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REVIEW ARTICLE

Effectiveness of root canal filling materials and techniques for treatment of apical periodontitis: A systematic review

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Abstract

Background: Apical periodontitis (AP) is an inflammatory disease of the apical periodontium as sequelae of pulp death. It is managed by disinfection and filling of the root canal space.

Objectives: The aim of this systematic review was to investigate whether obturation techniques and materials used for root canal filling led to the management of AP.

Methods: A systematic review protocol was written following the preferred reporting items for systematic reviews and meta-analyses (PRISMA) checklist and registered on the international prospective register of systematic reviews (PROSPERO; CRD42021260275) including two populations, interventions, comparisons, outcomes and time (PICOT) for the research questions querying the effectiveness of obturation techniques (PICOT 1) and materials (PICOT 2) for the management of AP. Electronic searches were conducted on PubMed, ScienceDirect, Scopus and Embase search engines. Searches on International Endodontic Journal, Journal of Endodontics, Clinical Oral Investigations, Journal of Dental Research and Journal of Dentistry websites were also conducted, until May 2021. Both primary (tooth survival) and secondary outcomes were evaluated. The risk of bias was assessed by Cochrane RoB2 for the randomized and ROBINS-I for the nonrandomized trials.

Results: The search strategy identified 1652 studies, with 1600 excluded on the title and abstract screening, leaving 52 studies for full-text screening. In total, 10 studies met the inclusion criteria. The obturation technique and materials used did not affect the outcome of AP. Vertical compaction resulted in faster resolution of periapical lesions. The oral health-related quality of life of patients treated with lateral condensation exhibited poorer outcomes compared with single matched cone after 6 months of recall.

Discussion: The inclusion and exclusion criteria used for this systematic review enabled the capture of all the literature available on the effect of obturation techniques and materials on the outcome of AP. The data were heterogenous, and a number of articles investigating obturation techniques had no information on the materials and techniques used as they looked at the quality of fill.

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Conclusions: Included studies did not find any difference between different procedures (PICOT 1) and materials (PICOT 2). The risk of bias was high, thus the findings should be interpreted with caution.

Registration: PROSPERO registration number: CRD42021260275.

KEYWORDS

apical periodontitis, gutta-percha, obturation materials, root canal filling, root canal sealers

INTRODUCTION

Apical periodontitis (AP) is an inflammatory response of periradicular tissues as a reaction to intraradicular bacterial infection (Nair, 2006; Ricucci & Siqueira Jr, 2010). A recent meta-analysis reported that AP is a highly prevalent disease with 52% of adult individuals presenting with at least one tooth affected by periapical pathosis (Tibúrcio-Machado et al., 2021). The incidence of AP has been reported to range from 16% to 86% and is associated with several person-related and tooth-related factors such as countries, systemic conditions, radiographic assessment for diagnosis and presence of a root filling (Kirkevang et al., 2007; Kirkevang et al., 2017; Tibúrcio-Machado et al., 2021).

The presence of preoperative AP is considered a strong and negative predictor of the outcome of root canal treatment, indicating that root canal infection might result in an endodontic failure (Chugal et al., 2001; Ng et al., 2011) and eventually increase the risk of tooth loss. Complete resolution of AP after initial treatment or retreatment ranges between 74% to 86% and functionality over time in 91%–97% of cases (Aquilino & Caplan, 2002; Dammaschke et al., 2003; Friedman & Mor, 2004; Stoll et al., 2005).

When AP has developed, irrespective of its frequent asymptomatic course, treatment is aimed at restoring the periradicular tissues to health by nonsurgical root canal treatment and, if necessary, in combination with a surgical endodontic approach (ESE Guidelines, 2006). The nonsurgical treatment of AP aims to eliminate the infection from the root canal space through chemo-mechanical preparation and to prevent re-infection by obturation of the root canal (Schilder, 1967). This fundamental step in root canal treatment is conventionally achieved with either a solid core and a sealer, or materials that can be modified and adapted to the shape of the root canal system (Schilder, 1967) and over the years, various materials and root canal filling techniques have been proposed (ESE Guidelines, 2006). It is clinically relevant to know the impact that the choice of materials and obturation techniques have on the effectiveness of root canal treatment.

Most of the currently employed obturation techniques, such as cold lateral condensation and warm vertical compaction, use gutta-percha and sealer. Gutta-percha was

introduced in dentistry in the mid-19th century as a root canal filling material to be used with classical filling techniques that were described several decades ago. The warm vertical technique is one of the most widely used obturation techniques (Ørstavik, 2017). Cold lateral condensation has been used frequently as a basis of comparison for other filling techniques (Dummer, 1991).

Combined with gutta-percha, endodontic sealers play a crucial role within obturation techniques, to fill the gaps, which are not obturated with gutta-percha. Epoxy resin-based sealers are frequently used as a reference material to which new sealers are compared (Viapiana et al., 2016) because they fulfil a key requirement of a root canal filling material by providing a stable apical seal (Bouillaguet et al., 2008). These materials associated with gutta-percha and used in vertical or lateral compaction techniques have been described as the gold standard for sealer cements (Viapiana et al., 2016). Over time, many alternatives to the traditional gutta-percha-based systems have been proposed to enhance the seal at sealer–core obturation material and sealer–radicular dentine interfaces (Pandey et al., 2020).

The European Society of Endontology ESE Guidelines (ESE, 2006) provide guidance on the quality of care to be provided in managing patients with the endodontic disease. Approximately 40%–60% of endodontic treatment failures are reported to be associated with inadequate obturation of the root canal system (Ingle et al., 2002; Ng et al., 2008) related to over- and underfilling (Damaschke et al., 2003; Stoll et al., 2005), and overall poor quality of root filling (Hoskinson et al., 2002; Ng et al., 2010). Despite the abundance of laboratory studies and the ever-increasing clinical employment of different materials and techniques, most of the published studies, which have evaluated the impact of root filling materials/techniques on treatment effectiveness, did not find any significant influence (Chu et al., 2005; Ng et al., 2007).

Systematic reviews of well-performed randomized controlled clinical trials are described as the gold standard of clinical evidence (Duncan et al., 2016). The development of clinical guidelines based on the systematic reviews contributes to improve the quality of dental and medical care for the general population by providing evidence-based recommendations relevant to clinicians and patients in

decision-making on appropriate health care for specific problems (Duncan et al., 2021).

The present study is part of a series of systematic reviews being undertaken by the European Society of Endodontology to provide evidence of the best quality of care for the management of patients requiring endodontic treatment. The purpose of this systematic review is to provide a comprehensive overview to verify: (i) the effectiveness of chemo-mechanical preparation and root canal filling with any type of nonlateral compaction technique in comparison with cold lateral compaction technique using gutta-percha in terms of clinical and patient-related outcomes, in permanent teeth with AP; (ii) the effectiveness of chemo-mechanical preparation and root canal filling with any other type of sealer in comparison with epoxy resin (AH Plus/AH 26) using gutta-percha in terms of clinical and patient-related outcomes, in permanent teeth with AP.

MATERIALS AND METHODS

The systematic review was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) (Moher et al., 2009). The review was registered on the international database of prospectively registered systematic reviews with a health-related outcome (PROSPERO) under number CRD42021260275.

Two review questions were set *a priori*:

PICOT 1 'In patients with apical periodontitis in permanent teeth (P) what is the effectiveness of chemo-mechanical preparation and root canal filling with any type of nonlateral compaction technique (I) in comparison with chemo-mechanical preparation and cold lateral compaction technique using gutta-percha (C) in terms of clinical and patient-related outcomes (O)?'

PICOT 2 'In patients with apical periodontitis in permanent teeth (P) what is the effectiveness of chemo-mechanical preparation and root canal filling with any other type of sealer (I) in comparison with chemo-mechanical preparation and root canal filling with epoxy resin (AH Plus/AH 26) using gutta-percha (C) in terms of clinical and patient-related outcomes (O)?'

Inclusion criteria were

Types of studies: Human experimental studies (Randomized Control Trials, Comparative Clinical trials—nonrandomized). Our search was supplemented

by longitudinal observational studies (retrospective and prospective comparative cohort and case-control studies) to ensure that all relevant clinical information that is often not tested in experimental studies is captured. Some outcome measures such as pain, tenderness, swelling and need for medication had a follow-up period of a minimum of 7 days and a maximum of 3 months, while radiographic evaluation was a minimum of 6 months.

Participants: Adults (>18 years old), systemically healthy individuals diagnosed with apical periodontitis.

Intervention: Nonsurgical primary root canal treatment in permanent teeth with radiographically confirmed apical periodontitis using techniques alternative to lateral condensation of gutta-percha and AH Plus sealer.

Comparison: Root canal treatment in permanent teeth using lateral condensation of gutta-percha and AH Plus sealer.

The outcomes were a combination of patient- and clinician-reported outcome measures. The most critical outcome was 'tooth survival'. Other critical outcomes included 'pain, tenderness, swelling, need for medication (analgesics, antibiotics)', 'radiographic evidence of reduction in apical lesion size (loose criteria)' and 'radiographic evidence of normal periodontal ligament space (strict criteria). Additional outcome(s) such as 'tooth function (fracture, restoration longevity)', 'need for further intervention', 'adverse effects (including exacerbation, restoration integrity, allergy)', 'oral health-related quality of life and 'presence of sinus tract' were also considered.

The exclusion criteria were studies performed with <6 months recall for the long-term outcomes, case studies, one-armed studies without a control group, experimental groups without radiographic evidence of apical periodontitis and all studies where the assessment was performed based on the quality of obturation without the details of the obturation method and material used.

Data collection and risk of bias (quality assessment)

The searches were conducted on Pubmed, ScienceDirect, Scopus and Embase search engines. Hand searches on International Endodontic Journal, Journal of Endodontics, Clinical Oral Investigations, Journal of Dental Research and Journal of Dentistry websites were also performed. The cut-off date was May 2021. The keywords for the searches are shown in Table 1. Only articles in English and with full texts were included. A two-stage screening (titles and abstract first and then full-text) was carried out in duplicate and independently by two reviewers (JC and CP). A data screening form was created at the full-text stage to verify study eligibility,

TABLE 1 Search criteria for the two PICOs related to management of apical periodontitis

Pico question	Key words
In patients with apical periodontitis in permanent teeth (P) what is the effectiveness of chemo-mechanical preparation and root canal filling with any type of nonlateral compaction technique (I) in comparison with chemo-mechanical preparation and cold lateral compaction technique using gutta-percha (C) in terms of clinical and patient-related outcomes (O)?	Apical periodontitis Apical periodontitis OR chemo-mechanical preparation Apical periodontitis OR root canal filling Apical periodontitis OR root canal filling OR obturation Chemo-mechanical preparation Apical periodontitis AND lateral condensation Apical periodontitis AND vertical compaction Apical periodontitis AND cold lateral compaction Apical periodontitis AND single cone Apical periodontitis AND gutta-percha
In patients with apical periodontitis in permanent teeth (P) what is the effectiveness of chemo-mechanical preparation and root canal filling with any other type of sealer (I) in comparison with chemo-mechanical preparation and root canal filling with epoxy resin (AH Plus/AH 26) using gutta-percha (C) in terms of clinical and patient-related outcomes (O)?	Apical periodontitis Apical periodontitis OR chemo-mechanical preparation Apical periodontitis OR root canal filling Apical periodontitis OR root canal filling OR obturation Sealer Apical periodontitis OR sealer AH Plus OR AH 26 Apical periodontitis AND sealer

Note: The searches were performed on different electronic databases and a selection of journals.

carry out the methodological quality assessment and extract data on study characteristics and outcomes. When in disagreement, the reviewers met to discuss the data and reach consensus. The final spreadsheet for each study included the following data in the final review: name and country of the first author, year published, name of the journal, type of study design, total number of participants, age distribution, number of participants with apical periodontitis, outcome measures employed, type of radiographic assessment and method of radiographic assessment. All extracted data were stored in tables. The reasons for the exclusion of studies after assessing the full text are shown in Table 2. Data extraction was performed by two reviewers (JC, CP).

The methodology used for the quality assessment was based on a critical appraisal of the included studies, performed depending on the type of study: for randomized control trials, RoB2 (<https://methods.cochrane.org/bias/resources/rob-2-revised-cochrane-risk-bias-tool-randomized-trials>) was used, while for controlled clinical trials (nonrandomized) ROBINS-I (<https://methods.cochrane.org/methods-cochrane/robins-i-tool>) was used. Two reviewers (JC and CP) scored the methodological qualities of the included studies.

For the RoB2, five domains were considered namely the randomization process (D1), deviations from the intended interventions (D2), missing outcome data (D3), measurement of outcome (D4) and selection of the reported result (D5). The replies included Yes, no probably yes, probably no or not applicable. For the nonrandomized studies the

risk of bias was recorded for the random sequence generation, allocation concealment, blinding of the participants and the personnel, blinding of the outcome assessment, incomplete outcome data, selective reporting and other forms of bias. The inter-reviewer reliability (percentage of agreement and kappa correlation coefficient) of the full-text analysis was calculated.

The eligible studies were assessed for the outcome measures including the following:

- ‘tooth survival’.
- ‘pain, tenderness, swelling, need for medication (analgesics, antibiotics)’.
- ‘radiographic evidence of reduction in apical lesion size (loose criteria)’ and ‘radiographic evidence of normal periodontal ligament space (strict criteria).
- Additional outcome(s) such as ‘tooth function (fracture, restoration longevity), ‘need for further intervention’, ‘adverse effects (including exacerbation, restoration integrity, allergy)’, ‘oral health-related quality of life and ‘presence of sinus tract’.

RESULTS

The outputs from the searchers performed and the exclusions are shown in Figure 1. All the publications that included a clinical study were collected at this stage to

TABLE 2 List of publications that were excluded after full-text search and reasons for exclusion

Name of the first author	Country of the first author	Year published	Name of the journal	Reasons for exclusion
Alsulaimani RS	Saudi Arabia	2016	BMC Oral Health	Wrong population
Akbar I	Saudi Arabia	2013	The Journal of Contemporary Dental Practice	Wrong study design
Albashaireh ZSM	Jordan	1998	Journal of Dentistry	Wrong study design
Al-Negrish ARS	Jordan	2006	Journal of Dentistry	Wrong population
Alonso-Ezpeleta LO	Spain	2012	Medicina Oral, Patologia Oral y Cirugia Bucal	Wrong population
Angerame D	Italy	2017	Giornale Italiano di Endodonzia	Wrong study design
Aslan T	Turkey	2021	International Endodontic Journal	Wrong population
Atav Ates A	Turkey	2019	Clinical Oral Investigations	Wrong outcome
Barborka BJ	Texas	2017	Journal of Endodontics	Wrong population
Bardini G	Italy	2020	Clinical Oral Investigations	Wrong study design
Brizuela C	Chile	2020	Journal of Dental Research	Wrong population
Cotton TP	USA	2008	Journal of Endodontics	Wrong study design
Cunha SA	Brazil	2020	Brazilian Dental Journal	Wrong population
Eyuboglu TF	Turkey	2017	Clinical Oral Investigations	Wrong study design
Fernández R	Colombia	2017	Journal of Endodontics	Wrong population
Ferreira NS	Brazil	2020	Brazilian Oral Research	Wrong population
Fleming CH	USA	2010	Journal of Endodontics	Wrong study design
Friedman S	Canada	1995	Journal of Endodontics	Insufficient information on data
He J	Texas	2017	Journal of Endodontics	Wrong population
Hommez GM	Belgium	2003	International Endodontic Journal	Wrong study design
Hoskinson SE	United Kingdom	2002	Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, Endodontics	Wrong population
Huumonen S	Norway	2003	International Endodontic Journal	Wrong population
Iqbal M	USA	2009	International Endodontic Journal	Wrong population
Jacoub MS	Egypt	2018	Future dental Journal	Wrong population
Koch M	Sweden	2015	International Endodontic Journal	Wrong outcomes
Lussi A	Switzerland	2002	International Endodontic Journal	Wrong population
Metska ME	The Netherlands	2013	Journal of Endodontics	Wrong population
Mohan SM	India	2009	Medical Journal Armed Forces India	Wrong population
Molven O	Norway	1988	International Endodontic Journal	Wrong population
Nino-Barrera JL	Colombia	2018	Acta Odontol Latinoam	Wrong population
Orstavik D	Norway	1993	International Endodontic Journal	Wrong population
Orstavik D	Norway	2004	European journal of Oral Sciences	Wrong population
Orstavik D	Norway	1987	Dental Traumatology	Wrong population
Reid RJ	Australia	1992	International Endodontic Journal	Wrong population
Restrepo-Restrepo FA	Colombia	2019	International Endodontic Journal	Insufficient information on data
Ricucci D	Italy	2016	Journal of Endodontics	Wrong population
Strange KA	USA	2019	Journal of Endodontics	Wrong population

(Continues)

TABLE 2 (Continued)

Name of the first author	Country of the first author	Year published	Name of the journal	Reasons for exclusion
Swathi UB	India	2020	International Journal of Research in Pharmaceutical Sciences	Wrong population
Tan HSG	Singapore	2021	Journal of Endodontics	Wrong population
Tennert C	Germany	2013	Clinical Oral Investigations	Wrong population
Waltimo TM	Norway	2001	Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, Endodontics	Wrong population
Yu YS	USA	2021	Clinical Oral Investigations	Wrong population

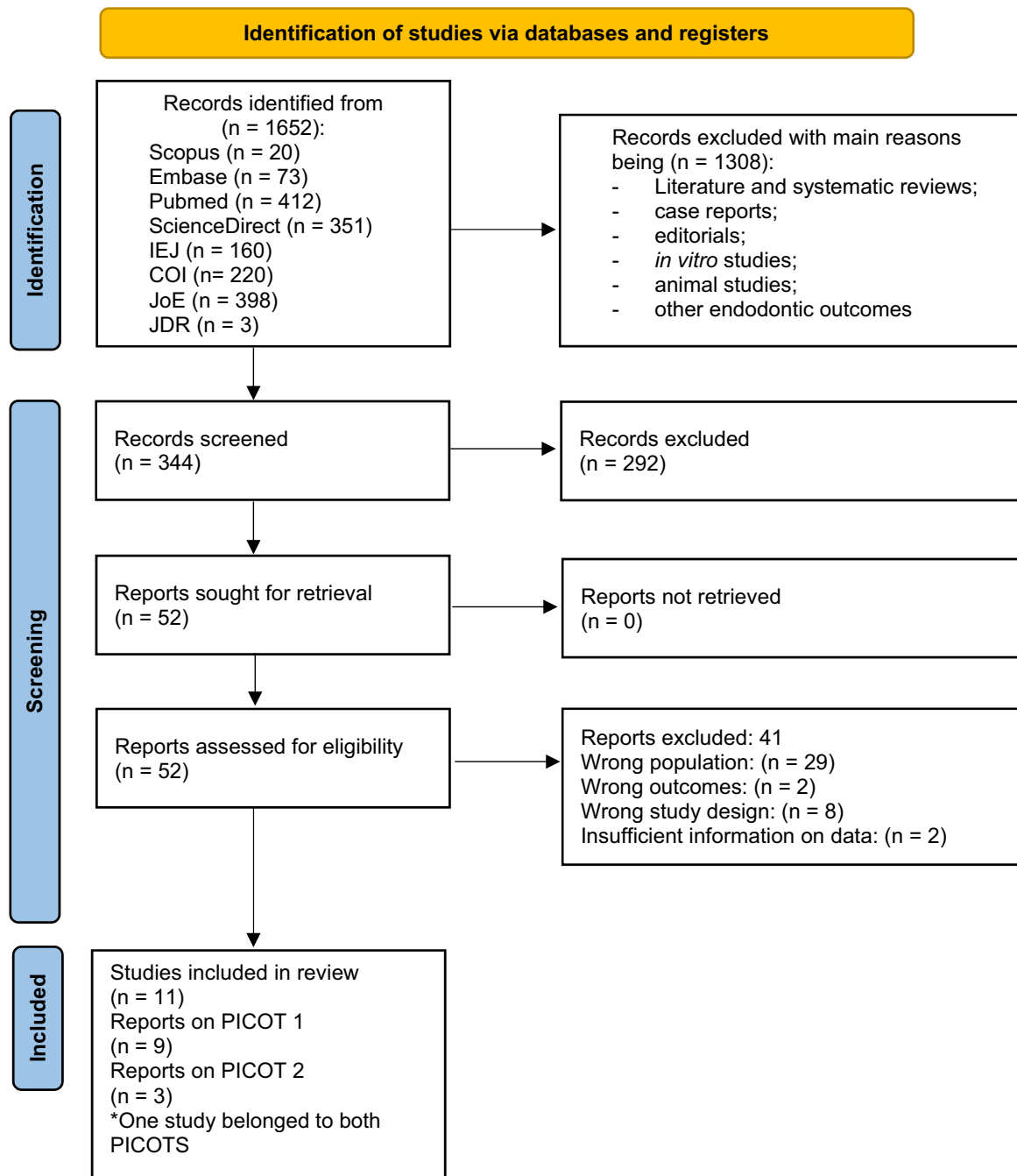


FIGURE 1 PRISMA flowchart with identification of the studies via databases and registers

ensure that nothing was missed. This was followed by full-text screening. The inter-reviewer reliability (percentage of agreement and kappa correlation coefficient) of the full-text analysis was 94% with a Kappa of 0.87.

The full-text screening resulted in 292 exclusions due to the presence of duplicates and publications that were not in the scope of the review. The final listing resulted in 52 outputs. There were exclusions from this list as indicated in [Table 2](#) with a total of 10 articles shortlisted with 9 for PICOT 1 ([Table 3](#)) and 2 articles for PICOT 2 ([Table 4](#)) with one article (Aqrabawi, 2006) eligible for both PICOTS.

The heterogeneity of the articles that were shortlisted was evident from the outset. The methodology used for the studies was different, and all studies presented a high risk of bias. This precluded statistical analyses and meta-analyses.

PICOT 1 – ‘In patients with apical periodontitis in permanent teeth (P) what is the effectiveness of chemo-mechanical preparation and root canal filling with any type of nonlateral compaction technique (I) in comparison with chemo-mechanical preparation and cold lateral compaction technique using gutta-percha (C) in terms of clinical and patient-related outcomes (O)?’

For PICOT 1, six studies (de Figueiredo, Lima, Lima, et al., 2020; de Figueiredo, Lima, Oliveira, et al., 2020; Diniz-de-Figueiredo et al., 2020; Kandemir Demirci & Çalışkan, 2016; Ozer & Aktener, 2009; Wong et al., 2015) were randomized control trials so RoB2 was used for the risk of bias assessment. Three studies (Aqrabawi, 2006; Chu et al., 2005; Michanowicz et al., 1989) were controlled clinical trials (nonrandomized) thus ROBINS-I was used for the risk of bias assessment. A detailed description of the risk of bias in the included studies is reported in [Tables 5](#) and [6](#). All the included randomized control trials were found at high risk of bias. The non-randomized clinical trials were found at moderate-to-high risk of bias.

The studies de Figueiredo, Lima, Lima, et al., 2020; de Figueiredo, Lima, Oliveira, et al., 2020; Diniz-de-Figueiredo et al., 2020 were one clinical study that was split up into three publications whereby the outcomes were separated. In this study the risk of bias was low for the Domains 1–4 with bias arising from the randomization process, deviations from the intended interventions, missing outcome data and measurement of the outcome was low. The randomization process was undertaken by creating a list from a website and the dentist did not open the envelope until the day of the intervention. The patient

was not aware of the choice of intervention. The sample size was calculated and the same evaluations were conducted across all the groups. All the outcome measures were available for all the groups and two independent blinded reviewers assessed the outcome. The valuers were calibrated before the start of the study. Drop-outs were equally divided between the groups. The oral health-related quality of life was reported in Diniz-de-Figueiredo et al., 2020, the periapical healing using the PAI score in de Figueiredo, Lima, Lima, et al., 2020 and the root canal filling quality and the occurrence of sealer extrusion reported in de Figueiredo, Lima, Oliveira, et al., 2020. A high risk of bias was shown in the reported result; as in each paper, only one outcome was measured. Kandemir Demirci & Çalışkan, 2016 also showed low risk of bias in D1-4 and high risk in D5 due to the limited outcomes measured.

Ozer & Aktener (2009) had some concerns in D1 and D5, high risk of bias in D2 and D4 and low risk in D3. There was no information provided whether the operators and the patients knew about the details of the intervention. There was also no information whether the outcome assessors were aware of the intervention and also whether the data were analysed according to pre-defined criteria. The outcome measures were also limited. Wong et al., 2015 was low risk of bias in D1-D3 and high risk for the D4 and D5 where the main concerns also were biased with the assessors knowing the intervention received and also the limited outcomes since only pain was assessed.

Aqrabawi (2006) study had no information on the randomization and allocation concealment with all the other criteria having critical concerns. Chu et al., 2005 had no information on allocation concealment, the blinding of the operator and patient and also the inclusion/exclusion criteria. Michanowicz et al. (1989) had no information on allocation concealment, the blinding of the operator. All studies were undertaken in a university setting. The risk of bias thus indicated a moderate-to-high risk of bias for these three studies.

Five out of the nine studies shown in [Table 3](#) compared heat-modified techniques to lateral condensation. Specifically, Thermafil (Chu et al., 2005; Kandemir Demirci & Çalışkan, 2016), vertical compaction (Aqrabawi, 2006) and thermoplasticized techniques (Michanowicz et al., 1989; Ozer & Aktener, 2009) were compared with lateral condensation. Three papers compared single cone to lateral condensation (de Figueiredo, Lima, Lima, et al., 2020; de Figueiredo, Lima, Oliveira, et al., 2020; Diniz-de-Figueiredo et al., 2020). The detailed analysis of these papers verified that the population sample was the same, so the data retrieved from these publications cannot be compared.

TABLE 3 Details of the articles pertaining to PICOT 1—'In patients with apical periodontitis in permanent teeth (P), what is the effectiveness of chemo-mechanical preparation and root canal filling with any type of nonlateral compaction technique (I) in comparison with chemo-mechanical preparation and cold lateral condensation technique using gutta-percha (C) in terms of clinical and patient-related outcomes (O)?'

Name of the first author	Country of the first author	Year published	Name of the journal	Type of study design	Total number of participants	Age distribution
Aqrabawi JA	Jordan	2006	The Journal of Contemporary Dental Practice	Prospective/retrospective study	290 patients, 340 teeth	Mean age 49 years
Chu CH	China	2005	International Endodontic Journal	Prospective study	79 patients	15–69 years (mean 48 ± 12 years)
De-Figueiredo FED	Brazil	2020	Clinical Oral Investigations	Randomized controlled pragmatic clinical trial	120 patients	33.3 ± 12.7 years old; (34.7 ± 13.8 years old)
De-Figueiredo FED	Brazil	2020	PLoS One	Randomized controlled pragmatic clinical trial	120 patients	36.9 ± 14.2 ; 34.2 ± 13.0 years old
Diniz-de-Figueiredo FE	Brazil	2020	International Endodontic Journal	Randomized controlled pragmatic clinical trial	120 patients	34.18 ± 12.99 years old
Kandemir Demirci G	Turkey	2016	Journal of Endodontics	Prospective randomized comparative study	120 anterior teeth in 100 patients	18–65 years
Michanowicz AE	USA	1989	Journal of Endodontics	Randomized clinical trial	100 with 50 per group	Not mentioned
Ozer SY	Turkey	2009	The Journal of Contemporary Dental Practice	Randomized controlled clinical trial	98 patients	52 years
Wong AW	Hong Kong	2015	BMC Oral Health	Randomized clinical trial	567 patients	18+

Number of participants with AP	Outcome measures employed	Type of radiographic assessment	Method of radiographic assessment	Details
177 teeth with AP	Periapical healing, pain, swelling, tenderness to palpation, percussion, tooth mobility, pocket depth and presence of caries	Periapical radiographs	PAI score	Vertical compaction with Kerr's sealer compared with lateral condensation with AH Plus
58 teeth with AP	Periapical healing, clinical signs, or symptoms such as pain, tenderness to percussion, mobility and soft tissue pathosis (abscess or sinus tract)	Periapical radiographs	Presence of AP (Pettersson criteria)	Thermafil compared with cold lateral condensation both with AH Plus
120 teeth with AP	Healing rate of AP, treatment success rate, quality of the root canal filling and life quality changes	Periapical radiographs	Healing rate of the AP according to the PAI score	Reciproc single file/single cone compared with hand filing and lateral condensation both with AH Plus
120 teeth with AP	Postoperative pain and radiographic healing of AP	Periapical radiographs	Healing rate of the AP according to the PAI score	Reciproc single file/single cone compared with hand filing and lateral condensation both with AH Plus
120 teeth with AP	Oral health-related quality of life	Periapical radiographs	No radiographic assessment was performed	Reciproc single file/single cone compared with hand filing and lateral condensation both with AH Plus
112 teeth with AP (smaller than 5 mm)	Clinical and periapical healing. Postoperative pain. Quality of root filling	Periapical radiographs	PAI score and obturation length evaluation	Thermafil and cold lateral with randomized choice and AH Plus sealer
26 experimental and 22 control had apical periodontitis	Radiographic healing	Periapical radiographs	Healed or not healed based on the presence of a periapical lesion	Ultrafil compared with and without sealer compared with cold lateral condensation using Calciobiotic sealer
All patients with AP	Clinical and radiographic healing. Pain, tenderness to percussion, mobility, sinus tract infection and abscess	Periapical radiographs	Presence of AP (Pettersson criteria)	Softcore compared with cold lateral condensation both with Diaket sealer
All patients with AP	Pain assessment 10-point Likert scale, ranging from no pain (score 0) to extreme pain (score 10); assessment after 1 and 7 days	Nil	Nil	Single/multiple visits cold lateral versus Thermafil with AH Plus sealer

TABLE 4 Details of the articles pertaining to PICOT 2—'In patients with apical periodontitis in permanent teeth (P) what is the effectiveness of chemo-mechanical preparation and root canal filling with any other type of sealer (I) in comparison with chemo-mechanical preparation and root canal filling with epoxy resin (AH Plus/AH 26) using gutta-percha (C) in terms of clinical and patient-related outcomes (O)?'

Country of the first author	Year published	Name of the journal	Total number of participants	Age distribution	Number of participants with AP	Outcome measures employed	Type of radiographic assessment	Method of radiographic assessment	Details
Aqrabawi JA	2006	The Journal of Contemporary Dental Practice	290 patients, 340 teeth	Mean age 49 years	177 teeth with AP	Periapical healing, pain, swelling, tenderness to palpation, percussion, tooth mobility, pocket depth and presence of caries	Periapical radiographs	PAI score	Vertical compaction with Kerr's sealer compared with lateral condensation with AH Plus
Graunaite I	2018	Journal of Endodontics	61 patients	Mean age 49.5 years	122 teeth with AP	Postoperative pain intensity at 24 h, 48 h, 72 h and 7 days after treatment	Nil	Nil	Warm vertical condensation technique and different obturation materials (ie, a gutta-percha point with AH Plus sealer and a bio ceramic-coated gutta-percha point with Totalfill sealer)

TABLE 5 Summary of risk of bias for included studies (PICOT 1) using RoBS2

Study	Experimental	Comparator	Outcome	Weight	D1	D2	D3	D4	D5	Overall		
de Figueiredo et al. (2020)	Single cone technique	Cold lateral compaction	Apical periodontitis healing	1	+	!	+	+	-	-	+	Low risk
de Figueiredo et al. (2020)	Single cone technique	Cold lateral compaction	Apical Periodontitis Healing and Post Operative Pain	1	+	+	+	+	-	-	+	Some concerns
de Figueiredo et al. (2020)	Single cone technique	Cold lateral compaction	Oral Health related Quality of life	1	+	+	+	+	-	-	+	High risk
Kandemir Demirci et al. (2016)	Carrier based	Cold lateral condensation	Treatment outcome	1	+	+	+	+	!	!	+	
Ozer & Aktener (2009)	Carrier based	Cold lateral compaction	Treatment outcome	1	!	-	+	-	!	-	+	
Wong et al. (2015)	Core Carrier	Cold lateral condensation	Post obturation Pain	1	+	+	+	-	!	-	+	

D1: Randomisation process
 D2: Deviations from the intended interventions
 D3: Missing outcome data
 D4: Measurement of the outcome
 D5: Selection of the reported result

Note: The domains D1-D5 included D1: Bias arising from the randomization process, D2: Bias due to deviations from the intended interventions, D3: Bias due to missing outcome data, D4: Bias in measurement of the outcome and D5: Bias in the section of the reported result.

Tooth survival

Tooth survival was similar in teeth treated using lateral condensation and Thermafil (Chu et al., 2005) where four teeth of the lateral condensation group and three teeth of the Thermafil group, that is a total of seven teeth were extracted due to fracture of tooth structure before the recall examination. The overall success rate was 96% with Thermafil and 98% in the cold lateral condensation group, showing slightly lower success rates over a 2-year recall period (Kandemir Demirci & Çalışkan, 2016) in the Thermafil group. However, this difference was not significant.

Radiographic evidence of reduction in apical lesion size (loose criteria) and radiographic evidence of normal periodontal ligament space

Management of AP using either lateral condensation with AH Plus or warm vertical compaction using Schilder's technique with Kerr's Pulp Canal Sealer led to different healing outcomes (Aqrabawi, 2006). Treatment was considered 'successful' when (a) the contours, width and structure of the periodontal margins were normal or (b) the periodontal contours were widened mainly adjacent to an excess of filling materials. All cases in which those criteria were not fulfilled were judged as 'unsuccessful'. In cases with apical lesions, the size of each lesion was calculated by taking the average of the lesion's largest dimension and its extent in the direction perpendicular to the largest dimension. The level of the root filling in relation to the root apex was also recorded. The overall success rate followed up to 5 years was 80.3%. There was a significantly higher success rate for cases with AP when treated with vertical condensation than when treated with lateral condensation (87% vs. 71%, respectively) (Aqrabawi, 2006).

Thermoplasticized gutta-percha led to a better resolution of periapical lesions compared with the lateral

condensation technique (Michanowicz et al., 1989). The cold lateral condensation resulted in the resolution of periapical lesions from 44% to 15% while in the thermoplasticized experimental gutta-percha group it decreased from 59% to 5%. In this study repair had taken place whether or not a calcium hydroxide-based sealer was used, concluding that the absence of a sealer did not make any difference to the outcome. A carrier-based system (Softcore) used in conjunction with Diaket sealer also exhibited similar outcomes to laterally condensed gutta-percha for the healing of AP (Ozer & Aktener, 2009).

Comparison of hand filing/lateral condensation to NiTi/single matched cone showed that both protocols resulted in a similar healing rate of AP. After 12 months, the success rate ranged from 73% to 78% (de Figueiredo, Lima, Lima, et al., 2020). The hand filing/lateral condensation compared with Reciproc/matched cone did not show any differences in the distribution of periapical status changes. However, cases with a PAI score of 4 or 5 at the baseline presented a reduction in healing rate when compared with those presenting lesions classified with a PAI score of 3 (de Figueiredo, Lima, Oliveira, et al., 2020).

Pain, tenderness, swelling, need for medication (analgesics, antibiotics)

A single-file Reciproc system combined with a single-cone technique was compared with hand filing using crown-down technique and obturation with gutta-percha and AH Plus sealer using lateral condensation technique for the management of anterior teeth with AP (de Figueiredo, Lima, Lima, et al., 2020). The patients were recalled for assessment of the pain after the intervention after 7 days and radiographic recall was at 12 months using the PAI score. Regardless of the assessment time, no difference in incidence, intensity of postoperative pain and incidence of flare-up were observed between the two endodontic protocols.

TABLE 6 Summary of risk of bias for included studies (PICOT 1) using ROBINS-I

Study	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete data outcome	Selective reporting	Other sources of bias	Overall
Aqrabawi 2006	NI	NI	Critical	Critical	Critical	Serious	US, SZC, C, DTD, SO, SE	Critical
Chu et al. 2005	Serious	NI	NI	Low	Moderate	Low	US, SZC, NIEC	Serious
Michanowicz et al. 1989	Low	NI	NI	Low	Low	Moderate	US, DTD, SZC, SMD, C	Moderate

Abbreviations: C, calibration; DTD, definition of trial design; NIEC, no information on inclusion/exclusion criteria; SE, single evaluator; SMD, statistical method definition; SO, single operator; SZC, sample size calculation; US, university setting.

The incidence of pain after 7 days of patients treated with Thermafil was similar to that of patients managed using lateral condensation (Wong et al., 2015).

Additional outcome(s) such as 'tooth function (fracture, restoration longevity), 'need for further intervention,' 'adverse effects (including exacerbation, restoration integrity, allergy),' 'oral health-related quality of life and 'presence of sinus tract'.

The oral health-related quality of life of patients treated with manual root canal preparation/lateral condensation exhibited poorer outcomes compared with Reciproc/single matched cone (Diniz-de-Figueiredo et al., 2020) after 6 months of recall. Patients with low-income status and treated with Reciproc/single-cone technique had better scores after 12 months.

The use of Thermafil reduced the treatment time (Chu et al., 2005; Kandemir Demirci & Çalışkan, 2016). Another carrier-based technique also showed reduced treatment time (Ozer & Aktener, 2009). More overfills were reported with Thermafil (Kandemir Demirci & Çalışkan, 2016) whilst warm vertical compaction using Schilder's technique had similar length control to lateral condensation (Aqrabawi, 2006). No significant differences were observed between the hand filing/lateral condensation and Reciproc/matched cone for root filling quality or sealer extrusion and both techniques resulted effective in the management of anterior teeth affected by AP (de Figueiredo, Lima, Oliveira, et al., 2020).

PICOT 2 – 'In patients with apical periodontitis in permanent teeth (P) what is the effectiveness of chemo-mechanical preparation and root canal filling with any other type of sealer (I) in comparison with chemo-mechanical preparation and root canal filling with epoxy resin (AH Plus/AH 26) using gutta-percha (C) in terms of clinical and patient-related outcomes (O)?'

Two studies were included in PICOT 2 (Table 4) with one (Graunaite et al., 2018) being a randomized controlled clinical trial thus risk of bias was assessed by ROBINS-I while one study (Aqrabawi, 2006) was a controlled clinical trial (nonrandomized) thus ROBINS-I was used for the risk of bias assessment. A detailed description of the risk of bias for Graunaite et al. (2018) is reported in Table 7 and classified as high risk of bias due to concerns with the randomization (D1) as there was missing information and also with the limitation of the measured outcomes (D5). Aqrabawi, 2006 was found at critical risk of bias (Table 8) as no information was given on the randomization procedure, on evaluation process (blinded or not) and missing data are provided on the measured outcomes.

TABLE 7 Summary of risk of bias for included studies (PICOT 2) using RoBS2

Study	Experimental	Comparator	Outcome	Weight	D1	D2	D3	D4	D5	Overall
Graunaite I. et al. 2018	Bioceramic sealer	Resin-based sealer	Post Operative Pain	1	!	+	+	+	!	-

+ Low risk
! Some concerns
- High risk

D1 Randomisation process
 D2 Deviations from the intended interventions
 D3 Missing outcome data
 D4 Measurement of the outcome
 D5 Selection of the reported result

Note: The domains D1-D5 included D1: Bias arising from the randomization process, D2: Bias due to deviations from the intended interventions, D3: Bias due to missing outcome data, D4: Bias in measurement of the outcome and D5: Bias in the section of the reported result.

Two studies compared AH Plus to alternative sealers (Table 4) namely zinc oxide eugenol-based sealer (Aqrabawi, 2006) and hydraulic cement sealer used with bioceramic-coated points (Graunaite et al., 2018). Aqrabawi (2006) also compared techniques thus is also listed in Table 3. However, the use of different sealers was not discussed in the latter study, which focused on technique comparison.

Pain, tenderness, swelling, need for medication (analgesics, antibiotics)

There was no difference in the pain reported by patients treated with AH Plus or Totalfill sealer over a period of 7 days (Graunaite et al., 2018).

Additional outcome(s) such as ‘tooth function (fracture, restoration longevity), ‘need for further intervention,’ ‘adverse effects (including exacerbation, restoration integrity, allergy), ‘oral health-related quality of life and ‘presence of sinus tract’.

No extrusions were reported for AH Plus and Totalfill sealer (Graunaite et al., 2018).

DISCUSSION

This systematic review was designed to obtain accurate and critical insights into root canal obturation techniques and materials because there was, and still is, a paucity of clinical information in the specialized literature on the superiority of available gold-standard materials compared with all the others. The current article reports both short-term outcomes for pain, tenderness and use of antibiotics/analgesics and more than 6-month follow-ups for radiographic healing of root canal treatments in permanent teeth affected by AP. The review questions were related to the obturation technique thus compared alternatives to the standard cold laterally condensed gutta-percha and also a second review question assessed the efficacy of

different sealers compared with AH Plus in the management of AP in permanent teeth.

At the abstract review stage, a large number of studies were eliminated since the research was undertaken by screening radiographs for adequacy and apical extent of the obturation without any information on the intra-operative procedures and materials. Further eliminations of publications from this review occurred at the full-text screening stage for the reasons given in Table 2. Most of the studies were not included due to the patient selection criteria since either all the groups did not present AP at the baseline, or the sample was mixed and the patients with AP were not scored separately.

Few studies fell within the remit of the research questions where alternative techniques and materials were compared with laterally condensed gutta-percha and AH Plus obturation technique. The cold lateral condensation technique and epoxy resin-based sealers are currently considered a classic reference treatment. The final selection resulted in only 10 publications with 9 comparing techniques (Table 3) and 2 comparing materials (Table 4) with one paper (Aqrabawi, 2006) comparing both.

The risk of bias in all the studies was high. The trial undertaken to assess the difference between single-file/single-cone technique and lateral condensation (de Figueiredo, Lima, Lima, et al., 2020; de Figueiredo, Lima, Oliveira, et al., 2020; Diniz-de-Figueiredo et al., 2020) had a high risk of bias due to the limited outcomes measured. In actual fact, this study should not have a risk of bias as there were a number of outcomes measured however these were split into different publications. The nonrandomized studies lacked a lot of information such as the blinding of the participants and operators, and the concealment of the allocation.

There was no difference in tooth survival of alternative techniques when compared with lateral condensation (Chu et al., 2005; Kandemir Demirci & Çalışkan, 2016). However, using radiographic methods, the techniques using gutta-percha modified by heat showed better resolution of periapical lesions (Aqrabawi, 2006; Michanowicz

TABLE 8 Summary of risk of bias for included studies (PICOT 2) using ROBINS-I

Study	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete data outcome	Selective reporting	Other sources of bias	Overall
Aqrabawi 2006	NI	NI	Critical	Critical	Critical	Serious	US, SZC, C, DTD, SO, SE	Critical

Abbreviations: C, calibration; DTD, definition of trial design; SE, single evaluator; SO, single operator; SZC, sample size calculation; US, university setting.

et al., 1989), which was not evident with carrier-based systems (Ozer & Aktener, 2009). As AP is an often asymptomatic pathosis, and its diagnosis is mainly made through radiographic images, most of the studies included in the current review used a radiographic assessment technique for diagnosis as this is the only way to differentiate cases with and without asymptomatic AP. Based on the reported data, all the studies used periapical radiographs to evaluate the preoperative periapical status. Treatment effectiveness was determined by radiographic examination alone (Michanowicz et al., 1989), or by clinical findings alone (Diniz-de-Figueiredo et al., 2020) or by the combination between radiographic and clinical findings in most of the included research (Aqrabawi, 2006; Chu et al., 2005; de Figueiredo, Lima, Lima, et al., 2020; de Figueiredo, Lima, Oliveira, et al., 2020; Kandemir Demirci & Çalışkan, 2016; Ozer & Aktener, 2009).

The Periapical Index (PAI) developed by Ørstavik et al. (1986) is a simplified version of the radiographic method of interpretation used by Brynolf (1967), which compared the histological progression of an AP with the appearance of the lesion in the radiographic image. It consists of five categories, numbered 1–5, usually dichotomized into ‘healthy’ and ‘diseased’ using the cut-off between PAI 2 and PAI 3 (Aqrabawi, 2006; de Figueiredo, Lima, Lima, et al., 2020; de Figueiredo, Lima, Oliveira, et al., 2020; Kandemir Demirci & Çalışkan, 2016). Two of the included articles (Chu et al., 2005; Ozer & Aktener, 2009) categorized the periapical status of the tooth into three groups (Strindberg, 1956) ‘Normal’, i.e. normal appearance of the surrounding osseous structure, ‘AP’ when periapical radiolucency was observed and ‘Periapical status not classified’ when the quality of the radiograph was not sufficient. This classification has also been attributed to a later study that also used the original Strasberg classification (Pettersson et al., 1991).

The literature search for data on tooth survival following root canal treatment of teeth affected by AP revealed that only one study amongst included ones reported information on the 3-year survival rate (Chu et al., 2005). Teeth extracted due to fracture of tooth structure before the recall examination were classified as failure and no significant difference in the treatment failure rates between the Thermafil and lateral condensation groups was reported. If these fractured cases were excluded from the analysis, the true endodontic failure rates for Thermafil and lateral condensation would be 11% and 12%, respectively. Other trials withdrew initially selected teeth from the final analysis or did not provide detailed data on fractures (de Figueiredo, Lima, Lima, et al., 2020; de Figueiredo, Lima, Oliveira, et al., 2020; Kandemir Demirci & Çalışkan, 2016; Michanowicz et al., 1989; Ozer & Aktener, 2009).

The studies evaluating postoperative pain were published between 2005 and 2020. Wong et al., 2015 only investigated the incidence of pain after 1 and 7 days and correlated this to single and multi-visit also comparing lateral condensation and Thermafil obturations. Other authors investigated the postoperative pain together with radiographic outcomes. Aqrabawi (2006) investigated postoperative pain and other clinical findings (swelling, tenderness to palpation and percussion, tooth mobility, pocket depth and presence of caries), but no detailed mention in the results section was made of these variables. There was an overall similar success rate with regards to the absence of signs and symptoms at the follow-up examination for vertical condensation compared with lateral condensation. Interestingly, the difference between vertical and lateral condensation in terms of resolution of AP was significant, reporting higher percentages of success for cases treated with vertical condensation than when treated with lateral condensation (87% vs. 71%, respectively). No significant difference regarding the incidence and intensity of postoperative pain was observed when matching taper single-cone filling and lateral compaction filling were compared (de Figueiredo, Lima, Lima, et al., 2020; de Figueiredo, Lima, Oliveira, et al., 2020). Another study compared the Thermafil technique with cold lateral condensation, revealing a similar incidence of postoperative pain after 7 days (Wong et al., 2015).

No significant difference in the distribution of radiographic healing was observed when matching-taper single-cone filling and lateral compaction filling were compared (de Figueiredo, Lima, Lima, et al., 2020, de Figueiredo, Lima, Oliveira, et al., 2020). The overall reported effectiveness at 12 months was 73% for cold lateral and 78% for single-cone technique. Results suggested the presence of a preoperative AP (PAI 4–5) as the only observed clinical aspect affecting the outcome with both filling techniques (de Figueiredo, Lima, Lima, et al., 2020, de Figueiredo, Lima, Oliveira, et al., 2020). Chu et al. (2005) compared carrier-based system or lateral condensation as a filling technique. The treatment outcome was categorized as success only when a treated tooth was both clinically sound (no clinical sign or symptom such as pain, tenderness to percussion, mobility and soft tissue pathosis like abscess or sinus tract) and rated as normal in the radiographic examination. No difference in the clinical and radiographic status was observed in presence of preoperative AP for teeth filled using Thermafil compared with those using lateral condensation after 36 months of observation (81% vs. 79%, respectively), suggesting that Thermafil is an acceptable alternative to the conventional cold lateral condensation technique. Another trial (Kandemir Demirci & Çalışkan, 2016), during the 2-year follow-up period, revealed no statistically significant difference in the

success rate of the teeth treated with Thermafil (96.4%) in comparison with those treated with cold lateral condensation (98.2%). Similar findings were reported (Ozer & Aktener, 2009) when cold lateral condensation was compared with carrier-based system Soft-Core in terms of 3-year success rate (80% vs. 85%, respectively) intended as the absence of signs and symptoms and normal radiographic appearance.

The oral health-related quality of life assessment was used by Diniz-de-Figueiredo et al., 2020. In this study, only this method of assessment was used to evaluate the difference between the single-file/single-cone obturation technique compared with hand filing and obturation with lateral condensation and AH Plus sealer. The single-cone technique with AH Plus sealer resulted in a better quality of life for the patients after 6-month recall. The comparisons made in this study were not only the materials and technique but also a different canal preparation system making precise comparisons difficult. Furthermore, AH Plus is not indicated for use with single-cone technique as it is a resin-based sealer and exhibits shrinkage (Marashdeh et al., 2019; Sonntag et al., 2015). The oral health-related quality of life is an integral part of general health and well-being and is recognized by the World Health Organization as it captures the disparities between populations and different groups. However, the condition and/or its symptoms being measured must also be responsive to treatment thus the measure must have effective evaluative properties (Sischo & Broder, 2011). In this study (Diniz-de-Figueiredo et al., 2020), a number of parameters were assessed that could have contributed to a better quality of life making the assessment carried out not as robust.

The only obvious difference highlighted by all those trials was the carrier-based systems employing less clinical working time than the cold lateral condensation. However, this aspect did not fall within the scope of this review. Further well-designed RCTs should be carried on with follow-up of at least 4 years and supported by an adequate sample size calculation to identify clinically significant differences in the long term between the efficacy of the various alternative filling techniques and sealers, if any exist.

The comparison of materials although very limited showed no difference in postoperative pain after 7 days when TotalFill was used as sealer (Graunaite et al., 2018).

The main strength of this systematic review was that it conformed to the protocol that was set on PROSPERO. The criteria set out eliminated some of the study heterogeneity as is the case with primary root canal therapy and retreatments, which were eliminated from the outset. The main shortcoming was the still existing heterogeneity of the studies selected as a result of which meta-analysis

could not be performed and the findings could only be described. Other factors that limited the review were the lack of information on whether the teeth treated were vital or not and also the exclusion of quality of fill as a criterion for evaluation of the effectiveness of managing AP. The quality of fill is usually assessed retrospectively on radiographs so no information on the obturation technique and materials used will be available.

CONCLUSIONS

Included studies did not find any difference between different procedures (PICOT 1) and materials (PICOT 2) in relation to tooth survival, pain, tenderness, swelling and need for medication, and few studies included information on radiographic evidence of reduction in apical lesion size and on the oral health-related quality of life. The risk of bias was high thus the findings should be interpreted with caution.

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CONFLICT OF INTEREST

Both authors declare no conflict of interest, and no funding was received related to this study.

AUTHOR CONTRIBUTIONS

Both authors contributed equally to the article.

ETHICAL APPROVAL

No ethical approval was necessary for the work undertaken.

DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

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