clinical status, psychological factors, systemic conditions, and tooth type (18,21,22).

Although frequently examined, these variables were not consistently assessed within fully adjusted multivariable models.

2.1. Demographic Variables

Individual variability in postoperative pain has been examined in relation to demographic characteristics, particularly age and gender. Several clinical studies have reported associations between age and postoperative pain outcomes. Younger adults (18–33 years) have been associated with higher flare-up rates in some cohorts, whereas older patients (>50 years) have been reported to experience more prolonged postoperative pain. Azim et al. identified age >50 years as a predictor of postoperative pain (OR 2.8), and similar associations have been reported in patients aged 40–60 years (18,20,23–25).

The influence of gender on PEP has also been investigated, although findings remain inconsistent

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across studies. Some studies have reported a higher incidence of postoperative pain and flare-ups in female patients. Naoum and Chandler (2002) and Walton (2002) both reported a higher frequency of postoperative pain in women (26,27). More recent studies, including those by Ali et al. (2016), Nair et al. (2017), Garcia-Font et al. (2018), and Shrestha et al. (2018), have also reported associations between female gender and increased postoperative pain or flare-up rates (28–31). In contrast, Ng et al. (2004) found no significant association between gender and postoperative pain (32).

2.2. Preoperative Clinical Status

Preoperative pulpal and periapical diagnoses have been consistently evaluated in relation to postoperative pain and flare-ups (21). Patients with symptomatic irreversible pulpitis or symptomatic apical periodontitis have been reported to experience moderate to severe postoperative pain within the first 48 hours, with incidence rates ranging from 40% to 60% (21,33).

Comparisons between pulpal status categories indicate differences in postoperative pain outcomes. Several studies have reported a higher incidence of postoperative pain in teeth with vital pulpal diagnoses compared with necrotic teeth (33). Sathorn et al. (2008) reported that the presence of preoperative symptoms was associated with an increased likelihood of postoperative pain following root canal treatment (34). Similarly, Alves et al. (2014) found that vital cases exhibited a higher incidence of postoperative pain after instrumentation (35).

Preoperative pain intensity has also been examined as a predictor of postoperative outcomes. Ng et al. (2004) reported that patients presenting with higher preoperative pain scores (VAS >7) were more likely to report persistent pain at 24–48 hours (36). However, variability in the reporting and categorization of baseline pain intensity across studies limits direct comparison and quantitative synthesis of these findings.

2.3. Psychological Modulators

Psychological factors have been investigated as potential determinants of postoperative pain following endodontic treatment. Dental anxiety, commonly assessed using the Dental Anxiety Scale (DAS), has been associated with increased postoperative pain intensity. van Wijk and Hoogstraten (2006) reported that higher DAS scores were predictive of greater postoperative pain following endodontic procedures (37). Subsequent evidence supports this association. A systematic review and meta-analysis reported that individuals with higher levels of dental anxiety consistently experienced greater postoperative dental pain, irrespective of procedural variables (38).

Pain catastrophizing has also been examined in relation to pain perception. Studies by George et al. (2006) and Feinmann et al. (2005) demonstrated that catastrophizing is associated with increased pain responses and may mediate the relationship between prior negative dental experiences and pain perception (39,40). Experimental studies in dental settings further indicate that individuals with higher catastrophizing scores exhibit greater pain responses under controlled conditions (41).

In contrast, sense of coherence (SOC) has been evaluated as a potential protective factor. Bergdahl and Bergdahl (2001) reported that higher SOC scores were associated with lower levels of dental anxiety and reduced pain intensity during dental procedures (42). Collectively, variables such as dental anxiety, dental fear, prior negative experiences, catastrophizing, and SOC have been identified as patient-related factors associated with variability in pain outcomes following dental treatment (18).

Despite these associations, psychological variables are not consistently incorporated into multivariable analyses in endodontic studies. Reviews focusing on endodontic outcomes indicate that, although preoperative anxiety is frequently associated with pain during treatment, postoperative pain outcomes are rarely adjusted for psychological status, limiting the ability to determine their independent contribution (43). In addition, variability in the use of validated assessment tools, such as DAS, has been reported across studies (44).

2.4. Systemic and Comorbid Conditions

Systemic conditions and comorbidities have been evaluated in relation to postoperative pain and flare-ups following endodontic treatment. Diabetes mellitus has been associated with delayed healing and higher complication rates in endodontic outcomes. Fouad and Burleson (1997) reported delayed periapical healing and increased complication rates in diabetic patients (45), while

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Segura-Egea et al. (2011) found an association between diabetes mellitus and increased severity of periapical disease as well as reduced predictability of endodontic treatment outcomes (46).

Evidence regarding immunosuppression and systemic inflammatory conditions is limited. Kwon et al. (2006) reported altered inflammatory responses and prolonged healing in immunocompromised patients receiving corticosteroids or chemotherapy (47). However, data specifically linking immunosuppression to postoperative endodontic pain remain scarce.

Parafunctional habits, particularly bruxism, have also been evaluated in relation to postoperative discomfort. Manfredini et al. (2011) reported an association between bruxism and increased orofacial pain symptoms (48). However, its specific relationship with PEP has been inconsistently reported across clinical studies.

Across studies, systemic conditions and comorbidities have been inconsistently reported, variably excluded, or insufficiently controlled for in clinical trials, limiting comparability and synthesis of their effects on postoperative endodontic pain.

2.5. Tooth Type as a Determinant of Postoperative Pain

Tooth type has been evaluated as a factor associated with postoperative pain and flare-ups following root canal treatment (22). Ng, Glennon, Setchell, and Gulabivala (2004) reported higher rates of post-obturation pain in molar teeth compared with premolars and anterior teeth, with an odds ratio of approximately 2.0 (22). In a related study, Glennon, Ng, Setchell, and Gulabivala (2004) also reported a higher likelihood of post-preparation pain in molar teeth compared with other tooth types (49).

Across studies, posterior teeth—particularly molars—have been more frequently associated with higher postoperative pain incidence compared with anterior teeth (22,49). However, in many studies, tooth type has been analyzed without consistent adjustment for other clinical variables such as pulpal diagnosis, preoperative pain, or operator-related factors.

3. Procedure-Related Factors

Procedure-related factors have been widely evaluated in relation to the incidence, intensity, and duration of postoperative endodontic pain. Clinical studies have examined variables including instrument design, kinematics, irrigation protocols, and obturation strategies, with reported associations between these procedural parameters and postoperative pain outcomes (19,32,33,50).

Across the literature, these variables are frequently assessed alongside patient-related and tooth-related factors, and are often not analyzed in isolation. Considerable heterogeneity exists in study design, instrumentation systems, pain assessment methods, and follow-up intervals, which limits direct comparison across studies.

The following subsections summarize the available evidence on specific procedural variables, including instrumentation type and kinematics, irrigation protocols, activation techniques, intracanal medicaments, obturation strategies, and treatment protocols, in relation to postoperative pain outcomes

3.1. Instrument Type and Kinematics: Manual Files, Continuous Rotary, and Reciprocation

Instrument type and kinematics have been extensively evaluated in relation to postoperative endodontic pain. Early clinical studies comparing manual stainless-steel hand files with engine-driven nickel–titanium (NiTi) rotary systems reported lower postoperative pain intensity and fewer flare-ups with rotary instrumentation (51).

Among engine-driven systems, two principal kinematic approaches are used: continuous rotation and reciprocation. Evidence from randomized clinical trials and systematic reviews is inconsistent. Several randomized clinical trials (Mollashahi et al., 2017 (52); Keskin et al., 2019 (53)) and laboratory studies (Ehsani et al., 2016 (54); Lu et al., 2015 (55)) reported no significant differences in postoperative pain between reciprocating and continuous-rotation systems.

In contrast, Nekoofar et al. (2015) reported higher postoperative pain scores, longer pain duration, and increased analgesic consumption in patients treated with the reciprocating WaveOne system compared with ProTaper Universal rotary instruments (56).

Meta-analytical evidence reflects similar variability. A 2021 meta-analysis reported slightly lower postoperative pain intensity with continuous rotary systems compared with reciprocating systems; however, the reported differences were small (57). An umbrella review published in 2025 also reported lower overall postoperative pain associated with continuous rotary systems, with some variation

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in early postoperative time points (58). Conversely, several randomized clinical trials comparing reciprocating and rotary systems reported no significant differences in pain scores at 6–48 hours (52,59).

Laboratory studies have shown that all instrumentation systems result in apical debris extrusion, with variability reported across different systems and kinematic approaches (54,60). However, clinical studies report variable associations between instrumentation systems and postoperative pain outcomes.

Glide-path preparation has also been evaluated. Randomized clinical trials have reported lower postoperative pain when mechanical glide-path preparation using engine-driven NiTi instruments was performed compared with manual glide-path preparation (53,61).

A summary of instrumentation kinematics and postoperative pain outcomes is presented in Table 2

3.2. Irrigation Protocols and Agitation Techniques

Irrigation variables—including irrigant concentration, volume, temperature, and activation technique—have been widely investigated in relation to postoperative endodontic pain between 2015 and 2025. Evidence from randomized clinical trials and systematic reviews remains heterogeneous.

Regarding sodium hypochlorite (NaOCl) concentration, several randomized clinical trials reported lower postoperative pain intensity and frequency with lower concentrations (e.g., 1.3%) compared with higher concentrations (5.25–8.25%), particularly in non-vital molars treated over multiple visits (62). In contrast, other studies reported no significant differences, or slightly improved early pain outcomes, with higher NaOCl concentrations in vital teeth treated in single-visit protocols (63). A randomized clinical trial comparing 2.5%, 5.25%, and 8.25% NaOCl, as well as chlorhexidine, found no statistically significant differences in postoperative pain among groups (64). Similarly, a 2023 meta-analysis reported a higher prevalence of postoperative pain in low-concentration NaOCl groups compared with high-concentration groups; however, the certainty of evidence was rated as very low due to heterogeneity and methodological limitations (65).

Adjunctive irrigation approaches have also been evaluated. A 2025 randomized clinical trial reported reduced postoperative pain with cryotreated NaOCl compared with conventional irrigation (66). This finding is supported by a 2022 systematic review and meta-analysis demonstrating reduced postoperative pain with intracanal cryotherapy, particularly within the first 48 hours (67).

Irrigation activation techniques—including passive ultrasonic irrigation (PUI), sonic devices, laser activation, and mechanical agitation systems—have been assessed in multiple studies. Randomized clinical trials comparing PUI with alternative activation methods such as EasyClean, XP-Endo Finisher, and diode laser systems reported no statistically significant differences in postoperative pain at various follow-up intervals (68–70). A 2022 systematic review and meta-analysis comparing ultrasonic and conventional syringe irrigation demonstrated lower postoperative pain scores with ultrasonic activation at early time points (6–48 hours), with no significant differences beyond 72 hours (71). A 2025 systematic review focusing on Er:YAG laser–activated irrigation (PIPS) reported reduced pain at 48 hours compared with conventional needle irrigation, with no differences at other time points (72).

Additional randomized trials comparing activated and non-activated irrigation techniques reported variable outcomes, with some studies demonstrating reduced early postoperative pain and others showing no significant differences (73,74). A scoping review of in vivo studies reported improved bacterial reduction with ultrasonic activation but inconsistent effects on postoperative pain across studies (75). A systematic review evaluating photobiomodulation and low-level laser therapy reported limited reductions in postoperative pain confined to early time points (76). Table 3 summarizes the available clinical evidence on the relationship between irrigant concentration and PEP. Table 4 presents comparative data on conventional and activated irrigation methods and their reported effects on postoperative pain across different clinical protocols.

3.3. Intracanal Medicaments and Postoperative Pain

Intracanal medicaments have been widely investigated in relation to postoperative pain in

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Year	Reference	Patient-related factors examined	Key finding (short)
1997	Delamaire M et al (42).	Diabetes — neutrophil chemotaxis, phagocytosis, oxidative burst	Demonstrated impaired PMN (neutrophil) functions in diabetes that can compromise early host defence and infection resolution.
2002	Walton RE et al (26).	Preoperative symptoms, pulp status, analgesic use, patient demographics	Classic review summarizing that more severe presenting symptoms and certain pulp diagnoses are associated with higher flare-up rates.
2004	Ng YL et al (47).	Gender, tooth type, preop pain, size periapical lesion, single-visit vs multivisit	Found 40.2% prevalence of post-obturation pain; female sex, molar teeth, pre-operative pain and small periapical lesions were associated with higher pain.
2007	Alba-Loureiro TC et al (50).	Diabetes — neutrophil dysfunction mechanisms	Detailed review of how hyperglycaemia alters neutrophil chemotaxis, phagocytosis and ROS production — mechanistic basis for impaired infection control in diabetics.
2012	Segura-Egea JJ et al (51).	Diabetes mellitus, glycemic control, periapical disease prevalence	Reported association between diabetes and higher prevalence/size of periapical lesions and worse healing after root canal treatment.
2016	Alí A, et al (52) .	Preoperative VAS pain intensity, tooth vitality, demographic covariates	Found preoperative pain intensity strongly predicted postoperative pain; higher preop VAS increased odds of persistent pain at 24–48 h.
2017	Nair M et al (28) ,	Preop symptoms, pulp status, patient factors	Retrospective series reporting higher flare-ups when preoperative symptoms were present; enumerated host and tooth factors.
2017	García-Font M et al (29).	Operator experience, patient sex, preop pain	Compared techniques and reported demographic associations; noted female patients more likely to report pain in some cohorts.
2021	Bassam S et al (7) .	Multivariable review — preop pain, pulp status, microbial factors, patient factors	Review emphasizing multifactorial etiology; lists patient-related variables (preop pain, anxiety, systemic disease) among contributors.
2021	Gao X, et al (49).	Multiple predictors including patient anxiety, preop pain, demographics	Demonstrated feasibility of multivariable prediction models where patient factors (preop pain, anxiety) improved predictive performance.
2023	Vitali FC, et al (19) .	Dental anxiety (DAS), dental fear, previous negative experiences, sense of coherence	Structural equation modelling showed dental anxiety, prior negative experiences and SOC are significant patient-level predictors of postoperative pain.
2024	Ballal NV, et al (53) .	Preop pain, technique interplay with patient pain	Recent studies continue to show preop pain intensity and patient factors remain important determinants of early postoperative pain.
2024–2025	Alhilou AM, et al (54).	Overview of systematic reviews — patient factors among many	Umbrella review summarizing multiple systematic reviews: patient factors (anxiety, preop pain, systemic disease) repeatedly appear but evidence quality is variable.

Table 1. Summary of studies comparing postoperative pain according to patient-related factors and number of visits during treatment

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Year	Author (et al.)	Study Design	Instrumentation Systems Compared	Tooth Condition / Sample	Postoperative Pain Outcome
2018–2023	Multiple authors	RCTs	Continuous rotary vs reciprocating single-file systems	Molars and premolars; vital and necrotic teeth	Most studies reported no statistically significant differences in postoperative pain when standardized protocols were used.
2020	Various RCTs	RCT	Reciprocating vs rotary systems	Single- and multi-rooted teeth	Some trials reported lower pain within the first 24 h with reciprocating systems, potentially related to shorter instrumentation time.
2021–2024	Various RCTs	RCT	Rotary NiTi systems	Complex canal anatomy	Several studies observed lower pain beyond 48–72 h, possibly due to reduced debris extrusion and improved canal centering.
2025	Puri et al. (140)	Umbrella review (SRs & MAs)	Rotary vs reciprocating NiTi systems	Pooled clinical evidence	Continuous rotary systems associated with lower overall postoperative pain; reciprocating systems showed transient early (≤24 h) pain reduction only.

Table 2. Instrumentation kinematics and PEP

Year	Author (et al.)	Study Design	Concentrations / Conditions Compared	Tooth Condition / Sample	Postoperative Pain Outcome
2019	Mostafa MEHHAA et al. (67)	RCT	1.3% vs 5.25% NaOCl	Necrotic mandibular molars, two-visit treatment	1.3% NaOCl associated with significantly lower pain incidence and intensity at all evaluated time points compared with 5.25%.
2021	Karataş et al. (68)	RCT	NaOCl at 2 °C, 25 °C, 45 °C (same concentration)	Single-visit RCT, various teeth	No significant difference in postoperative pain across temperatures when concentration was held constant.
2021	Demenech LS et al. (69)	RCT	2.5%, 5.25%, 8.25% NaOCl; 2% CHX	Single-session RCT, various teeth	No significant differences in pain intensity or analgesic use among concentrations; procedural factors (overfilling, preparation time) were more predictive of pain.
2023	Meta-analysis (70)	SR/MA	Low (0.5–3%) vs High (≥5%) NaOCl	Pooled RCTs (2015–2023)	Overall pain prevalence was 45% in low-concentration groups vs 39% in high-concentration groups; 24-h pain slightly higher with high concentration. Certainty of evidence rated *very low* due to heterogeneity.
2025	El-Faramawy et al. (71)	RCT	2.5% vs 5% NaOCl; room temperature vs cryotreated	Mandibular first molars, symptomatic irreversible pulpitis	Cryotreated 2.5% NaOCl showed the lowest pain at 6 h; cryotreated 5% also reduced pain compared with non-cooled solutions, indicating a temperature–concentration interaction.
2022	Hespanhol et al. (136)	SR/MA	Cryotherapy vs conventional irrigation (various NaOCl concentrations)	Teeth with apical periodontitis (pooled RCTs)	Intracanal cryotherapy significantly reduced postoperative pain, particularly within the first 48 h; effect more pronounced in symptomatic cases.

Table 3. Irrigation concentration and postendodontic pain

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Year	Author (et al.)	Study Design	Methods Compared	Tooth Condition / Sample	Postoperative Pain Outcome
2021	Karataş et al. (79)	RCT	Syringe irrigation at varying temperatures (no activation)	Single-visit RCT, various teeth	No significant variation in postoperative pain attributable to irrigant temperature alone.
2021	Rocas et al. (80)	RCT	Passive Ultrasonic Irrigation (UAI) vs Laser-Activated Irrigation (LAI)	Asymptomatic teeth undergoing primary RCT	LAI produced significantly lower pain at 6 h; no differences at 24, 48, or 72 h, and analgesic use was similar thereafter.
2023	Palanisamy R et al. (77)	RCT	PUI (Irrisafe tips) vs side-vented needle irrigation	Single-rooted necrotic teeth	PUI significantly reduced pain at 6 and 12 h and achieved higher rates of bacteria-free samples compared with needle irrigation.
2023	Mathevanan S et al. (81)	RCT	Conventional needle irrigation vs LAI vs PUI	Symptomatic irreversible pulpi-tis	Pain scores and analgesic intake were lowest with PUI, followed by LAI, and highest with conventional needle irrigation at 6, 24, and 48 h.
2025	Rai N et al. (78)	RCT	XP-Endo Finisher activation vs PUI vs conventional needle irrigation	Single-visit RCT	No statistically significant differences in postoperative pain or analgesic intake among groups, suggesting modern activation systems do not exacerbate pain in routine cases.
2022	Chalub et al. (137)	SR/MA	Ultrasonic activation vs conventional needle irrigation	Pooled RCTs	Ultrasonic irrigation significantly reduced pain at 6, 24, and 48 h; no differences beyond 72 h, indicating a transient early benefit.
2025	Schmidt et al. (138)	SR/MA	Er:YAG laser–activated irrigation (PIPS) vs needle irrigation	Pooled RCTs	Significant pain reduction observed at 48 h with PIPS; no significant differences at 24 h or ≥72 h.
2024	Elmsmari et al. (139)	SR/MA	Photobiomodulation / laser-assisted endodontic protocols	Pooled clinical trials	Only minimal and short-lived pain reduction (first 6–8 h); no sustained analgesic benefit beyond the first postoperative day.

Table 4. Irrigation / Activation Methods and Postoperative Pain

multi-visit root canal therapy. Among these, calcium hydroxide (CH) is the most frequently studied agent. Early narrative reviews reported antimicrobial activity and reductions in postoperative inflammation associated with CH use (77). In contrast, earlier medicaments such as phenolic compounds (e.g., cresols) have been associated with increased postoperative symptoms (78).

Systematic reviews and meta-analyses published over the last decade report inconsistent findings regarding the effect of calcium hydroxide on postoperative pain. A meta-analysis by Gondim et al. demonstrated modest short-term reductions in postoperative pain compared with no medicament, with effects largely confined to the first 1–14 days and characterized by wide confidence intervals and substantial heterogeneity (79). Similarly, a 2023 systematic review reported no consistent reduction in postoperative pain intensity or flare-up incidence with CH across different diagnostic categories (80). Comparable findings were reported in subsequent systematic reviews (80).

Randomized clinical trials published between 2023 and 2025 also demonstrate variable outcomes. Some studies reported reduced postoperative pain and flare-ups when CH was combined with adjunctive agents such as chlorhexidine gel, anti-inflammatory compounds, or antibiotic mixtures (81). In contrast,

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other trials found no statistically significant differences in postoperative pain when comparing CH, CH–iodoform combinations, or no intracanal medicament in necrotic teeth with apical periodontitis (82).

Recent randomized clinical trials have evaluated alternative intracanal medicaments with anti-inflammatory properties. One study reported significantly lower postoperative pain with diclofenac sodium compared with calcium hydroxide in cases of symptomatic irreversible pulpitis. The same study found no additional benefit when CH was combined with diclofenac compared with diclofenac alone (83).

Across studies, substantial heterogeneity was observed in study populations, pulpal and periapical diagnoses, medicament formulations, and pain assessment protocols. Variability in outcome reporting—including differences in pain scales, follow-up intervals, and analgesic use—was also noted. Table 5 presents a mapping of clinical studies evaluating intracanal medicaments and their reported postoperative pain outcomes.

3.4. Obturation Techniques and Sealer Selection — Effect on PEP

Obturation techniques and sealer types have been widely evaluated in relation to postoperative endodontic pain. Commonly studied obturation methods include cold lateral condensation, warm vertical compaction, thermoplasticized gutta-percha techniques, carrier-based systems, and sealer-based single-cone obturation. Frequently investigated sealer classes include epoxy-resin–based sealers, calcium-silicate/bioceramic sealers, and zinc oxide–eugenol (ZOE)–based sealers. Evidence published up to 2025 includes randomized controlled trials (RCTs), prospective cohort studies, and systematic reviews and meta-analyses (84,85).

Across RCTs and prospective clinical studies conducted between 2015 and 2025, no consistent or clinically significant differences in postoperative pain have been reported among obturation techniques when comparing warm vertical compaction, cold lateral compaction, carrier-based systems, and single-cone techniques. Reported differences were generally small and most frequently observed at early time points, particularly at 24 hours, with no significant differences at later intervals (48–72 hours) (86–88).

A 2024 randomized clinical trial comparing sealer-based single-cone obturation using a calcium-silicate sealer with warm vertical compaction using an epoxy-resin sealer reported no significant differences in postoperative pain trajectories or analgesic intake. A minor difference favoring the single-cone group at 24 hours was observed in selected subgroups, with no differences at later time points (89,90). Similarly, cohort studies comparing thermoplasticized techniques with cold lateral condensation reported inconsistent findings, with some studies indicating differences in early analgesic consumption and others reporting no significant differences (91). Multi-technique comparative studies reported variable findings in early postoperative pain and analgesic use, with no differences in long-term outcomes at one year (85,92).

Comparisons between calcium-silicate/bioceramic sealers and epoxy-resin–based sealers have been extensively reported. Systematic reviews and meta-analyses published through 2024 indicate slightly lower postoperative pain at 24 hours with calcium-silicate sealers in pooled analyses of RCTs; however, no significant differences were observed at later time points, including 48–72 hours and 7 days (84,85). A 2021 systematic review and meta-analysis similarly reported lower early postoperative pain and reduced analgesic intake with bioceramic sealers within the first 24–48 hours, with no sustained differences thereafter (93).

Recent RCTs published between 2023 and 2025 comparing epoxy-resin sealers (e.g., AH Plus) with calcium-silicate sealers (e.g., iRoot SP, TotalFill, NeoSealer Flo) reported mixed findings. Some trials found no statistically significant differences in postoperative pain, whereas others reported lower pain scores at early time points with specific calcium-silicate formulations. A 2025 multicenter randomized clinical trial reported lower postoperative pain at 24 hours with a calcium-silicate sealer compared with an epoxy-resin sealer, with no differences at 48–72 hours (89,94,95).

Earlier studies conducted between 2015 and 2019 reported higher early postoperative pain with zinc oxide–eugenol–based sealers compared with epoxy-resin and bioceramic sealers (89,94,96).

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Year	Authors (et al.)	Design / Context	Medicament(s) Compared	Main Outcome on Post-op Pain / Flare-up
2013	Anjaneyulu K. et al (89) (systematic review)	Review of clinical studies using CH alone or with other agents	Calcium hydroxide (CH) ± other medicaments	Concluded there was no clear evidence that CH alone consistently reduces post-treatment pain.
2020	Ahmad et al. (systematic review & meta-analysis) (90)	Primary RCTs in apical periodontitis / primary RCTs	CH vs no medicament / vs other ICMs	Found a statistically significant reduction in 24-h pain in CH vs no dressing; but at 72 h other medicaments (steroid-antibiotic, CHX) sometimes more effective.
2023	Meta-analysis group (various authors) (91)	Meta-analysis of RCTs / clinical trials in non-vital mature teeth	CH vs no ICM, vs TAP (triple antibiotic paste), vs combinations	CH reduced pain risk compared to no ICM in 1-14-day interval; CH was superior to TAP on day 1; similar to corticosteroid/antibiotic combinations.
2024	Angın et al. (et al.) — RCT in retreatment cases with post-treatment apical periodontitis (PTAP)(92)	Retreatment of single-rooted teeth	CH vs Chlorhexidine gel (CHX) vs CH + CHX	No statistically significant difference in VAS pain scores between groups across 7 days; all three medicaments clinically acceptable for PEP/flare-up control.
2024	Ghabraei et al. (et al.) — Randomized clinical trial on single-visit retreatment with intracanal cryotherapy (93)	Single-visit endodontic retreatment	CH with cryotherapy protocol vs (usual care)	Investigated effect of cryotherapy on postoperative pain; adds dimension of temperature modulation of ICMs.
2025	Kochhar et al. (et al.) — RCT on symptomatic apical periodontitis (94)	Primary RCT, symptomatic teeth	Calcium hydroxide (CH) combinations vs possibly other medicaments (as per study)	Explored combination medicament strategies for postoperative pain management (details per article) — suggests interest in optimizing CH performance.
2025	Fidanoğlu B. (et al.) — Randomized clinical trial on symptomatic irreversible pulpitis (95)	Teeth with irreversible pulpitis, first-visit treatment	CH vs Diclofenac sodium (DCS) vs CH + DCS	DCS (non-CH) was more effective than CH or CH + DCS in reducing post-treatment pain over one week ($p < 0.05$).

Table 5. Summary of clinical studies evaluating intracanal medicaments and postoperative pain

Across studies, variability was observed in study design, sample size, tooth type, pulpal status, obturation technique, analgesic protocols, and reporting of sealer extrusion. Differences in pain assessment time points and outcome measures were also noted. Table 6 presents a mapping of clinical studies evaluating obturation techniques and their reported post-endodontic pain outcomes.

3.5. Duration, Complexity, and Procedural Complications — Effect on PEP

Treatment duration, procedural complexity, and intraoperative complications have been investigated as factors associated with PEP . Evidence from randomized controlled trials, prospective clinical studies, and systematic reviews indicates variable associations across study designs.

A randomized controlled trial comparing single-reciprocating file instrumentation with additional apical enlargement in mandibular molars reported significantly higher pain incidence and intensity at 24 hours in the group with supplementary enlargement, with no significant differences at 48 hours or 7 days (97). Similarly, a prospective split-mouth clinical trial reported higher postoperative pain scores at multiple time points (12 hours, 24 hours, 72 hours, and 1 week) with increased apical preparation size (98). Studies evaluating procedural complexity have included multi-rooted teeth, retreatment cases, and anatomically challenging canals. These studies report longer treatment duration and greater procedural demands compared with uncomplicated cases. Several clinical studies and reviews identify treatment duration and procedural complexity as variables associated with increased postoperative pain, including analyses controlling for preoperative diagnosis and tooth type (1,98,99).

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Year	Author / Ref	Design	Population / Tooth Type	Intervention	Comparator	PEP Outcome s (Timepoints; Scale)	Main PEP Finding	Notes / RoB
2015–2022	Multiple older RCTs & cohort studies (101)	RCT / Prospective	Mixed	ZOE / resin / CSS	Various	PEP 24–72 h	ZOE sometimes associated with more intense PEP; modern sealers (AH Plus, CSS) generally comparable	Heterogeneous; fewer contemporary ZOE studies
2018	Paz A. et al., 2018 (106)	Prospective cohort	Adult teeth	Single cone + bioceramic	WVC / CLC	VAS daily for 7 days	Single cone reported higher early PEP in this cohort (contrasting result)	Older cohort; potential confounding; calls for RCTs
2021	Mekhdieva E. et al., 2021 (141)	SR & meta-analysis (RCTs)	Pooled RCTs (mixed tooth types)	Bioceramic sealers (CSS)	Epoxy-resin sealers (RBS)	PEP intensity & analgesic intake at ۴۸–۷۲ h; pooled mean differences	CSS associated with lower early (24–48 h) PEP and reduced analgesic use; no sustained differences at later time points	Low–moderate certainty; heterogeneity present
2024	Supare M. et al., 2024 (96)	SR & meta-analysis (RCTs)	Pooled RCTs (mixed)	CSS pooled	RBS pooled	Pooled VAS/incidence at 24, 48 h; ORs and mean diff	Small but statistically significant lower 24-h VAS with CSS; effect attenuates later	Evidence rated low–moderate; recommends more RCTs
2024	Alzoubi F. et al., 2024 (102)	RCT	Adult permanent teeth (mixed tooth types)	SBO: single-cone + CSS	WVC + epoxy-resin sealer (AH Plus)	PEP & analgesic intake at 6, 12, 24, 48, 72 h (VAS/NRS)	No clinically meaningful difference overall; small 24-h advantage for SBO in some subgroups	Moderate RoB; allocation/blinding described
2024	Ruiz-Cano A. et al., 2024 (98)	Prospective RCT	Mixed tooth types	SBO (single-cone + CSS)	WVC (epoxy sealer)	PEP at 24, 48, 72 h; analgesic use (VAS)	Similar PEP and analgesic intake; transient differences minimal	Low–moderate RoB
2024	Wahbi E. et al., 2024 (107)	RCT / clinical study	Mixed tooth types	Single cone + Total Fill (CSS)	AH Plus + warm compaction	PEP 24, 48, 72 h; analgesic intake	No significant difference in PeP between groups	Well-conducted; moderate RoB
2025	Hegde VR et al., 2025 (108)	SR & meta-analysis	Pooled RCTs	CSS vs AH Plus	AH Plus	PEP incidence/intensity pooled	CSS performed similarly to AH Plus overall; small early benefit in some analyses	Recent SR supports overall similarity
2025	Algar J. et al., 2025 (105)	RCT	Single-visit RCT, adult teeth	NeoSealer Flo (novel CSS)	AH Plus (resin)	PEP at 24 h and 7 d (VAS)	NeoSealer Flo associated with less PEP at 24 h and 7 d	Moderate RoB; noteworthy 7-day difference
2025	Ensinas P. et al., 2025 (125)	Multicenter RCT	Adult teeth, mixed types	Calcium sili cate–based sealer (NeoSealer Flo)	Resin-based sealer (AH Plus)	PEP at 24, 48, 72 h; VAS	CSS showed lower 24-h pain; 48–72 h pain similar; higher extrusion without clinical pain impact	Moderate RoB; multicenter design

Table 6. Obturation technique and PEP

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Intraoperative procedural complications—including ledge formation, canal transportation, perforations, and instrument separation—have also been evaluated in relation to postoperative pain. Clinical and laboratory studies report associations between these events and increased postoperative symptoms, including pain intensity and flare-up incidence (97–99).

Retreatment cases have been examined separately in multiple studies. Clinical investigations and systematic reviews report higher rates of postoperative pain and flare-ups in retreatment cases compared with primary root canal treatment, particularly in the presence of preoperative periapical pathology (100,101).

Variability in study design, definitions of procedural complexity, treatment duration, and reporting of operator-related variables has been noted across studies. Differences in outcome measures, follow-up intervals, and analgesic protocols further contribute to heterogeneity in reported findings.

Occlusal factors have also been investigated. A 2021 systematic review and meta-analysis evaluating occlusal adjustment following root canal treatment reported no statistically significant differences in postoperative pain intensity at early follow-up intervals (6–48 hours) between teeth with reduced occlusal contacts and those with maintained occlusion (102).). Table 7 presents a mapping of clinical studies evaluating treatment duration, procedural complexity, and related procedural factors in relation to reported post-endodontic pain outcomes.

3.6. Single-Visit versus Multiple-Visit Endodontics — Effect on PEP

Recent systematic reviews and randomized clinical trials evaluating single-visit (SV) and multiple-visit (MV) endodontic treatment demonstrate heterogeneous findings regarding PEP. A 2025 systematic review reported that the majority of included studies found no statistically significant difference in PEP between SV and MV protocols, while several studies reported lower PEP following SV treatment (103). Similarly, a meta-analysis of 29 controlled clinical trials involving 4,341 patients found no significant difference in overall postoperative pain risk or complication rates between SV and MV treatments, although a slightly higher flare-up incidence was observed in SV cases, with limited statistical certainty (104).

Evidence from individual randomized controlled trials provides variable results across different clinical scenarios. In nonsurgical retreatment, one RCT reported significantly fewer postoperative pain episodes in SV treatment compared with MV treatment using calcium hydroxide or chlorhexidine medicaments over a one-month follow-up period (105). In contrast, a 2025 randomized clinical trial in necrotic teeth reported no statistically significant differences in postoperative pain at 6, 24, 48, and 72 hours between SV and MV protocols (106).

Additional randomized clinical trials have reported inconsistent short-term outcomes. In mandibular premolars and molars, higher pain scores were observed following MV treatment at 12 and 48 hours, with no differences at later time points (107). Conversely, in patients with irreversible pulpitis, SV treatment was associated with higher pain intensity and increased analgesic intake at 24 hours, with no significant differences at one week or one month (108). Another clinical trial reported higher early postoperative pain at 6 and 12 hours in SV cases compared with MV cases, with no differences at 24 hours and low flare-up rates in both groups (109).

Adjunctive pharmacological interventions have also been evaluated. A 2022 systematic review and meta-analysis assessing systemic antibiotic use reported no significant reduction in postoperative pain at 24 hours and no decrease in flare-up incidence, regardless of treatment protocol (110).

Across studies, variability in outcomes is accompanied by methodological heterogeneity, including differences in pain assessment tools, follow-up intervals, pulpal status, tooth type, and reporting of analgesic consumption. Inconsistent stratification of cases and lack of standardized outcome reporting limit direct comparison between studies and reduce the certainty of evidence (103).). Table 8 presents a mapping of clinical studies comparing single-visit and multiple-visit endodontic treatment protocols in relation to reported post-endodontic pain outcomes.

3.4. Operator-Related Factors and PEP

Operator-related factors, including clinical experience and treatment delivery characteristics, have been evaluated in relation to PEP following endodontic treatment (111,112).

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Reference (Author, Year)	Study Type	Clinical Focus	Main PEP Finding
Di Spirito et al., 2022 (1)	Narrative/Systematic Review (clinical evidence only)	Multifactorial origins of postoperative pain	Reviews clinical evidence; confirms that procedural complexity, extrusion of debris, and mechanical irritation significantly increase PEP.
Wagh et al., 2022 (113)	Review of clinical flare-up literature	Flare-ups and inter-appointment pain	Clinical data show higher flare-ups in retreatment and complex cases; multi-visit treatments can reduce flare-ups in certain necrotic teeth.
Machado et al., 2020 (clinical) (2)	In vivo clinical study	Intentional foraminal enlargement (IFE) in necrotic teeth	Larger apical preparation and IFE associated with increased short-term postoperative pain in some patients.
Varghese et al., 2024/2025 (115)	Randomized clinical trial	Retreatment; different rotary/reciprocating NiTi systems in single-rooted retreatment	Postoperative pain peaked on day 1 and then declined, indicating that retreatment procedural complexity influences early pain patterns, though no system significantly reduced pain versus others.
Kataia et al., 2024 (RCT) (110)	Triple-blinded randomized clinical trial	Two different apical preparation sizes	Larger apical instrumentation significantly increases early postoperative pain (12–24 h), though pain normalizes by 72 h–1 week.
Amaral et al., 2021 (151)	Systematic review & meta-analysis	Occlusal reduction and postoperative endodontic pain	Occlusal reduction did not significantly reduce postoperative pain after instrumentation or obturation at 6–48 h; evidence certainty moderate.
Nagendrababu et al., 2019/2020 (152)	Randomized clinical trial	Occlusal reduction following root canal treatment	Occlusal reduction associated with lower pain at early time points (≈12 h), but differences diminished thereafter; no sustained long-term benefit.

Table 7. Duration, complexity, and procedural factors associated with PEP

A prospective clinical study comparing treatments performed by undergraduate and postgraduate clinicians using reciprocating instrumentation systems reported differences in postoperative pain profiles between operator groups (111). In addition, a retrospective analysis of more than 800 endodontic treatments found higher rates of procedural errors, including ledge formation and flare-ups, among less experienced clinicians compared with endodontic specialists (112).

Several observational and prospective studies have examined the effect of protocol standardization. A prospective observational study conducted in 2025 comparing bioceramic sealer–based treatments performed by postgraduate students and endodontic specialists reported comparable postoperative pain levels when instrumentation, irrigation, obturation, and analgesic protocols were standardized (92,113).

Across studies, operator-related variables evaluated in relation to postoperative pain include level of clinical experience, type of training, and treatment setting (single-operator versus multiple-operator care). Evidence regarding differences between single- and multi-practitioner treatment models remains limited and inconclusive (92,112,113).

Methodological heterogeneity is evident across studies, including variation in operator classification, procedural protocols, case selection, and outcome assessment. These factors limit direct comparison and reduce the certainty of conclusions regarding the independent effect of operator-related variables on postoperative pain. Table 9 presents a mapping of clinical studies evaluating operator-related factors in

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Reference (Author, Year)	Study Type	Population / Tooth Status	SV Intervention	MV Comparator	PEP Outcomes (Timepoints)	Main PEP Finding
Schwendicke & Göstemeyer, 2017 (117)	Systematic review & meta-analysis	Mixed RCTs (vital/non-vital pulps)	SV RCT	MV RCT	Short-term pain, flare-ups (24–48 h)	Comparable overall PEP; possible higher flare-up risk in SV (weak evidence)
Kumar G et al., 2025 (116)	Systematic review	Mixed clinical RCTs (n=612 records)	SV RCT	MV RCT	PEP incidence/intensity (24–48 h post-obturation)	Majority showed no difference; some less PEP in SV; high heterogeneity noted
Erdem Y., 2018 (118)	RCT	Retreatment cases (n=150)	SV retreatment	MV retreatment ($Ca(OH)_2$ or CHX)	1–7 days & 1 month pain	SV retreatment had fewer pain episodes early & at 1 month
Kamath DG et al., 2025 (119)	RCT	Necrotic teeth (n≈80)	SV RCT	MV RCT	6, 24, 48, 72 h	No significant pain difference at any time point
Gupta NK et al., 2022 (120)	RCT	Mandibular first molars (n≈70)	SV	MV	12, 48 h PEP	MV had higher early PEP vs SV (significant at 12 & 48 h)
Dhyani VK et al., 2020 (121)	RCT	Acute irreversible pulpitis (n≈60)	SV	MV	24 h, 1 wk, 1 mo	SV had higher mild PEP at 24 h; equal at 1 wk & 1 mo
Dr Omkar et al., 2021 (122)	RCT	Mixed permanent teeth	SV	MV	6–72 h POP	SV had higher pain at 6 & 12 h; similar beyond 24 h
Shamszadeh et al., 2020 (145)	Systematic review & meta-analysis	Patients with pulpal necrosis	Antibiotic effects (not SV/MV specific)	N/A	Post-operative endodontic symptoms	Antibiotics reduce post-op symptoms in pulpal necrosis; not directly SV vs MV comparison

Table 8. Single-Visit vs Multiple-Visit Endodontics in PEP

Author / Year	Study Type	Operator Type	Tooth Type	Intervention / Comparison	Main Findings Related to Postoperative Pain
García-Font et al., 2017(126)	Prospective Clinical Study	Undergraduate vs. Postgraduate clinicians	Single- & multi-rooted teeth	Standardized RCT protocol, different operator experience	Significant difference in pain profiles: less experienced operators showed higher early postoperative pain due to less precise instrumentation and greater debris extrusion.
Shao et al., 2024(127)	Large Retrospective Clinical Study (n ≈ 800+)	Residents vs. Specialists	All tooth groups	Comparison of complication rates based on operator experience	Residents showed significantly higher incidence of complications (ledge, apical extrusion, flare-ups), which correlate with higher postoperative pain. Experience strongly influenced outcomes.
Merfea M, 2024(128)	Prospective Observational Study	Postgraduate students vs. Endodontic specialists	Premolars & molars	Bioceramic sealer-based RCT with standardized protocols	No significant difference in postoperative pain, suggesting that strict adherence to standardized protocols may reduce operator-related variability.

Table 9. Operator related factors and PEP

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relation to reported post-endodontic pain outcomes.

3.5. Pain Assessment

Standardized pain assessment methods are widely used to evaluate postoperative outcomes in endodontic research. The Visual Analog Scale (VAS) and Numeric Rating Scale (NRS) are the most frequently reported unidimensional instruments for assessing postoperative pain intensity.

The VAS typically consists of a 100-mm line anchored by "no pain" and "worst imaginable pain," providing a continuous measure of pain intensity. A bibliometric analysis of postoperative endodontic pain studies identified VAS as the most commonly used assessment tool in the literature (114). The NRS, based on discrete numerical ratings (commonly 0–10), has been shown to correlate strongly with VAS scores (115).

Comparative studies and systematic reviews report differences in usability and measurement characteristics between these instruments. Evidence indicates that NRS is associated with lower error rates and higher patient preference, while VAS may be more prone to scoring and interpretation variability (116–120).

Across studies, postoperative pain has been assessed at variable time points, most commonly including early (e.g., 6–12 hours), short-term (24–72 hours), and extended follow-up intervals (e.g., 7 days). However, substantial heterogeneity exists in the timing and frequency of assessments, as well as in reporting of pain outcomes.

Discussion

This scoping review mapped current in vivo evidence (2015–2025) on factors influencing PEP, encompassing tooth-related variables, patient-related factors, procedural techniques, irrigation and obturation strategies, sealer types, operator-related variables, and pain assessment approaches. In line with the purpose of a scoping review, this synthesis highlights how evidence is distributed across domains, how it has been reported, and where important gaps remain. Overall, the findings confirm that PEP is a multifactorial phenomenon in which preoperative inflammatory status, anatomical complexity, and the degree of apical irritation appear to exert a greater influence than isolated differences in materials or techniques (130) .

Tooth-related and preoperative factors demonstrated consistent associations with postoperative pain. Molar teeth showed higher early pain levels than premolars and anterior teeth, likely reflecting increased anatomical complexity, longer treatment duration, and a higher risk of apical debris extrusion. Similarly, teeth with symptomatic irreversible pulpitis exhibited the highest postoperative pain intensity, which may be explained by elevated baseline inflammatory mediators, peripheral sensitization, and increased nociceptor excitability. In contrast, necrotic teeth generally presented with lower immediate pain but a greater susceptibility to flare-ups, particularly when apical extrusion of debris or irrigants occurred.

Procedural variables—including instrumentation kinematics, obturation technique, sealer type, and number of visits—showed limited clinically meaningful differences in postoperative pain when treatments were performed under controlled conditions. The apparent equivalence between rotary and reciprocating systems, as well as among obturation techniques, likely reflects the dominant role of procedural control, particularly the prevention of apical extrusion. Although calcium-silicate/bioceramic sealers demonstrated a modest reduction in early postoperative pain compared with epoxy-resin sealers in some studies, this effect was small and transient. These findings suggest that the biological response to apical irritation may outweigh differences in material properties.

The influence of treatment duration and procedural complexity provides further insight into the biological basis of postoperative pain. Prolonged instrumentation, additional apical enlargement, and retreatment procedures were consistently associated with increased early pain. This relationship is likely mediated by greater mechanical irritation of periapical tissues and increased extrusion of infected debris. The observation that pain differences typically peak within the first 24 hours and resolve thereafter supports the concept that postoperative pain is primarily an acute inflammatory response rather than a marker of long-term tissue damage. Retreatment procedures, in particular, may amplify this response due to disruption of established biofilms and increased procedural demands.

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Irrigation-related findings further reinforce the multifactorial nature of PEP. Variability in outcomes across studies suggests that factors such as apical extrusion, irrigant temperature, activation duration, and baseline inflammatory status may be more influential than irrigant concentration alone. Similarly, the inconsistent benefits observed with irrigation activation techniques indicate that their effect on postoperative pain is likely context-dependent rather than universally predictable.

Evidence regarding intracanal medicaments suggests that their role in postoperative pain modulation may be more complex than previously assumed. While calcium hydroxide remains widely used for its antimicrobial properties, its limited and inconsistent effect on pain reduction indicates that antimicrobial activity alone may not sufficiently address the inflammatory mechanisms underlying postoperative pain. Emerging evidence supporting intracanal anti-inflammatory agents highlights the potential importance of directly targeting inflammatory pathways; however, further high-quality trials are required to clarify their role.

The comparison between single-visit and multiple-visit treatment protocols illustrates the interaction between procedural and biological factors. Although overall differences in postoperative pain were minimal, early pain variations may be explained by differences in microbial control, duration of instrumentation, and the use of intracanal medicaments. Single-visit procedures may increase early inflammatory responses in infected cases due to the absence of inter-appointment disinfection, whereas multiple-visit approaches may reduce early inflammation through staged microbial control. However, these effects appear transient and are likely influenced by operator technique and case selection.

Operator-related factors represent an important but often underexplored source of variability in postoperative pain outcomes. Differences in clinical skill, experience, and decision-making may influence key procedural steps, including canal negotiation, instrumentation, and complication management. The observation that differences between operators diminish under standardized protocols suggests that adherence to evidence-based procedures may mitigate experience-related variability. In addition, continuity of care and careful procedural planning may contribute to more consistent outcomes, although current evidence remains limited.

Psychological factors also play a significant role in modulating postoperative pain perception. Anxiety, pain catastrophizing, and prior negative dental experiences may amplify pain responses through central and peripheral mechanisms, independent of procedural variables. Conversely, psychological resilience factors, such as sense of coherence, may attenuate perceived pain. The limited incorporation of these variables into clinical studies restricts understanding of their independent contribution and highlights an important area for future research.

Pain assessment methodology represents a further source of heterogeneity. Differences in scale selection, timing of assessment, and patient instruction may influence reported outcomes and complicate comparison across studies. While the Visual Analog Scale offers high sensitivity, its susceptibility to measurement variability may limit its reliability in some contexts. The Numeric Rating Scale appears to provide greater ease of use and consistency, particularly in clinical and remote settings. The limited use of multidimensional pain assessment tools also restricts evaluation of the complex sensory and affective components of postoperative pain.

Several important methodological limitations were identified across the included studies. These include heterogeneity in pain assessment protocols, inconsistent follow-up intervals, variable reporting of analgesic use, and inadequate control of confounding variables such as operator experience and treatment complexity. In addition, restriction to English-language publications introduces potential language bias and may have resulted in the exclusion of relevant evidence.

Taken together, these findings highlight the need for more standardized, rigorously designed clinical studies with clearly defined outcome measures and comprehensive reporting. Future research should aim to integrate biological, procedural, operator-related, and psychological variables within unified study designs to better elucidate the determinants of PEP and improve the clinical applicability of evidence.

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Future Directions

Future research on PEP should emphasize greater methodological standardization, adhering to established reporting frameworks such as PRISMA-ScR, JBI, and CONSORT guidelines. Studies should consistently employ validated pain assessment tools (e.g., Visual Analogue Scale [VAS] or Numeric Rating Scale [NRS]), clearly defined follow-up intervals, standardized postoperative analgesic protocols, and uniform diagnostic criteria for pulpal and periapical conditions, including symptomatic irreversible pulpitis and necrotic teeth. High-quality randomized controlled trials directly comparing obturation techniques, sealer types, irrigation activation systems, and single- versus multiple-visit strategies remain particularly necessary, especially in symptomatic and retreatment cases where postoperative pain patterns are more complex and variable.

Importantly, future trials should explicitly account for preoperative analgesic intake as a major confounding factor. Many patients with severe preoperative symptoms self-administer high doses of analgesics prior to treatment, while others tolerate pain without medication. Failure to control for this variability may substantially bias postoperative pain outcomes. Accordingly, improved randomization strategies—such as stratification based on preoperative pain intensity and prior analgesic consumption, or allocation into predefined subgroups—are needed to minimize confounding effects and allow more accurate attribution of postoperative pain to procedural or material-related variables.

Further investigation into operator-related factors is also warranted, including the influence of clinician experience, continuity of care (single versus multiple practitioners), and procedural errors on postoperative pain outcomes. Large-scale, multicenter studies with adequate statistical power and extended follow-up periods would strengthen the evidence base and improve generalizability across clinical settings.

Finally, emerging technologies—including artificial intelligence–based pain prediction models, real-time irrigation pressure monitoring, optimized irrigation activation systems, and next-generation bioactive sealers—deserve focused investigation for their potential to reduce apical irritation and postoperative discomfort. Integrating biological mechanisms, procedural variables, and patient-reported outcomes within future study designs will be essential for establishing a comprehensive, clinically applicable framework for predicting, preventing, and managing PEP.

Conclusion

This scoping review demonstrates that PEP is primarily governed by preoperative inflammatory status, procedural complexity, and the degree of apical irritation rather than by isolated differences in contemporary instruments, materials, or techniques. While advances in irrigation activation, obturation materials, and intracanal medicaments may modestly influence early pain in selected cases, their effects are generally transient and clinically limited when procedural control is optimized. Effective prevention of postoperative pain therefore relies on careful case selection, meticulous control of apical extrusion, thoughtful appointment planning, and attention to patient psychological factors. Future high-quality randomized trials should prioritize standardized pain assessment, stratification by diagnostic complexity, and integration of operator- and patient-centered variables to refine predictive models and improve patient-centered outcomes in endodontic care.

Declarations

Availability of Data and Materials

Data sharing is not applicable to this article as no new datasets were generated or analyzed during the current scoping review. All data extracted from included studies are presented in the summary tables and reference citations.

Competing Interests

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funding agency in the public, commercial, or not-for-profit sectors.

Authors' Contributions

Somayeh Majidi: Conceptualization, Investigation, Writing – original draft, Data curation, Formal analysis.

Sholeh Ghabraei: Methodology, Validation, Writing – review & editing, Visualization, Project administration.

Hadi Assadian: Conceptualization, Supervision, Resources, Writing – review & editing, Corresponding author.

Declaration of Generative Artificial Intelligence (AI) Utilization

To ensure the highest standards of clarity and readability, this manuscript underwent a thorough review and editing process supported by advanced artificial intelligence (AI) tools. The AI assistance focused solely on refining sentence structure, enhancing coherence, and improving overall language flow without altering the original scientific content or intent. Importantly, AI was not involved in the conception of the study, development of the main ideas, or interpretation of the results, and therefore is not considered an author of this work. This approach facilitated clearer communication of complex ideas and helped eliminate ambiguities, thereby making the manuscript more accessible and engaging for a diverse readership. The use of AI in this capacity serves as a valuable supplement to the authors' expertise, ensuring the presentation of the research is both precise and polished.

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