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Review article

Outcome of root canal retreatment filled with gutta-percha techniques: a systematic review and meta-analysis

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ABSTRACT

Objective

The present systematic review and meta-analysis aimed to evaluate the success rate of root canal retreatment filled with gutta-percha and the variables related to retreatment success.

Methods Eligibility criteria and information sources

The PRISMA guidelines were followed for the present review. The study protocol was registered in the International Prospective Database of Systematic Reviews (PROSPERO). Bibliographic research was performed using different databases (PubMed, Scopus, ScienceDirect, and Cochrane) to select studies published until 10 December 2022. Clinical studies evaluating the success of root canal retreatment filled with gutta-percha with at least a 1-year follow-up were selected.

Risk of Bias

Risk assessment was performed using the Newcastle–Ottawa scale. Funnel plots were used to detect publication bias and asymmetry was assessed using Egger's tests.

Results Included studies

From the initially identified studies, after excluding duplicates, 10 studies and one unpublished study fulfilled

the inclusion criteria for quantitative analysis.

Synthesis of results

The success rate of non-surgical root canal retreatment was 71% (95% CI: 66%–76%) with strict criteria and 87% (79% – 93%) with loose criteria for 1-3 years of follow-up, and 77% (66% – 86%) with strict criteria for a 4-5 years of follow-up.

Description of the effect

: Endodontically retreated teeth with periapical lesions had a lower success rate under strict criteria. The tooth type, dental arch, initial periapical index (PAI) score, and the number of visits also affected the treatment success rate under strict criteria. For the loose criteria, teeth with larger periapical lesions and higher initial PAI scores had a lower success rate.

Discussion Limitations of evidence

: Only two studies evaluated radiographic outcomes using cone-beam computed tomography (CBCT), and only two were randomized controlled trials. Most of the included studies did not have an accurate record of many variables that could affect the retreatment success.

Interpretation

According to the present systematic review and meta-analysis, non-surgical root canal retreatment results in favourable outcomes. The presence of a periapical radiolucency, periapical lesions >5mm, a higher initial PAI score, multiple-visit retreatments, and mandibular and molar teeth resulted in a lower success rate.

Registration

CRD42021283134 (PROSPERO).

Clinical significance

Non-surgical root canal retreatment filled with gutta-percha techniques is a relatively predictable procedure with a high success rate. Several variables can affect retreatment success, mainly the presence and size of a PA lesion and the type of tooth.

Keywords

Endodontics; outcome assessment; periapical periodontitis; root canal retreatment; systematic review, treatment outcome

1. INTRODUCTION

Root canal treatment is a reliable procedure that aims to restore or maintain the health of apical tissues to maintain tooth functioning for as long as possible [1]. However, treatment failure has been reported to be approximately 15-25% depending on whether strict or loose criteria are used to evaluate the treatment [2,3].

Persistent intracanal bacterial infections present in unclear areas within the root canal complex [4,5], including the canal isthmus, lateral canals, and ramifications in the apical third, have been described as the leading cause of an unsuccessful outcomes [5]. Other reasons that could lead to root canal treatment failure are related to procedural errors, such as inadequate working length preparation and/or obturation, or, more specifically, perforations and instrument fractures that impede healing, jeopardising the treatment outcome [3], [4], [5]. The global prevalence of apical periodontitis (AP) in root canal-filled teeth is 39% [6]. Although transverse studies of patients seeking dental treatment have not contributed to increasing scientific evidence regarding the success or failure of root canal treatment or retreatment, the results underline the importance of considering AP as a highly prevalent condition in root-filled teeth.

The main treatment options for endodontic failure include surgical or non-surgical root canal retreatment. Buchi *et al.* [7] concluded that the criteria or clear evidence for the selection of surgical or non-surgical management of endodontic failure still needs to be clearly defined. Thus, the choice of surgical or non-surgical retreatment may be influenced by several factors, including training and the level of experience [8]. In cases where the root canal anatomy is not altered and the aetiology of failure can be associated with missed or underfilled canals, a non-surgical approach is recommended to resolve endodontic failure [9]. Non-surgical root canal retreatment consists primarily of achieving proper chemomechanical disinfection by removing the previous filling material, adequate instrumentation, and copious irrigation. Once this first stage is successfully completed, the root canal system can be filled at the same visit, or an intracanal medication can be used between sessions in a multiple-session approach [10].

Different studies and several systematic reviews have evaluated root canal retreatment outcomes, reporting weighted success rates ranging from 75-80% [11], [12], [13], [14], [15]. However, these reviews included studies evaluating treatment survival [13], or postoperative discomfort data only [15], and retreatment cases in which periapical (PA) surgery was previously performed [12], [13], [14]. These reviews also included studies with a small sample size [12,15], less than a 1-year follow-up [11,12,14], less than 80% of recall rate [11], [12], [13], [14], [15], or combined units of measurement, such as roots and teeth [11,12]. All these factors may represent a risk of bias when extrapolating the results to current clinical practice. Accordingly, Ng *et al.* [12] and Torabinejad *et al.* [13] recognized the limitations of the included data and stated the need for more clinical trials reporting in a standardized format that permits adequate comparison for systematic reviews and meta-analyses.

Over the last decade, there has been an increase in the use of magnification devices such as loupes and microscopes in dentistry. Magnification devices with integrated light sources have improved visual acuity in endodontic settings [16]. In addition, several improvements have been introduced to root canal desobturation and preparation instruments, including modifications to instrument alloys and cross-sections [17,18]. These improvements not only can reduce complications and the risk of iatrogenic damage during endodontic procedures [19] but also improve retreatment success. Moreover, several studies addressing root canal retreatment outcomes have been published since previous reviews were published. Thus, the main aim of the present systematic review and meta-analysis was to evaluate revised treatment outcomes of non-surgical root canal retreatment. The secondary aim was to analyse the variables to identify possible associations with retreatment outcomes.

2. MATERIALS AND METHODS

2.1. Protocol registration

The Preferred Reporting Items for Systematic Reviews and Meta- Analyses (PRISMA) guidelines (Page *et al.* 2021) were followed in conducting the present systematic review (*supplementary material 1; supplemental tables S1a-S1b)*. The initial protocol was uploaded to the PROSPERO international prospective database of systematic reviews (CRD42021283134).

2.2. Eligibility criteria

The present systematic review was focused on answering the following question following the PICO framework: “What is the success rate of root canal retreatment in permanent teeth filled with gutta-percha?”

2.3. Information sources and search strategy

An electronic search of articles was performed using four different databases without date or language restrictions. Medline was reviewed through the PubMed (National Center for Biotechnology Information, U.S. National Library of Medicine). Cochrane (The Cochrane Library, John Wiley & Sons, Ltd), ScienceDirect, and Scopus (Elsevier, Relx Group plc) databases were also revised. In addition, grey literature was reviewed (OpenGrey, Networked Digital Library of Theses and Dissertations, UK's national thesis service (EThOS), and Digital Access to Research Theses – Europe (DART-Europe)).

2.4. Search strategy

A similar search strategy, adapted for each database search engine, was performed until 10 December 2022. The strategy consisted of combining different key terms relevant to the research subject following the structure shown in Table 1.

Table 1. Search strategy *(example from the PubMed database)*

(("Secondary"[Title/Abstract] AND "root canal t*"[Title/Abstract]) OR "secondary root canal t*"[Title/Abstract] OR ("nonsurgical"[Title/Abstract] AND "retreatment"[Title/Abstract]) OR ("nonsurgical"[Title/Abstract] AND "root canal t*"[Title/Abstract]) OR ("root canal"[Title/Abstract] AND "retreatment"[Title/Abstract]) OR "root canal retreatment" [Title/Abstract] OR ("endodont*"[Title/Abstract] AND "retreatment"[Title/Abstract]) OR "endodontic retreatment" [Title/Abstract] OR ("endodontic"[Title] AND "outcome"[Title]) OR ("endodontic"[Title] AND "prognosis"[Title]) OR ("root canal"[Title/Abstract] AND "retreatment"[Title/Abstract] AND "prognosis"[Title/Abstract]) OR ("root canal" [Title/Abstract] AND "retreatment"[Title/Abstract] AND "outcome"[Title/Abstract]))
Search results: 1893

2.5. Study selection and data collection process

Two authors (M.E. and J.G.O.) with a Master's Degree in Endodontics and university teaching experience of more than 6 and 12 years individually screened the different databases to identify potentially relevant studies that met the inclusion and exclusion criteria. The selected studies were reviewed for the final selection. Study data were extracted and entered into an Excel worksheet (Microsoft Excel 2016, Microsoft, Redmond, WA, USA), previously configured to include different study features such as name, type of study, year of

publication, sample size, dropouts, patient age and sex, teeth group, procedure details, restoration, and follow-up details. Reasons for exclusion after the full-text review, which were also recorded. Any possible controversy during study selection and data extraction was resolved by an agreement between the same authors. In case an agreement was not reached, a third investigator was consulted (T.N).

2.6. Inclusion and exclusion criteria

Inclusion criteria:

- Clinical trials, randomized controlled studies (RCTs), case-control studies, cross-sectional studies, and cohort studies.
- Studies on endodontically retreated permanent teeth.
- At least 1 year of follow-up after root canal retreatment.
- Articles in which success was measured or could be measured.
- Final sample size larger than 40.
- Dropout rate less than 20%.

Exclusion criteria:

- Animal and laboratory studies.
- Non-restorable teeth, teeth with a previous endodontic PA surgery, a root resorption, or root fracture.

2.7. Data items

Data collected from the studies selected for this systematic review included the demographic features of the patients (age and sex), tooth-related characteristics (arch location and dental group, presence and size of apical radiolucency, and periodontal involvement), and treatment-related features (number and operator experience, rubber dam isolation, desobturation and preparation system, solvent use, irrigating solution and activation, obturation technique, pre- and postoperative extension of root canal filling, final restoration type, number of visits, and procedural complications, including perforations and instrument fractures).

2.8. Risk of bias in individual studies

Two investigators (T.N. and J.G.O.) independently assessed the risk of bias for each of the selected studies, and discrepancies were resolved via discussion. In accordance with the study type, the Cochrane risk-of-bias tool (RoB 2) [20] or a modification of the Newcastle-Ottawa scale [21] was used for single-arm studies. The Oxford Centre for Evidence-Based Medicine - Levels of Evidence recommendations were used to grade studies according to the level of evidence [22].

2.9. Summary, synthesis, and statistical analysis of results

The outcome measures were standardized as binary data (success/failure) according to the data reported in the different studies. Success was based on the clinical and radiographic evaluations reported in the different studies and readjusted according to two main criteria [12]: strict criteria (absence of clinical signs and

symptoms and radiographically normal periodontal ligament space) and loose criteria (absence of clinical signs and symptoms and absence or reduction of apical radiolucency in the control radiograph).

R software (version 4.2.1, R Foundation, Vienna, Austria; metafor package) [23] was used for statistical data analysis. The weighted and pooled estimates of success from all studies were obtained by using a random-effects model. Furthermore, to make the assumptions of normal distribution more applicable to significance testing and to stabilise the variance, the Freeman-Tukey transformation was performed. The data were analysed for both strict and loose criteria in two groups according to the study follow-up (1-3 years or 4-5 years), and the results were visualized using forest plots. The Cochrane Q test and I^2 values were used to measure the level of heterogeneity between studies (I^2 > 60% was considered heterogeneous). The significance level was set at 0.05 and confidence intervals were 95%.

2.10. Risk of bias across studies

Potential publication bias was evaluated using funnel plots, and asymmetry was assessed using Egger's linear regression tests, considering $p<0.05$ to represent significant publication bias.

2.11. Additional analyses

The effect of each study on the global treatment effect if study bias was present, was analysed using a sensitivity analysis. The effects of demographic, pre-, intra-, and postoperative variables (patients age and sex, tooth arch location and dental group, presence and size of apical radiolucency, periodontal status, type and number of operators, desobturation and preparation system, solvent use, irrigating solution, obturation technique, sealer type, pre- and postoperative root canal filing extension, number of visits, type of final restoration and procedural complications) on the retreatment success rate (strict and loose criteria) were assessed, and the estimated success and 95% confidence interval (95% CI) were calculated by using a random-effects model.

3. RESULTS

3.1. Study selection

The selection process for the present systematic review performed by the researchers (M.E. and J.G.O.) is shown in the flow diagram in Figure 1. Following the initial identification of articles and the removal of duplicates, 66 studies were screened for eligibility. After a full-text evaluation of this group of studies, 57 were excluded for the reasons shown in the *supplementary material 2 (supplemental table S2).* Finally, with the inclusion of one study performed by the present study researchers' group and unpublished at the time of the present study search, the final selection consisted of 10 studies.

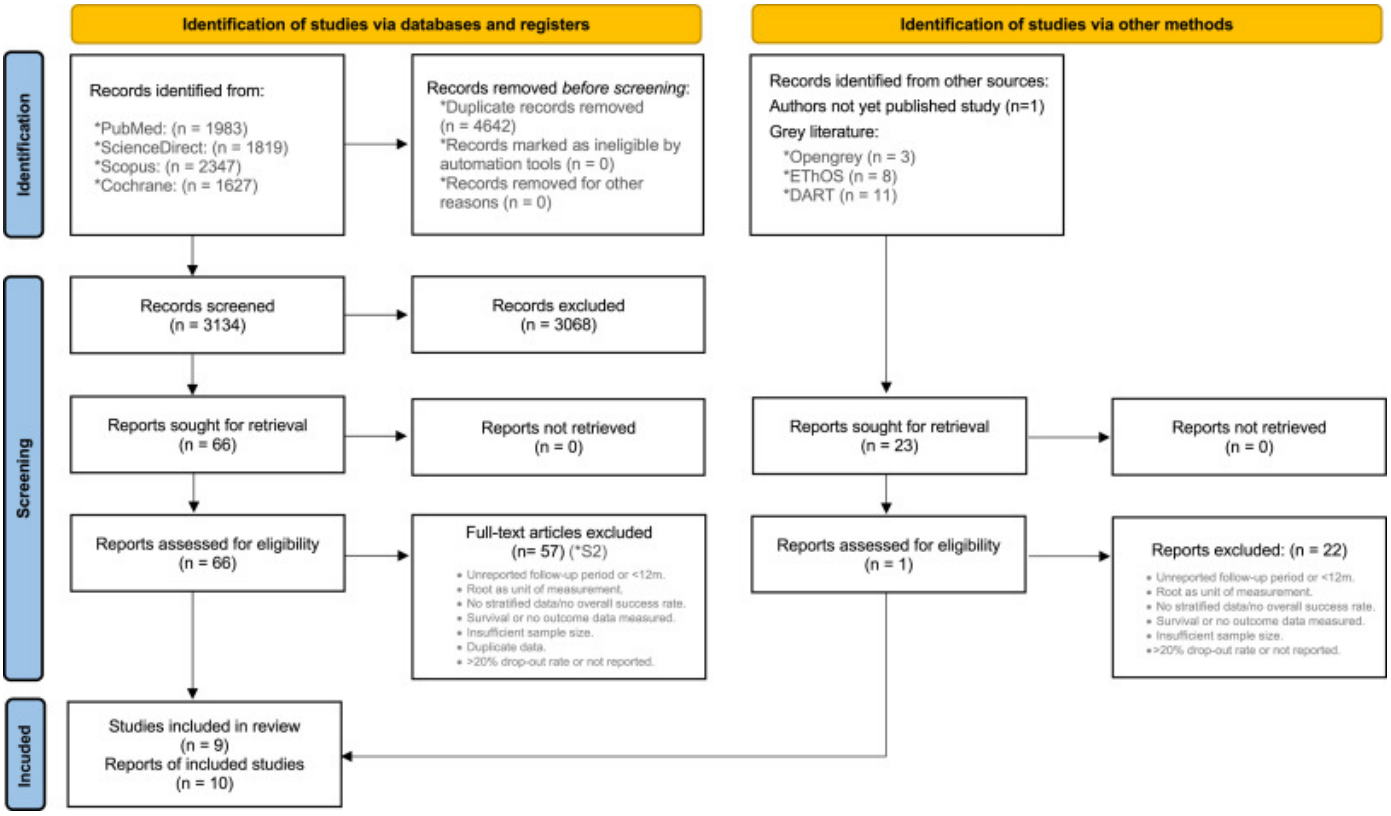

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Figure 1. PRISMA 2020 Flow Diagram

3.2. Study methodological features

Table 2 presents the details of the included studies. Of the ten studies, there were two RCTs [24,25], seven single-arm prospective studies [26], [27], [28], [29], [30], [31], [32], and one single-arm ambispective study [33]. Nine of the included studies were published between 1998 and 2022. Most studies (n=7) were conducted in Europe [24,[26], [27], [28], [29],31,33], followed by two in Asia [25,32] and one in North America [30].

Table 2. Included studies general features

Study	Study design	Country	Recall rate	Sample	Follow-up	Operator	Number of operators	2 evaluators	Calibration	Radiographic evaluation	Reliabili test
Sundqvist 1998	PSC	Sweden	93	50	5	NR	NR	Yes	trained'	PA	NR
Gorni 2004	PDC	Italy	94.2[p]	452	2	Specialist	Multiple	Yes	Yes	PA	Yes
Davies 2016	PSC	UK	86.3	98	1	Postgrad	Multiple	Yes	Yes	PA + CBCT	Yes

Neskovic 2016	PSC	Serbia	100	49	2	NR	Single	Yes	NR	PA	NR
He 2017	PSC	USA	82.6	52	2	Postgrad	Multiple	Yes	Yes	PA	NR
Al-Nuaimi 2017	PSC	UK	87.2	137	1	Postgrad	Multiple	Yes	Yes	PA + CBCT	Yes
Zandi 2019	RCT	Norway	100	45	1	Specialist	Single	Yes	Yes	PA	Yes
Serefoglu 2021	PSC	Turkey	85.8	103	2.4	Specialist	Single	Yes	Yes	PA	Yes
Karaoglan 2022	RCT	Turkey	89	89	2	Specialist	Single	Yes	Yes	PA	Yes
Olivieri 2023	ASC	Spain	80.1	129	2.3	Postgrad	Multiple	Yes	Yes	PA	Yes

PSC: Prospective single arm clinical trial; PDC: Prospective double arm clinical trial; ASC: Ambispective single arm clinical trial; RCT: Randomized clinical trial; NR: Not reported;

*Recall rate of endodontic treatment and retreatment, individual retreatment rate not provided; *p*Recall rate of patients, retreatment rate not provided; PA: Periapical radiograph; CBCT: Cone-Beam Computed Tomography;

** Modifications made from the original classification; PAI: Periapical Index.

For the radiographic assessment of treatment success, ten studies used PA radiographs, of which two also used cone-beam computed tomography (CBCT) [28,31]. Five studies categorized PA radiographs using the periapical index (PAI) to establish treatment success [24,25,29,32,33] while the other five [[26], [27], [28],30,31] used reduced categorisations such as the Strindberg criteria or similar [34]. All studies evaluated the retreatment outcomes based on clinical criteria and strict or loose radiographic standards. Follow-up assessments across the studies ranged from 1-5 years. Two observers evaluated the radiographic images in all studies and mentioned previously calibrating them, except in one study in which calibration was not mentioned [29]. Seven studies reported intra- or inter-agreement reliability test results [24,25,27,28,[31], [32], [33]]. Only two studies [25,33] described having previously calculated the sample size. The recall rate across all included studies ranged from 80.1-100%.

3.3. Risk of bias within studies

There was no discrepancy between the two evaluators owing the risk-of-bias appraisal. Seven out of the ten included studies were single-arm investigations and three included a group comparison [24,25,27]. Gorni & Galiani [27] compared retreatment between teeth that had their original root canal morphology retained or altered, Zandi *et al.* [24] compared two irrigating solutions, and Karaoglan *et al.* [25] compared one- and two-visit retreatments. However, as the present review aimed to evaluate the outcome of non-surgical root canal

retreatment, these studies were also evaluated using a modified Newcastle-Otawa scale for study comparison, removing the selection of the non-exposed cohort and comparability items as a single-group meta-analysis was performed. Each study was graded with one star for all six evaluation items. Detailed information regarding each item in all the included studies is shown in *supplementary material 3 (supplemental table S3).* All studies assessed retreatment outcomes using clinical and radiographic criteria (employing PA radiographs or CBCT images) by at least two evaluators, seven of which also included reliability test results [24,25,27,28, [31], [32], [33]] (Figure 2).

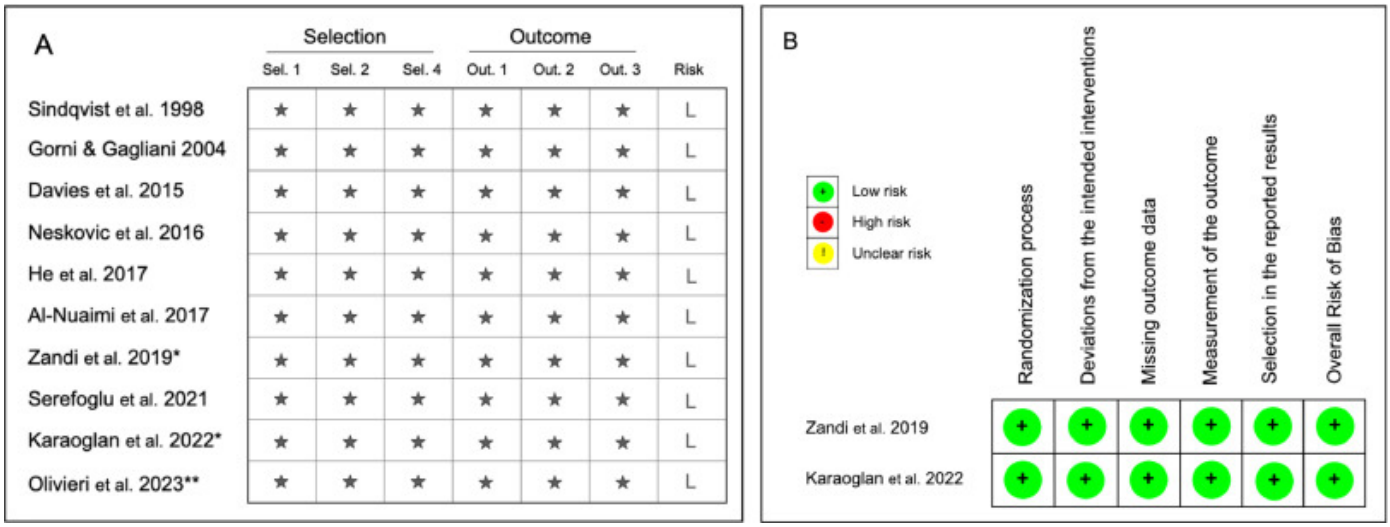

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Figure 2. Risk of bias summary for the different studies (A: Newcastle-Ottawa quality assessment scale (NOS) modified for single group cohort studies and B: Rob2 Cochrane Collaboration's tool for randomized controlled trials).

3.4. Results of individual studies and synthesis of results

When using strict criteria, the weighted pooled (clinical + radiographic) success rate of the included studies, based on a random-effects model using PA radiographs to evaluate radiographic outcome, was of 0.73 (95% CI, 0.67-0.78) with a significant heterogeneity across the studies (I^2 = 73%) (Figure 3A). The outcome of interest (retreatment success) was also evaluated in a short (1-3 years) and long (4-5 years) follow-up periods with a resulting weighted pooled success rate of 0.71 (95% CI, 0.66 - 0.77) with moderate heterogeneity across the studies (I^2 61.37%) and 0.77 (95% CI, 0.67-0.86) with no heterogeneity across the studies (I^2 = 0.0%) (Figure 3B).

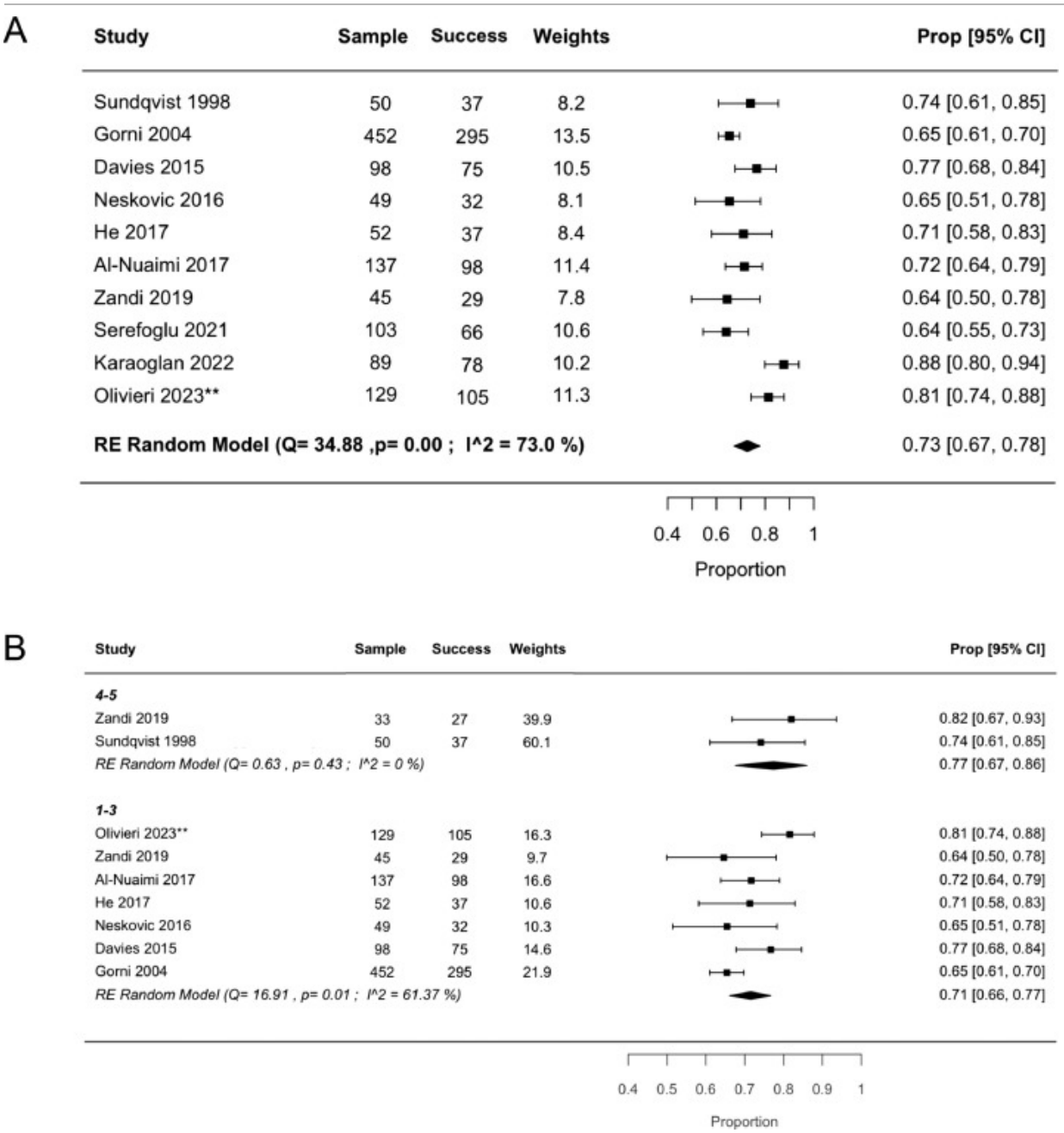

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Figure 3. Meta-analysis results for included studies according to STRICT CRITERIA of success. A: General data. B: Data according to the follow-up period.

When using loose criteria to evaluate the retreatment success, the weighted pooled (clinical + radiographic) success rate of the included studies, based on a random-effects model and using PA radiographs to evaluate radiographic outcome, was 0.86 (95% CI, 0.79-0.91) with significant heterogeneity across studies (I^2 = 86.4%) (Figure 4A). Retreatment success was also evaluated in a short (1-3 years) follow-up period with a resulting weighted pooled success rate of 0.87 (95% CI, 0.79-0.93) with significant heterogeneity across the studies (I^2 = 88.5%). Only one study reported data over a long follow-up [26] impeding further analysis. (Figure 4B).

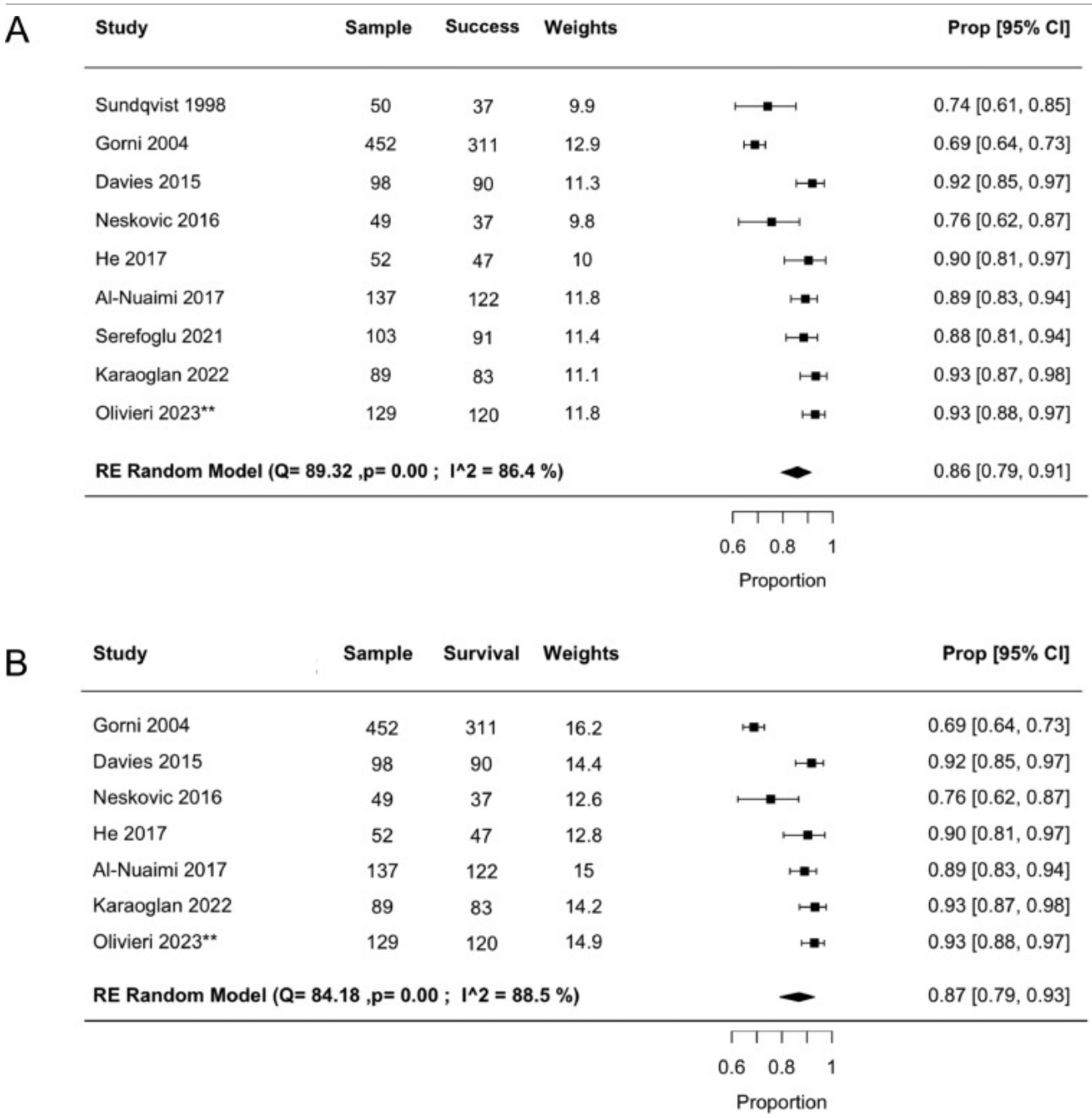

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Figure 4. Meta-analysis results for included studies according to LOOSE CRITERIA of success. A: General data. B: Data according to 1-3 follow-up period.

Two studies used CBCT images to evaluate radiographic outcomes [28,30,31]. The weighted pooled (clinical + radiographic) success rate was 0.55 (95% CI, 0.43-0.67) with moderate heterogeneity across the studies (I^2 = 71.2%) and 0.79 (95% CI, 0.73-0.85) with low heterogeneity across the studies (I^2 = 25.2%) for strict and loose criteria, respectively (Figure 5).

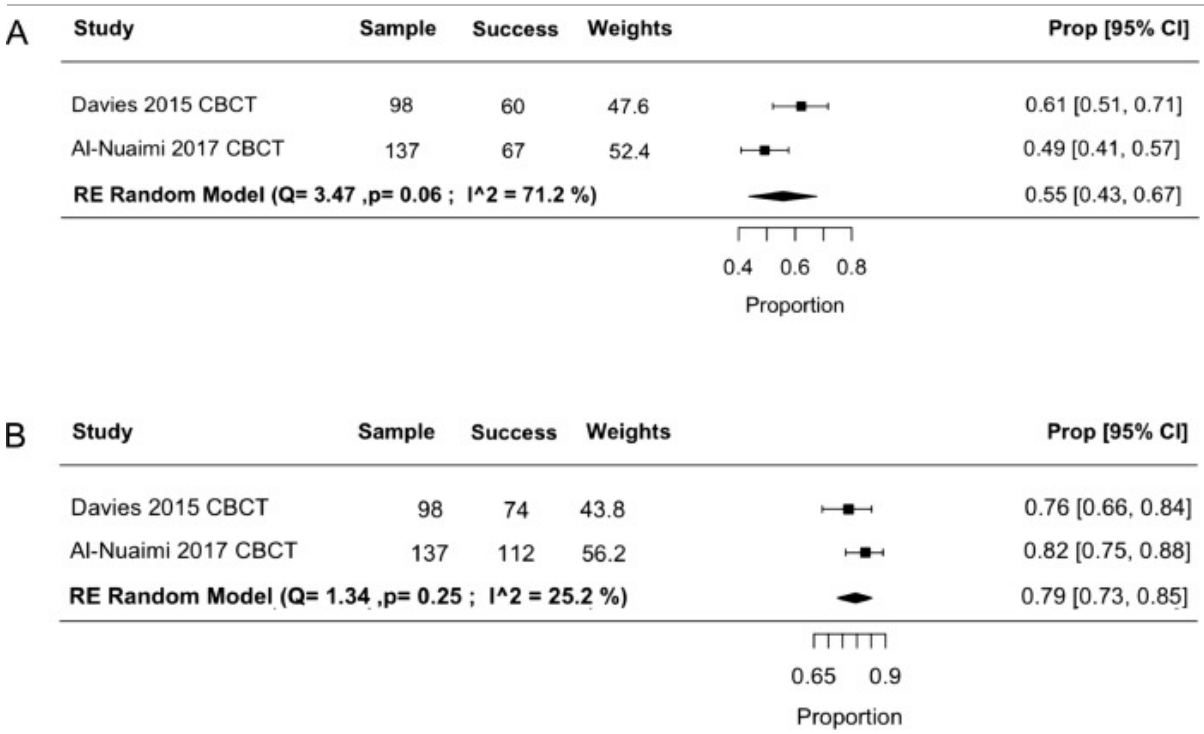

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Figure 5. Meta-analysis success general results for included studies (CBCT). A: Strict criteria. B: Loose criteria.

3.5. Risk of bias across studies

The results observed in the funnel plots are displayed in *supplementary material 4 (supplemental figure S4).* Egger's test results indicated no publication bias. For outcome results using PA radiographs (strict criteria), the p-values of Egger's test were 0.92 for the global data and 0.83 for the 1-3 follow-up period. For loose criteria, the p-values of Egger's test were 0.84 for the global data and 0.47 for the 1-3 follow-up period. A limited number of studies evaluated strict or loose criteria outcomes in a 4-5 follow-up period using PA radiographs or CBCT images. Thus, impeding further analysis.

3.6. Additional analysis

The stability of the results and evaluation of the impact of individual datasets were tested using sensitivity analyses showing that no study had a significant impact on the pooled results that were robust and stable.

3.7. Study variables and retreatment success

Most of the studies evaluated different preoperative, intraoperative, or post-operative variables and their associations with retreatment success. The main observations related to the effects of different variables and retreatment success are described below.

3.7.1. Demographic variables

Although most studies recorded sex as a variable, only three studies stratified retreatment success according to sex [30,32,33]. The success rate after 2-4-years of follow-up was 78% in women and 66% in men according

to strict criteria, and 90-91% for both sexes under loose criteria. No differences were found in patient sex under either criterion when evaluating retreatment success (Table 3).

Table 3. Pooled weighted success rates by pre-operative clinical factors based on strict criteria

		Strict criteria			Loose criteria		
Variable	Category	Studies	Teeth	Weighted pooled success rate	Studies	Teeth	Weighted pooled success rate
Sex	Female	3	148	0.78 (0.71; 0.84)	3	148	0.91 (0.86; 0.96)
	Male	3	136	0.66 (0.47; 0.83)	3	136	0.90 (0.81; 0.97)
Tooth	Anterior	2	47	0.92 (0.81; 0.99)[a]	2	47	0.96 (0.88; 1.00)
	Premolars	2	53	0.79 (0.67; 0.89)[ab]	2	53	0.91 (0.81; 0.98)
	Molars	4	282	0.70 (0.64; 0.75)[b]	7	282	0.91 (0.87; 0.94)
Dental arch	Maxillary	2	95	0.87 (0.79; 0.93)[a]	2	95	0.95 (0.89; 0.99)
	Mandibular	3	189	0.66 (0.59; 0.73)[b]	3	189	0.89 (0.84; 0.93)
Initial AP	No AP	5	196	0.97 (0.88; 1.00)[a]	5	196	0.97 (0.88; 0.93)
	AP	9	909	0.67 (0.58; 0.75)[b]	8	864	0.83 (0.73; 0.91)
Size AP	< 5	3	159	0.94 (0.74; 1.00)	3	159	0.98 (0.94; 1.00)[a]
	> 5	3	97	0.59 (0.44; 0.75)	3	97	0.87 (0.79; 0.93)[b]
Initial PAI	PAI 1.2	1	40	0.97 (0.89; 1.00)[a]	1	40	1.00 (0.96; 1.00)[a]
	PAI 3	1	40	0.97 (0.89; 1.00)[a]	1	40	0.97 (0.89; 1.00)[a]
	PAI 4	2	83	0.64 (0.48; 0.78)[b]	2	83	0.85 (0.75; 0.94)[b]
	PAI 5	2	69	0.55 (0.43; 0.67)[b]	2	69	0.72 (0.31; 0.98)[a]
Operator	Postgrad/Student	3	318	0.75 (0.68; 0.82)	3	318	0.91 (0.87; 0.94)
	Specialist	4	689	0.71 (0.58; 0.82)	3	644	0.84 (0.68; 0.96)
Number of operators	Single	4	286	0.71 (0.58; 0.83)	3	241	0.87 (0.76; 0.95)
	Multiple	5	868	0.73 (0.67; 0.79)	5	868	0.87 (0.78; 0.94)
Solvent	No Solvent	7	651	0.75 (0.68; 0.81)	5	556	0.91 (0.88; 0.93)
	Solvent	3	553	0.66 (0.62; 0.69)	3	553	0.78 (0.64; 0.89)
Desobturation	Manual	4	373	0.76 (0.66; 0.85)	4	373	0.88 (0.82; 094)
	Mechanical	5	741	0.70 (0.63; 0.77)	4	721	0.86 (0.75; 0.94)
Preparation	Manual	3	158	0.75 (0.56; 0.89)	3	158	0.86 (0.64; 0.98)
	Mechanical	6	956	0.72 (0.67; 0.77)	6	956	0.87 (0.80; 0.93)
Irrigation	L%NaOCl	5	407	0.69 (0.64; 0.75)	4	387	0.87 (0.82; 0.92)

	H%NaOCl	3	633	0.73 (0.62; 0.82)	3	633	0.85 (0.68; 0.96)
	CHX	1	25	0.64 (0.44; 0.82)	-	-	-
Obturation Technique	Cold GP	5	336	0.72 (0.61; 0.81)	4	291	0.84 (0.73; 0.92)
	Warm GP	5	868	0.73 (0.67; 0.79)	5	868	0.87 (0.78; 0.94)
Sealer	ZOE-based	3	687	0.70 (0.63; 0.76)	3	687	0.84 (0.68; 0.95)
	Resin-based	6	437	0.75 (0.65; 0.83)	5	392	0.89 (0.86; 0.93)
Visits	Single	2	74	0.88 (0.79; 0.95)[a]	2	74	0.95 (0.88; 0.99)
	Multiple	9	678	0.73 (0.68; 0.77)[b]	7	583	0.89 (0.86; 0.92)
Filling extension (preoperative)	Ok	3	106	0.74 (0.64; 0.83)	3	106	0.89 (0.82; 0.94)
	Short	3	200	0.79 (0.61; 0.93)	3	200	0.92 (0.87; 0.95)
	Long	3	20	0.71 (0.47; 0.91)	3	20	0.88 (0.57; 1.00)
Filling extension (postoperative)	Ok	3	300	0.76 (0.67; 0.84)	3	300	0.89 (0.81; 0.96)
	Short	2	20	0.36 (0.00; 1.00)	2	20	0.59 (0.10; 1.00)
	Long	1	10	-	1	10	-
Restoration	Direct	2	127	0.73 (0.54; 0.88)	2	127	0.92 (0.87; 0.96)
	Indirect	4	294	0.74 (0.68; 0.79)	4	294	0.89 (0.86; 0.93)

AP: Apical Periodontitis; GP: Gutta-percha; ZOE: Zinc Oxide-Eugenol.

ab

Variables that share the same script letter are not statistically significant.

Age was also recorded in all included clinical studies. However, stratification related to retreatment success was not reported across most studies, and grouping differed in some of the studies, making comparison not possible. Olivieri *et al.* [33] stratified data into two groups (<40 and >40 years old) and reported success rates of 93.1% (strict criteria) and 96.5% (loose criteria) in patients younger than 40 years and 77% (strict criteria) and 92% (loose criteria) in older patients. He et al. [30] observed success rates of 69.2% (strict criteria) and 89.7% (loose criteria) in patients younger than 60 years. They observed success rates of 76.9% (strict criteria) and 92.3% (loose criteria) in patients aged >60 years. Serefoglu *et al.* [32] stratified age groups using 35 years as a cut-off. They observed that younger patients had success rates of 75.5% (strict criteria) and 90.6% (loose criteria), while older patients had success rates of 52% (strict criteria) and 86% (loose criteria). No study reported differences between the different age groups.

3.7.2. Location and tooth type

Two studies included success data related to the position of the tooth in the maxillary or the mandibular arches [30,33], and one included only mandibular molars [32]. According to the present analysis, root canal retreatment in mandibular teeth had a lower success rate than maxillary teeth after 2-4-years of follow-up

(strict criteria). However, no differences were found when loose criteria were applied (Table 3).

The tooth type was significantly associated with retreatment success. Anterior teeth showed a higher success rate than molars under strict criteria; however, no differences were found when loose criteria were considered. Four studies were included for tooth type analysis: three used strict criteria [28,30,33], and four used loose criteria [28,30,32,33]. Davies *et al.* [28] and Olivieri *et al.* [33] also found differences between anterior and posterior teeth in their studies ($p<0.05$) (Table 3).

3.7.3. Periapical radiolucency

Selection criteria in four studies included only teeth with a PA radiolucency [[24], [25], [26],32]. In the six other studies [[27], [28], [29], [30], [31],33], the retreatment procedures were included in both teeth with or without a PA radiolucency. All of these studies found a higher success rate in teeth without PA radiolucencies, making the difference in four of them statistically significant [27,29,31,33] ($p<0.05$). The presence of a PA radiolucency associated with the retreated tooth in the present analysis was directly related to lower retreatment success under strict criteria. Teeth with a previous PA radiolucency had a weighted pooled success rate of 67% (strict criteria) and 83% (loose criteria), compared to 97% (for both strict and loose criteria) in teeth without a PA lesion (Table 3).

Three of the ten studies compared and analysed differences in the healing rate of root canal-retreated teeth with regard to PA radiolucency size [25,30,33]. Two categorized lesions with a cut-off of 5 mm [30,33], and Karaoglan *et al.* [25] used a cut-off of 6 mm. Healing rates in these three studies were higher in teeth with smaller lesions. However, only two of the studies reported significant differences [25,33], and only one of these in both strict and loose criteria [25] ($p<0.05$). When performing the present weighted analysis, in cases where the PA lesion was greater than 5 mm, the success rate statistically decreased only when the loose criteria were used for radiographic evaluation, but not under strict criteria (Table 3).

Two studies reported success rates based on initial PAI scores [32,33]. Serefoglu *et al.* [32] only included retreatment cases with initial PAI scores of 4 and 5 and found no differences ($p>0.05$). Olivieri et al. [33] observed differences in the success rate of retreatment cases with an initial PAI score of 1-2 compared with higher scores (PAI 4-5) ($p<0.05$) when evaluating success using strict criteria. When comparing the stratified data in the present review, differences were found between the initial PAI scores according to the strict and loose criteria models. An initial PAI score of 1-3 resulted in a higher success rate than PAI scores of 4 or 5 (strict criteria). Differences were found between PAI 1-2 compared to PAI 4 under the loose criteria (Table 3).

3.7.4. Number of operators and experience

In four studies, a single operator performed all retreatment procedures [24,25,29,32], and in the remaining five studies, multiple operators were used [27,28,30,31,33]. Analysis of these variables showed no differences between groups with either strict or loose criteria (Table 3).

None of the ten studies compared differences in retreatment success rates according to operator experience. Retreatments were performed by specialists in four [24,25,27,32], by endodontic postgraduate students in three [30,31,33], and by both in one [28]. No significant differences were observed between groups. Thus, operator experience did not affect the retreatment outcomes (Table 3).

3.7.5. Rubber dam isolation

All studies reported using rubber dam isolation except two that did not specifically mention its use [27,29]; however, none reported not using it. Thus, precluding any possible comparison, the most reasonable scenario was that rubber dam isolation was also performed in those studies; however, they failed to mention it.

3.7.6. Root canal desobturation and instrumentation

Manual (K-Flex, K-Files, and H-Files) and Gates Glidden instruments were used for canal desobturation in five studies [24,25,28,29,31]. In four [27,30,32,33], mechanical rotary or reciprocating NiTi instruments were used during root canal desobturation. After root canal desobturation, root canal preparation was completed with manual files in two studies [25,29], with mechanical NiTi instruments in six studies, and in two it was not reported or included unclear information. To date, no study has compared the success rates on the use of mechanical and manual instruments. The present analysis comparing both groups revealed no differences in the use of manual or mechanical NiTi instruments during root canal retreatment procedures for either the strict or loose criteria (Table 3). There are insufficient and inconsistent data to evaluate the possible effects of preparation size or taper on the success rate of root canal retreatment. Some studies reported a minimum or range of preparation sizes, but none reported stratified data related to treatment success.

3.7.7. Solvent

Chloroform, xylene, ethyl acetate and thymol, halothane, and xylol have been used in studies on root canal desobturation. Three of the ten studies included in the present systematic review reported the use of one of these solvents [27,29,30], whereas seven specifically mentioned not using any solvent [[24], [25], [26],28,[31], [32], [33]]. A comparison of studies that did or did not use a solvent showed no differences in the success rate with either strict or loose criteria (Table 3).

3.7.8. Irrigation

Only one study [24] directly compared the success rates of two irrigant solutions. Zandi *et al.* [24] evaluated retreatment success with either 1% sodium hypochlorite (NaOCl) or 2% chlorhexidine digluconate (CHX) and found no significant difference ($p>0.05$). The most common irrigant was NaOCl, which was used at concentrations ranging from 0.5-5.25% across all the included studies. For the present analysis, NaOCl concentrations ranging from 0.5-2.5% were classified as low-concentration NaOCl (LNaOCl) [24,25,28,29,31,32] and concentrations ranging from 4.2-5.25% were classified as high-concentration NaOCl (HNaOCl) [27,30,33]. According to the present analysis, there were no significant differences in retreatment success based on the irrigant solution employed in either criteria model (Table 3).

Six studies reported the use of chelating solutions for smear layer removal. Disodium edetate (EDTA) solutions were used in five studies at concentrations of 5% [25] and 17% [28,[30], [31], [32]], whereas 10% citric acid was used in two studies [29,33]. Three studies did not use or mention any solution for smear layer removal [24,26,27]. Thus, there are limited data to evaluate the effect of the use of a chelating solution on retreatment outcomes.

Irrigant activation was reported in four studies. Two used a manual dynamic technique [25,32] and two used a passive ultrasonic irrigation technique [28,30]. The remaining studies did not activate or report irrigant activation. As such, this factor could not be analysed in retreatment outcomes.

3.7.9. Intracanal medication

All studies reported the use of a calcium hydroxide paste when performing root canal retreatment at more than one visit. Thus, a comparison of different intracanal medications was not possible.

3.7.10. Retreatment obturation technique and sealer

Five studies used a cold lateral compaction gutta-percha technique for root canal retreatment obturation [[24], [25], [26],29,32] and five used a warm gutta-percha technique [27,28,30,31,33]. No study directly compared these two techniques to evaluate their success.

Regarding the endodontic sealer employed, three studies used a zinc-oxide-eugenol-based sealer [27,28,31] and six used a resin-based sealer [24,25,29,30,32,33]. Group analysis in the present review found no differences related to the retreatment obturation technique or the sealer used in terms of success rate (Table 3).

3.7.11. Number of visits

Only two studies included stratified data for comparison between single- and multiple-visit retreatment [25,33], one of which was an RCT that specifically compared the success rate of single- and two-visit retreatment [25]. No differences in success rates were found in either study ($p>0.05$). Most studies included in this systematic review performed all root canal retreatments in multiple visits [24,26,[28], [29], [30], [31], [32]]. No differences in success rates were observed between single- and multiple-visit retreatments under loose criteria. However, when evaluating success under strict criteria, single-visit retreatments showed a higher success rate than multiple-visit retreatments (Table 3).

3.7.12. Root canal filling apical extension

The root canal filling extension across studies was classified mainly as short (>2 mm from the radiographic apex), flush (within 0-2 mm of the radiographic apex), or long (beyond the radiographic apex). When evaluating preoperative root canal filling extensions, three studies included stratified data and evaluated this variable for retreatment success [25,32,33]. No study reported statistically significant differences among the three categories ($p>0.05$), nor did the present group analysis (Table 3). Data on the extrusion of endodontic sealers during root canal retreatment in relation to retreatment success were not included in any study.

3.7.13. Restoration

Different types of final restorations were performed in various studies. One study performed crown restorations in all included retreatment cases [30], and in another study, indirect cusp coverage was performed [31]. Only two studies included stratified data on both types of restorations (direct and indirect) and treatment outcomes [32,33]. No significant differences were found between the type of final restoration and retreatment success; the same result was observed in the present analysis. The quality of the final restoration was assessed in two studies [31,33], neither of which found significant differences in retreatment success ($p>0.05$). Assessment of restoration quality as ‘adequate’ or ‘inadequate’ was based on radiographic and clinical criteria defined by Hommez *et al.* [35,33] or similar to that proposed by Craveiro *et al.* [36,31]. Al-Nuaimi *et al.* [31] also found no significant association between retreatment success and the number of remaining coronal walls ($p>0.05$). However, the data were insufficient for a proper analysis.

Data on the effect of an intracanal posts on retreatment outcomes are scarce. Only one study included data on the success rate of retreated teeth restored with or without an intracanal post and on the presence of a preoperative intracanal post [33], and reported no differences between groups ($p>0.05$). More data are required to perform a group analysis.

3.7.14. Perforations

Five studies included data on perforations and success rates. Gorni and Galiani [27] included 43 cases with prior root perforations, which were sealed with either fibrin adhesive, zinc-oxide-ethoxybenzoic acid-added cement, or amalgam, and reported success rates of 51.6% (strict criteria) and 60.5% (loose criteria) after retreatment. Al-Nuaimi *et al.* [31] analysed 12 cases with prior perforations, and 11 were considered to have favourable outcomes (loose criteria) after one year. Only two studies reported data on the success rate of perforated teeth during root canal retreatment [31,33]. Al-Nuaimi *et al.* [31] reported only one perforation, which was considered healed after 1 year, and Olivieri *et al.* [33] reported six cases, four of which healed after 2-3 years. Insufficient data were available for group analysis.

3.7.15. Broken instruments

Only one study included data on the success rate of teeth retreated with a previously broken instrument [27], and no study included data on the success rate of teeth in which the instrument had broken during the retreatment procedure. Gorni and Galiani [27] included 61 teeth with an intracanal instrument fragment, 58 (95%) of which healed, and one was considered healing.

3.7.16. Magnification

Eight studies reported the use of magnification devices to aid root canal retreatment; loupes were used in two studies [25,27], an operative microscope in four [24,28,30,31], and either loupes or an operative microscope in two [32,33]. Only two studies [26,29] did not use or did not mention this aspect in their articles, impeding any possible group comparison.

There were insufficient data on possible associations of several variables with retreatment success, such as final apical preparation size, pre- and postoperative pain, flare-ups, when the final restoration was placed, or patient toxic habits and systemic diseases.

4. Discussion

The results of the present systematic review and meta-analysis results demonstrate that non-surgical root canal retreatment results in a favourable success rate. When performing a systematic review and meta-analysis, the first aim seems to be to gather as much data as possible, sometimes without prioritising the quality of the information collected. The present review aimed to select and analyse the highest-quality available information using strict study inclusion criteria. Although studies on root canal retreatment have been published for more than 90 years, the vast majority of studies that fulfilled the inclusion criteria for the present review were published during the last decade [24,25,[28], [29], [30], [31], [32], [33]]. The high number of studies analysing the prognosis of root canal retreatment in recent years highlights the interest in this topic. Improvements in methodological design and data reporting across studies has also been evident. Recent studies have considered factors such as the number of evaluators analysing radiographic images and their

prior calibration, reliability tests, higher follow-up rates, stratified data for analysis, and the provision of a clear study typology. In addition, most recent studies have reported having received ethical approval, which is rare in past studies. This indicates that data and patient protection regulations have been adequately adopted across different countries. Clinical studies require arduous efforts by the researchers involved. Completing the initially proposed study protocol comprises serious challenges, and recent studies including items of bias control, such as those described above, are encouraging and reflect the determination of researchers and journal editorial groups to perform and include increasingly enhanced evidence-based data. However, only two studies [25,33] have reported a sample size calculation, which might be a point that still needs to be improved.

The present systematic review included studies that analysed teeth as a measurement unit. When evaluating the worst-appearing root in multi-rooted teeth, the possibility of detecting AP increases considerably [4,37]. Comparing or combining data from different units of measurement, such as teeth and roots, may be imprecise, particularly when evaluating bi- or multi-radicular teeth, as evaluating roots may tend to overestimate treatment outcomes. Clinically, an upper molar with a PA lesion in one root is considered non-healed, even if the other roots present normal periradicular tissues. Davies *et al.* [28] evaluated the radiographic success of root canal retreatment using both teeth and roots as the units of measurement. They reported higher success rates when analysing roots than when analysing teeth using both PA radiographs and CBCT. Indeed, when evaluating the roots as a unit or combining the results with other units of measurement, the sample size increases considerably. However, one of the aims of a systematic review and meta-analysis should be to evaluate the same units of measurement for outcome assessment. In addition, combining data seems inadequate from a clinical perspective.

As borne out in many studies, achieving an adequate recall rate is the most problematic aspect of conducting a clinical study, especially in longitudinal studies evaluating treatment outcomes. A follow-up loss of up to 5% is considered of little concern, but may potentially pose severe threats to validity if it is over 20% [38] and may impact treatment outcome results [39]. Therefore, the present systematic review only included studies with at least 80% follow-up. However, analysis was also performed on studies with a higher percentage of loss to follow-up (*supplementary material 5 (supplemental table S5)*, and the success rate appears to be overestimated when including studies with fewer recalls using strict criteria. In addition, one frequently observed aspect of systematic reviews and meta-analyses is the grouping of studies with different follow-up periods. We believe that comparing data from different follow-up periods may not be the most accurate methodological approach. Healing is a longitudinal process; therefore, the point at which it is evaluated is possibly relevant and mixing may be inappropriate. However, as seems to be a standard practice, in the present meta-analysis, the results of a grouped analysis were also included for comparison with previous reviews.

Reporting the stratified data of the recorded variables across studies is also a significant limitation. Most studies describe the different variables being recorded, including demographic, pre-, intra-, and postoperative data. However, some studies did not report correlations between these variables and retreatment success. In addition, other studies included stratified data from the initially screened population but not from cases followed up. Some of these aspects hinder data recollection and subsequent analysis for variable correlation to retreatment success, which led us to highlight another limitation of the present systematic review and meta-analysis. Since all raw data from the included studies were not available to evaluate the effect of the interaction of the independent variables (predictive factors) on the dependent variable (success/failure), ruling out the presence or absence of confounding factors was not possible.

The presence of a PA lesion has been observed to affect the success of root canal treatment and retreatment [40,41]. Ng *et al.* [12] reported a 76.4% and 82.7% pooled success rates of root canal retreatment according to clinical and radiographic strict and loose criteria respectively. However, the success rate in teeth with preoperative PA radiolucency decreased to 65.7% (strict criteria) [12]. Similarly, in the present study analysis, a significant difference was observed with a 30% reduction in healing under strict criteria and a 14% reduction under loose evaluation criteria. However, the differences were significant only under the strict criteria model. When evaluating radiographic success, regeneration of periradicular tissues is required, including intact lamina dura, elimination of the PA lesion, and normal periodontal ligament space (Strindberg 1956). Hence, teeth with a PA lesion are expected to have a lower success rate or more protracted regeneration than teeth that do not require bone regeneration. Accordingly, studies analysing retreatment success under strict criteria across time show higher success in longer follow-ups [24,29,42].

In the present analysis, endodontically retreated teeth with larger PA lesions and teeth with higher PAI scores (PAI 4-5), had a lower success rate than those teeth with smaller lesions or lower PAI scores (PAI 1-3) under strict radiographic criteria. In addition, differences were found between teeth with initial PAI scores of 4 and 1-2 when using loose criteria. It has been suggested that larger PA lesions hold major infection and bacterial diversity [43] and may be more difficult to eliminate or confront [44]. Bacterial organisation in larger lesions may explain the reduced success rates. In addition, long-standing infections can be present within the complexity of root canals, such as accessory canals, or penetrate deeper into the dentinal tubules [45], jeopardising retreatment outcomes. Moreover, larger lesions are more likely to present with cystic structures [46,47]. However, as no differences were found when the loose criteria were used, it is possible that larger lesions only take more time to heal, as a reduction in size in the follow-up examination is considered a success when using loose criteria. It is important to note that only two studies evaluated radiographic healing using CBCT. Zhang *et al.* [48] observed that 75.8% of PA lesions healed completely after 4 years, 13.8% were almost completely healed (>84% reduction), and only four (6.9%) increased in volume. No relationship was found between the size of the PA lesion and treatment success [48].

The aetiology of endodontic failure is multifactorial, including several hosts and other factors, being the presence of bacteria within the root canal one of the leading causes [5]. The root canal systems in multiradicular teeth are complex structures with a higher prevalence of intracanal ramifications and irregularities than those in uniradicular anterior teeth. These areas can harbour a number of bacteria that are more difficult to reach during chemo-mechanical preparation. Accordingly, in the present analysis, anterior teeth had a higher success rate than molar teeth under strict criteria. Moreover, two recent studies [49,50] reported similar results. In contrast, Ng *et al.* [12] observed a lower success rate in anterior teeth. However, the results were pooled from only two studies, both using roots as a unit of measurement, and in one of these studies, 65% of root canal-retreated teeth did not present a PA lesion [51]. When analysing only teeth with PA lesions, Sjögren *et al.* [51] found that anterior teeth had a higher success rate than molar teeth.

Numerous studies have shown no difference in success between single and multiple appointments in primary root canal treatments [52], [53], [54]. Nevertheless, evidence regarding single versus multiple appointments in root canal-retreated teeth is scarce. According to our results, non-surgical retreatments performed in one appointment exhibited a significantly higher success rate than multiple visits under strict criteria. In seven of the ten studies included, retreatment procedures were performed in a multiple-visit approach [24,26,[28], [29], [30], [31], [32]]. Only two studies included stratified data to compare single- and multiple-visit retreatments [25,33], of which only one was a RCT [25]. Karaoğlan *et al.* [25] compared single- and two-visit

retreatments in teeth with asymptomatic AP, showing high success rates in both groups (95.5% vs. 91.1% respectively) with no significant differences. It is important to consider that whenever the choice of whether performing a retreatment in one or more visits is not randomized, it could be interpreted that the decision was made according to the level of difficulty or preoperative signs or symptoms, thereby causing bias in the results.

The present review included studies that met similar clinical and radiographic success evaluation criteria. The clinical criteria included the absence or presence of any level of pain or discomfort on palpation, percussion, or biting, and the presence or absence of a sinus tract. For radiographic evaluation, the results were classified into two general groups according to strict or loose success criteria. However, one limitation of the present systematic review is that the criteria used to define success differed slightly across studies. Five studies used PAI scoring to evaluate healing [24,25,29,32,33]. However, is difficult to establish where small bone structure changes are present. Most studies using the PAI considered healing when scoring a PAI 1 or 2. However, only PAI 1 has an exact criterion for radiographic healing as the one defined by Strindberg [34]: complete resolution of the PA lesion, with an intact lamina dura, normal contours of the periodontal ligament, or widening around the root filling excess [34]. A similar definition of radiographic healing was proposed by Rudd *et al.* [55] which included the presence of a normal lamina dura, but with a maximum of periodontal space widening of twice the normal size and a maximum defect of 1 mm^2 around the lamina dura adjacent to the filling material. However, these differences may not be clinically relevant, especially in cases with a previous PA radiolucency.

Despite the improved methodological standards of recent studies, more controlled studies are still necessary that randomise retreatment according to different variables and to long follow-up periods. Moreover, stratified data with the maximum number of possible variables are required, even if they seem insufficient for analysis, because only then a sufficient number of samples for variables that are not common will be available, such as pre- and intraoperative complications (root perforations and fractured instruments) that prevent reaching an adequate working length to meet the retreatment success criteria. In addition, in order to evaluate radiographic success, more studies including CBCT analyses may be required. Although regularly performing a CBCT during follow-up examinations should not be recommended in all cases [56], it has been advocated in cases with contradictory or non-specific clinical signs or symptoms associated with previously endodontically treated teeth [57]. CBCT technology is of a great importance in root canal treatment planning and evaluation [58,59]. It provides three-dimensional images with greater diagnostic accuracy than PA radiography [59]. In addition, it has been confirmed as a suitable diagnostic tool for detecting missed canals and PA radiolucencies [58,60]. However, it has some limitations such as artefact generation, noise and scatter levels, and a higher radiation dose compared with PA radiography [61]. PA radiographs are still widely used in retreatment studies [24,25,[28], [29], [30], [31], [32], [33]] and are still the main method used in endodontics in both clinical practice and studies settings. However, the compression of three-dimensional structures into a two-dimensional view, geometric distortion, and superimposition of structures, are some of their main limitations [62].

Understanding the effect of the different variables on the prognosis of endodontic retreatment is necessary for recommending evidence-based clinical protocols and guiding future research. Unfortunately, information regarding the extent to which several factors, such as systemic diseases like hypertension or diabetes and toxic habits like smoking and alcohol consumption, have an impact on the retreatment prognosis has not yet been addressed. Having enough quality data for an adequate clinical decision-making process is essential.

Hence, studies are required to aid clinicians in providing a proper treatment plan that best suits patients based on their preferences and clinical characteristics.

Finally, we encourage researchers to continue pursuing excellence with a view to achieving a higher level of evidence for root canal retreatment.

5. Conclusions

According to the results of the present systematic review and meta-analysis, non-surgical root canal retreatment results in favourable outcomes. The presence of a PA radiolucency, PA lesions >5mm, multiple-visit retreatments, and retreatments in the mandibular or molar teeth result in a reduced success rate.

CRediT authorship contribution statement

Juan Gonzalo Olivieri: Conceptualization, Investigation, Methodology, Writing – original draft, Writing – review & editing. **Marc Encinas:** Investigation, Methodology. **Tousif Nathani:** Investigation. **Queralt Miró:** Formal analysis, Validation, Writing – review & editing. **Fernando Duran-Sindreu:** Writing – review & editing.

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Appendix. Supplementary materials

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