The effect of retrograde material type and surgical techniques on the success rate of surgical endodontic retreatment: systematic review of prospective randomized clinical trials

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Abstract

Background: Endodontic surgical procedures, when performed, require retrograde filling materials that are biocompatible, non-toxic, non-irritant, dimensionally stable, and ideally promote bone formation. Precise evaluation of retrograde filling materials in clinical trials is necessary to give holistic view for properties of material and potential outcome from its use. The purpose of this review is to evaluate the effect of retrograde material type and surgical techniques on the success rate of surgical endodontic retreatment.

Methods: An electronic search was performed in the time frame between 1st of January 2000 to 1st of September 2020 using database.

Sources

Web of Science, PubMed and redundant hand searches through their references. Seven inclusion–exclusion criteria were set for the selection and identification of relevant articles. Risk of bias was conducted for the included studies.

Results: Nine randomized clinical trials (RCTs) fulfilled the inclusion criteria for this systematic review. The outcome of this review revealed that none of the reviewed trials totally-fulfilled CONSORT 2010 criteria.

Conclusions: In light of the outcome of this review, there is no enough evidence to support the superiority of certain retrograde filling material or surgical technique over another in the success rate of surgical endodontics retreatment. The variety of methodologies and strategies, such as patient selection, the method of treatment and study analysis, led to doubtful credibility of the obtained clinical evidence. Further prospective randomized controlled clinical trials evaluating the specific effect of the various used materials are needed.

Keywords: Apicectomy, Endodontic surgery, RCT, Retrograde filling

Background

The ultimate goal of endodontic treatment is to achieve complete elimination of bacterial components and toxins during the mechanical shaping of the root canal system with a subsequent filling of that system with materials to provide a three-dimensional seal of that root canal system from coronal to apical aspects of that system [1, 2].

Despite the high success rates achieved with initial root canal treatment, endodontic failures can still occur...
The causality of failure can largely be attributed to bacterial invasion from inadequate cleansing of the root canal system, inaccessible areas when encountering complexities and irregularities of the root canal system, and from foreign body reactions such as extrusion of filling material and broken files or extra radicular biofilm [4, 5]. When there is non-surgical endodontic treatment failure, retreatment is typically considered, provided the tooth is restorable, and the canals are accessible. However, when non-surgical treatment cannot be achieved, surgical retreatment becomes a viable treatment modality [6].

Endodontic surgical procedures, when performed, require retrograde filling materials that are biocompatible, non-toxic, non-irritant, dimensionally stable, and ideally promote bone formation [7, 8]. Many different materials that have been suggested for use as a retrograde filling material, such as amalgam, composite resin, reinforced zinc oxide–eugenol cement (IRM; Dentsply), super ethoxybenzoic acid (Super-EBA; Bosworth Co, Skokie, IL) cement, and glass ionomer cement [9]. With such an array of choices, the clinician can encounter considerable confusion as to which material would work best in the various clinical situations that they face. Precise evaluation of retrograde filling materials in clinical trials is necessary to give an accurate picture of the properties of the material and the potential outcome from its use.

Systematic reviews and meta-analytical studies are considered the highest level of evidence that supports evidence-based decision making, which is described as the “formalized process of using a specific set of skills for identifying, searching for and interpreting clinical and scientific evidence so that it can be used at the point of care” [10].

There are several prospective randomized clinical trials that assess the effect of root-end filling materials [11–21]. And there are narrative reviews focused on the effect of retrograde filling material itself. Assessment of the differences in the materials used, adopted techniques, and heterogeneity in studies of previous articles are required for a better understanding of surgical endodontic treatment protocols and to assess which variables affect clinical outcomes [22–25].

The systematic review by Pinto et al. [26] focused only one on evaluating only endodontic microsurgeries when used with different retrograde filling materials. Another systematic review by Seltzer et al. [23] compared endodontic microsurgery and tradition root-end surgery and concluded that there is a significant better prognosis in case of microsurgery. To date, there are no systematic reviews that evaluate the methodologies of prospective randomized clinical trials with a focus on the effect of different root-end filling materials. Hence, the evidence supporting the use of specific root-end filling material with a particular technique as a useful and efficacious technique remains weak. Accordingly, the objectives of this systematic review are to (1) assess the clinical outcome of using different root-end filling materials in previously published prospective randomized controlled clinical trials and (2) evaluate quality and extent of compliance of these studies with the requirements of ideal randomized clinical trials.

**Methods**

The protocol for this systematic review was adopted from the PRISMA checklist for reporting systematic reviews [27] with registration number (20180029).

**Formulating review questions**

A well-defined review question was developed by using the Patient Population, Intervention, Comparison, and Outcome (PICO) framework to establish a systematic review of the current literature regarding radiographic outcomes of endodontic surgical retreatment in patients who have had prior endodontic treatment but have recurrent periapical pathosis and/or clinical symptoms.

“P”—population—is the patients with teeth that were previously Endodontically treated and had periapical pathosis.
“I”—the type of surgery (e.g., modern endodontic surgery).
“C”—the comparison group: is the type of retrograde filling material used.
“O”—the definition of outcome: according to the healing criteria of Rud et al./or Molven et al. [28, 29].

The critical questions of this systematic review were these:

1. What is the effect of using retrograde filling?
2. Does the use of specific material, device, or technique in surgery improve healing of the lesion or reduce patient post-operative discomfort?
3. Did the adopted methodologies in previously published studies fulfil the ideal requirements of a randomized clinical trial?

**Search methodology**

An exhaustive broad literature search was done through three electronic databases, WEB OF SCIENCE, ELSEVIER, and PubMed searching for topic-related studies, regardless of the publication type using four keywords:
Exclusion criteria consisted of studies that did not meet the above inclusion criteria, which are: (1) non-randomized studies, non-English studies, (2) one arm studies, (3) lab or animal studies, (4) case reports, (5) reviews or opinion papers, (6) retrospective studies, (7) studies less than 12 months follow up, re-surgery studies, (8) detailed success rate not given or success rate calculation from raw data not possible, (9) use of guided tissue regeneration, (10) outcomes not evaluated according to the criteria above, (11) no sample design provided and (12) presence of a through and through lesion or a lesion of combined periodontal endodontic origin.

Data extraction and quality assessment
Study quality and internal validity were assessed for each included trial according to the CONSORT 2010 checklist [30] by examining information such as ethical approval, study settings, sample size calculation, number of patients, type of teeth treated, number of surgeons, use of magnification (none, loupes, microscope), materials used, the age range of patients, follow-up period/intervals, and specific outcomes. These data were put into data extraction sheets, which were also used to evaluate information about elements of randomization, concealment of treatment allocation, blinding, and the handling of patient attrition.

Risk assessment of selected studies
The same five reviewers independently assessed the risk of bias of included studies. Also, the final decision is reached by the approval of at least three reviewers. Disagreements were resolved after substantive discussion. The risk of bias assessment is built according to instructions provided by Higgins AND GREEN 2011 [31].

Five points were considered for each study: selection bias, performance bias, detection bias, attrition bias, and reporting bias. For every article, the risk was judged as low, unclear, or high. If a study had a low risk for each item, then it was judged to have a low risk of bias and a high level of evidence. If a study had an unclear risk for at least one item, but no item had a score at high risk, then the study is judged to have an unclear risk of bias and a moderate level of evidence. If a study had a high risk of bias at any of the previously mentioned items, the study is judged to be at high risk of bias and low level of evidence.

Results and data analysis
Excluded studies
The flow chart of the article screening process is presented in (Fig. 1). The electronic search and hand search gave after removal of duplicates, 327 records. After the screening of titles and abstracts, the following categories were excluded: 13 non-English studies, 97 out of subject studies and laboratory studies, 21 animal studies, 52 review articles, 30 retrospective studies, 94 case reports and case series, 3 prospective clinical studies but
Fig. 1 Prisma flow diagram
non-randomized and finally 17 full-text articles assessed for eligibility but 8 articles were excluded because 2 articles studied patient with exclusion criteria, 3 articles were out of our scope of research with different objectives, and 3 articles were a follow-up. We considered nine articles potentially eligible for inclusion.

In our analysis, eight articles didn’t meet our criteria for eligibility. The study of Pecora et al. [32] was excluded because the studied patients had exclusion criteria (through and through periapical lesions) which will require bone grafting, while the study conducted by Da Silva et al. [33] had evaluation criteria of success and failure other than our inclusion criteria. The scope of the studies conducted by Taschieri et al., de Lange et al., Shearer et al. [34–36] aimed to test the effect of ultrasonic preparation and effect of magnification on periapical surgery thus they were excluded. Meanwhile, Chong et al. [37] assessed mainly the post-operative pain after two years, in addition; the studies of Kim et al. and Kruse et al. [19, 20] were a follow up to previously included studies but were included in this systematic review.

Characteristics of included studies

Nine studies met the inclusion criteria. The chosen randomized clinical trials had the following geographic distribution 3 trials in Sweden 33% Platt and Wannfors [13], Walivaara et al. [16], Walivaara et al. [17], 2 trials in Denmark 22% Jensen et al. [11]; Christiansen et al. [15], 1 trial in Netherlands 11% Lindeboom et al. [14], 1 trial in London 11% Chong et al. [12], 1 trial in china 11% Zhou et al. [21] and finally 1 trial was conducted in South Korea 11% Song and Kim–Kim et al. [18, 19] with total 77% of the trials in Europe and 22% in Asia.

Four studies (44%) clearly stated the funding sources, and 77% of the trials received ethical approval from relevant Institutional Review Boards (IRB). From the assessment of the methodologies, participant eligibility criteria were clearly stated in four studies, 40%, while the others were incompletely illustrated. The number of operators was as follows: (one) in four studies 44%, (two) in three studies 33%, (three) in one study 11%, and (four) in one study 11%. Concerning the blinding of evaluators, only five studies (55%) succeeded. Conversely, for blindness to treatment, no study managed to achieve it, neither the patients nor the operators.

Regarding sample size calculation, only 5 studies performed the analysis while the remaining studies did not clearly state this issue. In comparing long-term follow-up, 3 trials (33%) showed a follow-up period of more than one year. Variables such as type of the tooth, age, sex, and smoking, which can affect the results, were fully documented and included in only two studies (22%), while in 6 trials, it was not wholly illustrated. One study didn’t even discuss the topic. The size of the treated lesion was mentioned in four studies (44%), while other studies provided no information.

Four studies (45%) used no bevel or slight bevelling technique in root-end resection, while the other five studies (55%) indicated that the root apex was cut using traditional bevelling techniques. Magnification was used in 77% of the studies during surgical procedures ranging from loupes to operating microscope. The same studies also used ultrasonic for root-end cavity preparation. Furthermore, 44% of the included studies indicated the provided antibiotic prescriptions after surgery. At the same time, there is no mention of such, in the other studies, which may affect the results, as shown in Table 1.

The analysis of investigated materials mentioned in these studies illustrated: MTA (mineral trioxide aggregate) was tested in 55% of the trials, IRM (Intermediate restorative material) in 44%, Super EBA 22%, Ultrafill gutta-percha 11%, just smoothening of gutta-percha 11%, R.E. composite (Retroplast) 11%, C.S. Glass ionomer (Chelon silver) 11%, Ketac silver Glass ionomer 11%, iRoot BP plus 11% and Compomer Dyract 11%. Assessment of the frequency of testing root-end filling materials in the studies was illustrated in Table 2.

In terms of success and failure, the outcome of each study for each material is illustrated in Table 3. Each one of the nine included studies compared two types of retrograde filling materials. MTA was evaluated against IRM in two studies Chong et al. and Lindeboom et al. [12, 14]. Both studies involved 222 teeth. Results after one year follow up showed no significant of difference between the two materials with no superiority of one material over the other. The same clinical results were noted when MTA was compared to Super EBA in the studies of Song and Kim, Kim et al. [18, 19] on 192 patients with no significant of difference between the two materials even after four years follow up. Also, the study of Zhou et al. [21] compared MTA with i Root BP Plus and conducted on 120 patients reported no significant of difference between the materials.

When MTA was compared against gutta-percha (GP) in the study by Christiansen et al. [15] on 46 teeth, followed up six years later by Kuruse et al. [20], MTA showed superiority and significant of difference over gutta-percha. Nevertheless, IRM showed no superiority when compared to either GP or Super-EBA in two studies, Walivaara et al. [16, 17], respectively, with no significant of difference. Retroplast composite resin showed superior results when compared to Chelon silver in the study of Jensen et al. [11] on 134 participants with higher significance; also, Dyract compomer had superior results.
### Table 1 Illustration of information of included studies

|                | Jensen et al. [11] | Chong et al. [12] | Platt and Wannfors [13] | Lindesmo et al. [14] | Christiansen et al. [15] to Kruse et al. [20] | Walivaara et al. [16] | Walivaara et al. [17] | Song and Kim [18] and Kim et al. [19] | Zhou et al. [21] |
|----------------|---------------------|-------------------|--------------------------|----------------------|-----------------------------------------------|----------------------|----------------------|----------------------------------------|------------------|
| **Trial design** | RCT                 | RCT               | RCT                      | RCT                  | RCT                                           | RCT                  | RCT                  | RCT                      | RCT              |
| **Location**    | Denmark             | London            | Sweden                   | Netherlands          | Denmark                                       | Sweden               | Sweden               | Korea                    | China            |
| **Recruitment period** | ?                   | ?                 | 1/2000–12/2002           | ?                    | ?                                             | ?                     | 9/2006–12/2008        | 2/2003–10/2010          | 12/2012–2/2015 |
| **Source of funding** | √                   | ?                 | √                       | ?                    | ?                                             | √                    | ?                     | √                       | ?                |
| **Ethical approval** | √                   | √                 | √                       | √                    | ?                                             | ?                    | ?                     | √                       | √                |
| **Informed consent** | ?                   | ?                 | ?                       | ?                    | ?                                             | ?                    | ?                     | ?                       | ?                |
| **Eligibility criteria** | IC                 | IC                | IC                      | IC                   | IC                                             | IC                   | IC                   | IC                       | ?                |
| **Number of surgeons** | 4                   | 2                 | 1                       | 3                    | 2                                             | 2                    | 1                    | 1                       |      |
| **Blindness of the patients/operator/evaluator** | ?/√                  | x/√               | x/√                     | √/√                  | ?/x/√                                         | ?/x/√                | ?/x/√                | ?/√                     | ?/√              |
| **Sample size**  | 134Pt/134T          | 183Pt/183T        | 28Pt/34T                 | 90Pt/100T            | 44Pt/52T                                      | 139Pt/160T           | 164Pt/206T            | 260Pt/260T              | 240Pt/240T       |
| **S.S.c**       | √                   | √                 | x                       | √/×                  | ×                                             | ×                    | ×/×                  | ×                       | √/√              |
| **After 1 year F. up** | 122Pt/122T         | 122Pt/122T        | 28Pt/34T                 | 90Pt/100T            | 39Pt/46T                                      | 131Pt/147T           | 153Pt/194T            | 192Pt/192T              | 120Pt/130T       |
| **More than 1 years F. up** | x                  | x                 | x                       | x/×                  | 39 teeth                                      | ×                    | 12–21 Month           | ×                       | 122 4 years      |
| **Drop out**    | 12Pt/12T            | 61Pt/61T          | x                       | x/×                  | 5 Pt/6 T (1Y)                                | 8 Pt/13 T            | 9Pt/12 T              | 68Pt (1Y)               | 82 Pt/82T        |
| **Age at baseline** | Age range of 49    | 33–83             | 17–64                    | Average 43.4         | Range 30–77 years mean 546                   | Average 58.5 –       | –                    | ≤ 45 = 136, > 45 = 22 |                  |
| **Gender**      | F/M ratio = 1.8:1   | ?                 | 49% Female               | 57 F/33 M            | 24F/20 M                                      | 81 F/58 M            | 99 F/65 M             | 69 F/123 M              | 94 F/64M         |
| **Smokers**     | 48%                | ?                 | ?                        | ?                    | 16/44                                         | ?                    | ?                    | ?                       | ?                |
| **Clinical variables analysis** | √                   | x                 | IC                      | √/×                  | IC                                            | IC                   | IC                   | √                       |      |
| **Teeth treated** | Max 27 Ant 39Pm16 M | Ant teeth 1st PM, MB root of molar | Ant teeth | Single rooted ant teeth and PM | Max 17 incisors, 24 canines and PM | 46 incisor | 40 incisor | Max 73 Ant 31 PM, 28 M | Max 73 Ant 21 Ant, 11 PM |
| Jensen et al. [11] | Chong et al. [12] | Platt and Wannfors [13] | Lindeboom et al. [14] | Christiansen et al. [15] to Kruse et al. [20] | Walivaara et al. [16] | Walivaara et al. [17] | Song and Kim [18] and Kim et al. [19] | Zhou et al. [21] |
|------------------|------------------|-----------------|----------------|--------------------------------|----------------|----------------|-------------------------------|----------------|---|
| Size of lesion   |                  |                 | not > 10 mm    |                                                | not > 10 mm | < 5 mm = 52, 5–10 mm = 35, > 10 mm = 6 |                  |                  |                  |
| Use of magnification | ×                | ×               | √              | √                                               | √              | √              | √                            | √              |√ |
| Use of ultrasonic preparation | ×                | ×               | √              | √                                               | √              | √              | √                            | √              |√ |
| Angel of resection (bevelling) | √                | ×               | √              | √                                               | ×              | √              | √                            | ×              | × |
| Antibiotics prophylaxis | √                | ×               | ×              | ×                                               | ×              | x              | x                            | √              | x |
| Comparison       | Retro Plast CS G! | MTA versus IRM  | Compomer Dynact versus Ketac Silver GI | MTA versus IRM (MTA) versus smoothing of orthograde gutta-percha root filing | IRM versus super EBA | IRM versus super EBA | MTA versus I root Bp plus | MTA versus super EBA plus |

√ = yes, ? = not clear / not available, × = no.RCT = randomized clinical trial. IC = incomplete. S. Scal = sample size calculation. F. UP = follow up. MTA = mineral trioxide aggregate. IRM = intermediate restorative material. EBA = ethoxy benzoic acid. CS = chelon silver. GI = glass ionomer, Pt = patient, T = tooth, Max = maxillary, Mand = mandibular, ANT = anterior, PM = premolar, M = molar.
Table 2  Frequency of test materials in included studies

|                  | MTA | EBA | iRoot BP Plus | IRM | Ketac Silver | Compomer | Chelon-Silver | Retroplast | GP |
|------------------|-----|-----|---------------|-----|--------------|-----------|---------------|------------|----|
| Number of studies tested | 5   | 2   | 1             | 4   | 1            | 1         | 1             | 1          | 2  |
| Percentage (%)    | 55  | 22  | 11            | 44  | 11           | 11        | 11            | 11         | 22 |

5, success; F, failure; Sig of Dif, significance of difference

against Ketac Silver in the study of Platt and Wannfors [13].

Risk of bias analysis

After analyzing the data, only one study, Lindeboom et al. [14], was judged to be at low risk of bias while two studies Christiansen et al. [15] and Zhou et al. [21] were judged to be at unclear risk. The remaining six studies Jensen et al., Chong et al., Platt and Wannfors, Wälivaara et al., Wälivaara et al. and Song and Kim, Kim et al. [11–13, 16–18] are considered to be at high risk of bias. So, we have, according to the level of evidence, 66% of the studies had a high risk of bias, 22% moderate risk, and only 11% had a low risk of bias.

Through all studies, it seems that random sequence bias had a 22% high risk of bias and 77% low risk of bias. Meanwhile, allocation concealment took 44% high risk of bias and 11% unclear risk of bias and 44% low risk of bias. Regarding blinding of participants was the highest risk of bias with 55% between studies and 22% unclear risk and lowest percent 22% for low risk of bias. Conversely, in the blinding of outcome assessment, high risk took 33%, and low risk took 66%. For attrition bias 44% low risk, 33% for unclear risk, and 22% for high risk of bias. Likely in reporting bias, we found 66% for low risk and 33% for unclear risk. Lastly, for other types of bias, the highest percentage was for unclear bias 44% and 33% for high risk and 22% for low risk of bias, as shown in (Fig. 2).

Discussion

After reviewing all the previous randomized clinical trials, no clinical trial has completely fulfilled the requirements of the CONSORT 2010 checklist for quality assessment of randomized clinical trials [30]. The clinical trials performed by Lindeboom et al. and Zhou et al. are the only clinical trials that achieved accepted percent from the required items of the checklist including: demonstration of the ethical approval, eligibility criteria, sample size calculation, number of surgeons and evaluators, the blinding of evaluators to treatment, number and reasons of drop out of patients and use of modern tools in performing the operations [14, 21].

Throughout the studies analyzed, MTA was the most frequently compared material with other filling materials. Four studies showed no significant difference in success rates between the use of MTA and IRM as a retrograde filling material for the first two articles and super EBA in the third and iRoot BP plus in the fourth respectively [12, 14, 18, 21]. Only one study showed significant difference when using MTA in comparison with Gutta Percha. [15, 20] The study of Jensen et al. revealed a higher success rate with significant difference of Retroplast over Chelon silver [11]. Platt and Wannfors study also reported superiority of Compomer over Ketac Silver [13]. Meanwhile, IRM showed no significant difference when compared to Gutta Percha [16]. It was surprising that the same results obtained by Wälivaara et al. [17] when compared IRM to Super EBA, which lead to doubtful clinical evidence.

It should be noted that missing information can influence the success rate analysis of clinical variables, including the type and status of the teeth being treated, quality of previous root filling, patient status such as age, sex, smoking, and alcohol consumption. The techniques and parameters followed can affect the treatment outcome, and it is important to be equally distributed among the participants [22].

Regarding the lesion size Kim [38] stated that the size of the apical lesion is a significant determinant of treatment outcome, Jansson et al. [39] also found poor prognosis with larger periapical lesions—however, Grung et al. [40] found no relationship between lesion size and prognosis. Only four of the viewed trials mentioned the size of the lesion, while six did not. Lindeboom et al. [14] and Zhou et al. [21] included patients with lesion size not exceeding 10 mm. This inclusion can affect the results because, according to Christiansen et al. rate of successful healing was attributed to the size of the lesion; the smaller the lesion, the higher the rate of success [15].

The correlation between the type of the tooth being treated and the success and failure rates is not clearly defined yet. Many articles reported higher success rates associated with anterior teeth after endodontic surgery, which may be attributed to more accessibility and more precise visualization of the operating field, all these factors lead to better handling and improved apical seal attainment [41–43]. These factors may explain the success rate results of Platt and Wannfors and Christiansen et al. [13, 15].

Most of the investigators adopted modern techniques, including magnification devices, like loups and
Table 3. Assessment of the outcomes of tested materials

| Study                          | Materials          | Significance of difference |
|--------------------------------|--------------------|-----------------------------|
|                                | MTA                |                             |
|                                | S%    | F%    | S%    | F%    | S%    | F%    | S%    | F%    | S%    | F%    | S%    | F%    | S%    | F%    | S%    | F%    | S%    | F%    | S%    | F%    |
| Jensen et al. [11]             | –      | –      | –      | –      | –      | –      | 52    | 48    | 82    | 18    | –      | –      | Yes   |
| Chong et al. [12]              | 84     | 16     | –      | –      | –      | –      | 76    | 24    | –      | –      | –      | –      | No    |
| Platt and Wännfors [13]        | –      | –      | –      | –      | –      | –      | 44    | 56    | 89    | 11    | –      | –      | Yes   |
| Lindeboom et al. [14]          | 92     | 8      | –      | –      | –      | –      | 86    | 14    | –      | –      | –      | –      | No    |
| Christiansen et al. [15]       | 96     | 4      | –      | –      | –      | –      | 90    | 6     | –      | –      | –      | –      | No    |
| Wålivaara et al. [16]          | –      | –      | –      | –      | –      | –      | 84    | 15    | 89    | 10    | 52     | 48     | Yes   |
| Wålivaara et al. [17]          | –      | –      | 81.6   | 18.4   | –      | –      | 90    | 6     | –      | –      | –      | –      | No    |
| Song et al. [43]               | 95.6   | 4.4    | 93.1   | 6.9    | –      | –      | –      | –      | –      | –      | –      | –      | No    |
| Kim et al. [19]–4 years (follow up) | 91.6   | 8.4    | 89.9   | 10.1   | –      | –      | –      | –      | –      | –      | –      | –      | No    |
| Kurse et al. [20]–6 years (follow up) | 84     | 16     | –      | –      | –      | –      | –      | –      | –      | –      | –      | –      | No    |
| Zhou et al. [21]               | 93.1   | 6.9    | –      | –      | 94.4   | 5.6    | –      | –      | –      | –      | –      | –      | No    |
microscope to improve the visualization during the treatment. Also, they used microsurgical ultrasonic tips for preparation which have been proven to be faster compared to rotary burs and require less bone removal [44]. Jensen et al. [11] and Platt and Wannfors [13] did not adopt modern techniques but used the traditional root-end resection with a bur. It was not clinically proved yet the difference in the rate of lesions healing of treated cases using either loupes or surgical microscope except in improvement in the visualization and illumination of the surgical field, details of the apical part of the root, and more conservative bone removal [38, 45, 46].

The combination of magnification with modern techniques of root-end resection and ultrasonic preparation

![Risk of bias of included studies](image)
allows for more conservative preparations, less exposure of dentinal tubules, more efficient disinfection, and more effective adaptation and sealing of the retrograde filling to the root canal walls and consequently increased chances for higher success rates [23].

It would not be appropriate to conclude that healing/success would be based solely on clinical and radiographic outcomes after a follow-up period of only one year, ignoring that success versus failure might be influenced by an extended follow-up period. Moreover, judging lesions that failed to decrease in size during this period might show improvement with longer follow up periods and thereby become successful [47].

By assessing the risk of bias, via random sequence generation, we considered the randomization methods followed are accepted in all trials and considered to be at low risk except in Jensen et al. [11] and Wälivaara et al. [16] which were considered to be at high risk of bias. The methods used were not reported in Jensen et al. [11], while in Wälivaara et al. [16], patients were assigned according to their date of birth. We found that allocation concealment was not stated or attempted in Jensen et al. [11] and Platt and Wannfors [13]. Therefore, the studies of Wälivaara et al. [16, 17] were considered to be at high risk of bias, while Song and Kim [18] and Song et al. [43] was unclear at this point. We considered the studies of Chong et al. [12]; Lindeboom et al. [14]; Christiansen et al. [15] and Zhou et al. [21] have adequate allocation concealment methodology. Furthermore, the presence of different follow-up investigators as in the studies of Christiansen et al. [15]; Kruse et al. [20] and Song and Kim [18]; Kim et al. [19] decreased the risk of bias.

Our study has several limitations, starting with the exclusion of non-English studies, prospective studies, but lack of randomization and short follow up period studies. The quality of the selected RCTs varied. Randomization was adequate in most trials; however, analyses did not identify a correlation between retrograde filling type and surgical technique, and favorable healing outcomes.

Publication bias might appear in some trials regarding the allocation concealment, participant, and outcome assessment. Larger trials, generally, analyzed with more methodological rigor than smaller ones, and through methodological assessment of all trials suggest that shortage of reporting in some items may have led to an overestimation of the effect of some retrograde fillings. In addition, the applicability of this review might be affected because there are no data for other populations in the world where the intervention might perform differently.

Conclusions
The current scientific evidence shows that none of the used materials was significantly better than the other in clinical application except when comparing glass ionomer cement to composite materials or MTA to gutta-percha. The variety of methodologies and strategies, starting from patient selection to the method of treatment and analysis, led to doubtful credibility of the obtained clinical evidence. Further prospective randomized controlled clinical trials evaluating the specific effect of the various used materials and following the ideal requirements of clinical trials are needed.

Abbreviations
ANT: Anterior; CS: Chelon silver; F UP: Follow-up; GI: Glass ionomer; GP: Gutta percha; IC: Incomplete; IRM: Intermediate restorative material; M: Molar; Max: Maxillary; Mand: Mandibular; MTA: Mineral trioxide aggregate; Pt: Patient; PICO: Patient population, intervention, comparison, and outcome; PM: Premolar; RCT: Randomized clinical trials; S. S Cal: Sample size calculation; Super EBA: Super ethoxybenzoic acid; T: Tooth.

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Authors’ contributions
AA participated in all the steps of the research process plus writing the initial form of the manuscript. HH participated in all the steps of the research process and was responsible for planning and guiding the study plan and final editing of the manuscript. JC participated in all the steps of the research process. AZ participated in all the steps of the research process and participated in writing and editing the final manuscript. XX participated in all the steps of the research process and was the major contributor in writing the manuscript and put the study design. All authors have read and approved the manuscript.

Availability of data and materials
All data generated or analyzed during this study are included in this published article.

Declarations
Ethics approval and consent to participate
Not applicable.

Consent for publication
Not applicable.

Competing interests
The authors declare that they have no competing interests.

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