

Single-visit versus multiple-visits endodontic treatment of apical periodontitis: A meta-analysis of outcome assessed by intra oral radiographs

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Abstract

The established multiple-visit treatment for necrotic teeth with apical periodontitis has been challenged by single-visit treatment. However, there is no clear support for the one or the other treatment in the literature. The aim of this meta-analysis was to investigate if non-surgical primary root canal treatment carried out in single-visit or multiple-visit makes any difference in terms of radiographic healing in necrotic teeth with apical periodontitis. The null hypothesis was: there is no difference in the rate of apical healing for the two treatment modalities. The literature search was organized through the National Centre for Biotechnology Information (NCBI) at the U.S. National Library of Medicine (NLM) the National Library of Medicine (NLM)) using PubMed database and EMBASE Ovid to select articles with single-visit or multiple-visit included teeth with pulp necrosis and apical periodontitis. Of the 60 identified studies, only eight studies were included in current meta-analysis. The main reasons for exclusions were teeth with other diagnosis except necrotic pulp and apical periodontitis, studies with no comparison between single- and multiple-visit endodontics within the same study and studies without healing rate appearance. Results from each of the included studies were entered into the statistical program Stata, Version 15 (Texas, USA). The odds ratio (OR) and the 95% confidence interval for each study were calculated (dependent variable: single-visit/multiple-visit, independent variables: healed/not healed based on intra oral radiographs) with the random effect model. There was no significant difference in radiographic evidence of periapical healing between single-visit endodontics and multiple-visit treatment modalities, of the primary root canal treatment in necrotic teeth with apical periodontitis (OR = 1.10, 95% CI: 0.67-1.83) as evaluated on intra oral radiographs. Thus, the null hypothesis could not be rejected.

Background

Untreated necrotic pulp tissue will by time be infected and develop apical periodontitis as a response to microorganisms in the root canal system [1–3]. The success of root canal treatment is directly dependent on the elimination or eradication of root canal infection [4–8]. Mechanical instrumentation alone causes a complete elimination of bacteria in only 20–43 % of cases [9]. Additional irrigation with antibacterial reagents such as 0.5 % sodium hypochlorite provides disinfection in 40–60 % of root canal treatments [10]. Inter-appointment root canal medication with calcium hydroxide, commonly used in multiple-visit endodontic treatment, reduces the bacterial count, but it does not ensure total eradication of microorganisms in the root canal system [11]. The antimicrobial properties of calcium hydroxide are related to the release of hydroxyl ions. Hydroxyl ions kill bacteria by damaging the cytoplasmic membrane, protein denaturation, and damage to the DNA. Bacterial cells use proton pumps to manage pH homeostasis within a narrow physiological range so that enzymes and proteins function normally [12]. It has been demonstrated that some microorganisms such as *Enterococcus faecalis* and *Candida albicans* can resist the effectiveness of calcium hydroxide medications in root canals [13–16].

Extensive controversy exists over the question of whether it is desirable to complete root canal treatment of teeth with apical periodontitis in a single-visit session. Single-visit root canal treatment aims to entomb the remaining microorganisms, and depriving them from nutrition [17–20]. Root canal treatment in a

single-visit is gaining popularity over the traditional multiple-visit endodontics because of several advantages; chair-side time reduction, less susceptibility to reinfection through the temporary filling and root canal dressing [18, 21–23], costs reduction, high patient acceptance [24] and reduced flare-up rate [25, 26]. It has also been shown that calcium hydroxide may be difficult to remove from the irregular root canal walls [27]. Remaining calcium hydroxide on the canal walls affects the quality of the root filling negatively [28–31]. According to an *in vitro* study, residue calcium hydroxide can hinder the penetration of sealers into the dentinal tubules [32]. Calcium hydroxide paste can result in degenerative changes and necrosis as shown by intense inflammatory responses in animal models [33], and histology [34–36].

For evaluating the healing of apical periodontitis after root canal treatment, periapical radiographs are needed. Radiographic appearance of the periapical tissue can be evaluated according to classification of Reit and Gröndahl [37] from 1983 (5-point scale), the Periapical Index (PAI) by Ørstavik et al. (5-point scale) [38], or the 3-point scale developed by Halse and Molven [39].

The aim of this meta-analysis was to investigate if non-surgical primary root canal treatment carried out in single-visit or multiple-visit makes any difference in terms of radiographic healing in necrotic teeth with apical periodontitis. The null hypothesis is that there is no difference in the rate of apical healing for the two treatment modalities in primary endodontic therapies in permanent necrotic teeth with preoperative apical periodontitis as assessed by intra oral radiographs.

Methods

Without a well-focused question, it is difficult to identify appropriate resources and search for relevant evidence. To form the question and facilitate the literature search, the PICO framework was used [40], and is presented in Table 1.

A professional librarian specializing in literature search in medical topics carried out a search in PubMed and EMBASE databases together with the authors. The literature searches were carried out October 2th, 2018, and the search strategy is given in Table 2. A systematic search for unpublished studies was not carried out.

Due to different search methodologies in the two databases, the number of search terms are unequal. According to results from the search strategy 34 studies were identified by EMBASE [4, 7, 17, 18, 25, 26, 41-68] and 48 by PubMed database [4, 5, 7, 17-19, 26, 43-47, 49-51, 55, 56, 58, 59, 62, 65-92]. Several studies were duplicates [4, 7, 17, 18, 26, 43-47, 49-51, 55, 56, 58, 59, 62, 65-68]. A total of 60 original studies were reviewed, including randomized clinical trials (RCT) and follow-up studies (non-RCT). The flow of the study process and final number of included studies are shown in Fig. 1. Inclusion criteria for this meta-analysis are given in Table 3. There were no restriction to index used for scoring apical periodontitis on intra oral radiographs. Criteria for exclusion are given in Table 4.

To avoid bias and confirm or refute individual findings, so called meta-analytical methods was used to aggregate information from different studies and provide quantitative estimates of the effect. In the

present study, data from relevant literature were combined statistically to provide a quantitative estimate of the strength of association between the radiographic healing rate of root canal treatment and number of treatment visits.

The PPISMA statement for reporting meta-analyses was acknowledged [93].

Statistical methods

All data were entered and analyzed in Stata, Version 15 (Texas, USA). Logistic regression analysis was used to calculate the odds ratio (OR), the 95 % confidence interval (CI) and the standard error (SE) of the OR for each study (dependent variable: single-visit versus multiple-visit, independent variables: healed/not healed). To account for the possibility that there are a true (random) difference between the included studies (e.g. patient groups) and variation by chance between the studies, the random effect model was applied to calculate the overall effect size (summary OR), as described by Fleiss (62). Forest plot were designed for the different analyses.

Results

From the 60 identified papers, a total of 52 papers were excluded according to our exclusion criteria. Excluded studies and the reason for exclusion from the present meta-analysis are presented in Table 4.

Of all identified studies through the literature search strategies given in Tables 2, only eight studies were included in our final analysis, see Table 5. For studies using either «incomplete» [18] or «uncertain» [4, 57] healing, the teeth in these groups were categorized as «not healed». In all of the eight included studies [4, 18, 23, 50, 55, 57, 73, 81], the teeth in the multiple-visit groups were root filled in the second session (some studies call this the two-visit group).

In all included studies rubber dam was applied and the root canal irrigation regimen included sodium hypochlorite concentrations of 0.5 % [57], 1 % [18], 2 % [4], 2.5 % [23, 73], 3 % [81] and 5.25 % [50, 55]. Three studies [50, 55, 73] used 17 % ethylenediaminetetraacetate in addition, whereas by one study the irrigation was completed using 5 % iodine-potassium-iodine solution (Lugol's solution) for 10 minutes [57]. In cases with multiple-visit treatment the intra-canal medication was placed for at least one week before root canal treatment was completed. Calcium hydroxide was the inter-appointment medication in all included studies. In two studies calcium hydroxide was not mixed with sterile saline; Penesis et al. [55] used calcium hydroxide powder mixed with 2 % chlorhexidine liquid, and Gill et al. [73] used calcium hydroxide with iodoform paste (Vitapax) as inter-appointment medication of multiple-visit treatment teeth. Six studies obturated root canals with lateral condensation technique using gutta-percha and different sealers. The other two studies used either warm lateral-compaction technique and sealer [4] or warm vertical condensation technique and sealer [55]. In all included studies the teeth were coronally

sealed by the operator performing the endodontic treatment. More detailed information about treatment procedure and evaluation in each of the included studies are presented in Table 5.

The results showed an overall OR of 1.10 (95% CI: 0.67-1.83) for non-healed outcome for the multiple-visit group as compared to the single-visit group indicating no increased risk for the multiple-visit group versus the single visit group. The calculated OR for each included study is shown in Fig. 2. Only the study by Paredes-Vieyra & Enriquez [50] showed a significant risk (odds ratio of 3.5, 95% CI:1,23-9.90) for non-healing in the multiple-visit group, which means that there is a 3.5 times the odds of non-healing in the multiple-visit group as compared to the single-visit group. The remaining seven studies [4, 18, 23, 55, 57, 73, 81] and the overall analysis showed no difference between outcomes of the two different treatment groups. In Fig. 2, the overall OR for the non-RCT (OR 1.03, 95% CI: 0.57-1.88) and the RCT (OR 1.17, 95% CI: 0.66-2.10) studies are also presented separately, and show close values for the OR.

The studies using the PAI-index for radiographic evaluation of healing were analyzed separately, with an overall OR of 1.10 (95% CI: 0.64-1.89). This indicate that there is no difference between the two treatment modalities regarding index used for scoring of radiographic healing of apical periodontitis (Fig. 3).

Discussion

The findings of the present meta-analysis showed no statistical difference between single-visit and multiple-visit treatment modalities. This means that there is no difference between the treatment regimens, or, alternatively, the sample size is too small to demonstrate a true difference. Trope et al. [66] demonstrated a radiographic healing rate of 64 % in single-visit versus 74 % in multiple-visit treatment. However, the difference was not significant. They calculated the need for a sample size of 354 teeth in each treatment group for demonstrating significant differences based on power set at 80 %. The number of treated teeth in the present meta-analysis, 351 in single-visit and 315 in multiple-visit treatment, approached the calculated number by Trope. A larger sample size is desired, giving a higher power in the statistical analysis, but there are lack of randomized clinical trial in multi-centre settings in the field of endodontology [94]. In this meta-analysis 65 teeth out of 351 (18 %) in the single-visit group and 63 out of 315 (20 %) in the multiple-visit group were not healed (Table 5), given a difference of 1.5 % between the two treatment groups. According to calculations in Stata, 10844 teeth are needed in each treatment groups to achieve a significance different between the two treatment regimens at this low level.

The present meta-analysis included clinical follow-up studies, and was not limited to randomized clinical trials. Clinical follow-up studies are lower in the hierarchy of evidence. Only three [50, 55, 57] of the eight included studies in the current meta-analysis were randomized controlled trials. Of the 666 teeth included in present meta-analysis, 434 were included in the three abovementioned RCTs. The remaining five studies were follow-up studies. A systematic review and meta-analysis by Sathorn at el. [5] in 2005 aimed to answer if single-visit treatment results in a lower healing rate then multiple-visit treatment with calcium hydroxide dressing. They included only three studies [4, 18, 66], all of them ordinary follow-up studies and concluded that there was no statistically significance in healing between single-visit and multiple-visit

root canal treatment, which is in agreement with the findings of the present study with an extension of included studies.

Lucena et al. reported quality assessment of randomized clinical trials limited to English language articles published in the field of endodontology between 1997 and 2012 as poor. Sample description, no adherence to Helsinki Declaration regarding ethical aspects, lack of information on randomization methods and no previous sample size estimation or inappropriate sample size estimation and inappropriate reports of statistical analysis contributed to the weakness and limitations [95]. However, the present study showed no difference comparing radiographic outcome of RTCs and non-RCTs.

Clinical trials in endodontics cannot easily be completely blinded. For example, when comparing single-visit versus multiple-visit treatment, both patients and dentists are inevitably aware of their randomized assignment. However, a blinded assessment of outcome can often be achieved, as recorded in six of the included studies in the present meta-analysis [4, 18, 50, 55, 57, 66, 73]. In six of the eight included studies, the evaluation of radiographic outcome was carried out blinded and not performed by the operators. One study [18] mentioned that the radiographs were judged by the operators involved in the treatment, however the examiners did not know whether the tooth belonged to the single-visit or the multiple-visit group. Dorasani et al. [81] did not clearly describe the radiographic evaluation procedure. On the other hand, many investigators believe that the data obtained are less reliable than those obtained from double-blind trials [96].

Although published literature is the main source of evidence for clinical decision-making, there are still concerns that many studies, in particular those with negative results, are not published. Since there is a tendency that studies with positive results would more likely be published than studies with negative results, publication bias is a concern for most meta-analyses and systematic reviews. There was no test of publication bias performed in our meta-analysis, due to the very small number of identified randomized controlled trials. The literature search in PubMed and EMBASE databases used most relevant terms related to the null hypothesis, thus, we claim that a possible selection bias was minimized. Nonetheless, language limitations and size of apical lesion are examples for limitations that can contribute to selection bias.

In all included studies, the patients were randomly assigned to each treatment groups, and root canal treatment was performed according to standardized protocols, using rubber dam and establishment of asepsis. The teeth in five of the included studies [4, 50, 66, 73, 81] were treated by one operator, in one study by two operators [18] and in another study by four operators [57]. In one of the included studies [55] the number of operators were reported to be more than one. However, it was not exactly clear how many persons that had been involved in the treatment processes. A low number of operators in each study may increase the internal validity of each of them.

Five of the included studies used the PAI-index [50, 55, 66, 73, 81], which is reasonably accurate, reproducible and able to discriminate between sub-populations. According to Ørstavik et al. [38] PAI-score 3 was seen as disease, by which changes in bone structure could be detected with some mineral loss. It is applicable to use the PAI-score for the analysis of periapical radiographs in clinical trials, epidemiological and in retrospective studies of endodontic outcome [38]. Thus, included studies using the PAI-index should be comparable. By doing separate calculations on the studies using the PAI-index for final assessment of outcome, the overall OR were close to the overall OR for all included studies. As such, the different indices are relatively close when it comes to evaluation outcome on intraoral radiographs reported on a dichotomous scale as healed or not-healed. The important aspect for the present meta-analysis is that, regardless of the index used, the same index was used for both study groups in each study.

In the present meta-analysis, only teeth with definite preoperative apical periodontitis were included to make the comparison between the treatment protocols viable. There was no evidence of a difference, in terms of radiological healing between teeth treated in a single-visit compared with teeth following a multiple-visit protocol (OR=1.10). Our finding is consistent with the results of a meta-analysis from 2005 where only three of the eight identified studies in this meta-analysis were analyzed [5].

The observation time in four of the included studies was 12 months [55, 66, 73, 81], in two of them 24 months [50, 57] and in the remaining two studies almost five years [4, 18]. However, it has been concluded that simple calculation of success rates would overestimate the chance of complete periapical healing within the first years after therapy, but underestimate it over longer observation periods [97]. It has also been demonstrated that there is a gradual increase of periapical healing over a period of four years [4, 18]. Several studies choose a 12-months follow-up evaluation as an end-point due to the resource-intensive nature of clinical studies and difficulty of controlling patient loss over time [98-100]. By using the PAI-index, evidence of periapical changes in bone density associated with healing should be apparent at 12 months and longer observation times might not be necessary [101]. The 1-year follow-up was first recommended by Ørstavik [102], who showed a peak in incidence of healing or emerging chronic apical periodontitis (CAP) at 1 year. Risk assessments at 2, 3, and 4 years did not indicate an added risk that filled roots developed CAP during this period. Although complete healing of preoperative CAP in some instances required 4 years to heal, initial signs of healing (although incomplete) were visible in at least 89% of all healed teeth after 1 year. The fact that the included studies had a follow-up time of 12 month or more adds to the validity of the study.

Except for the study by Paredes-Vieyra & Enriquez [50], which presented a significant risk (odds ratio of 3.5) in favour of single-visit endodontics, all other included studies showed no significant difference between the treatment modalities. The same finding was reported in a meta-analysis by Schwendicke & Gostemeyer [44]. In this study, the aim was to study several factors such as pain and flare-ups related to one-visit versus multiple-visit root canal treatment. Their main inclusion criteria was randomized controlled trials or controlled trials without signs of selection bias and studies comparing single-visit with multiple-visit root canal treatment in permanent teeth with closed apices, regardless of the preoperative

condition. In two other systematic reviews, the radiographic healing in single-visit root canal treatment appeared to be slightly more effective than multiple-visit treatment, however without reaching statistical significance [5, 7].

Conclusions

Based on identified studies, there was no significant difference in radiographic evidence of periapical healing between single-visit endodontics and multiple-visit treatment modalities, and the null hypothesis could not be rejected. However, the total number of included teeth in this analysis is too small to support this as a final conclusion to the research question.

Declarations

Abbreviations

CI – confidence interval

OR – odds ratio

PAI – periapical index

RCT – randomized controlled trial

SE – standard error

Ethical approval and consent to participate

Not applicable

Consent for publication

Not applicable

Availability of data and material

The datasets analysed during the current study are available from the corresponding author on reasonable request.

Competing interest

The authors declare that they have no competing interests.

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Authors' contribution

Author BDM and AB has contributed in the determination of search strategy (together with the librarian), selection of relevant studies, data extraction and analyses, and drafting the manuscript. Both authors has revised and approved the final version of the manuscript.

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Tables

Figures

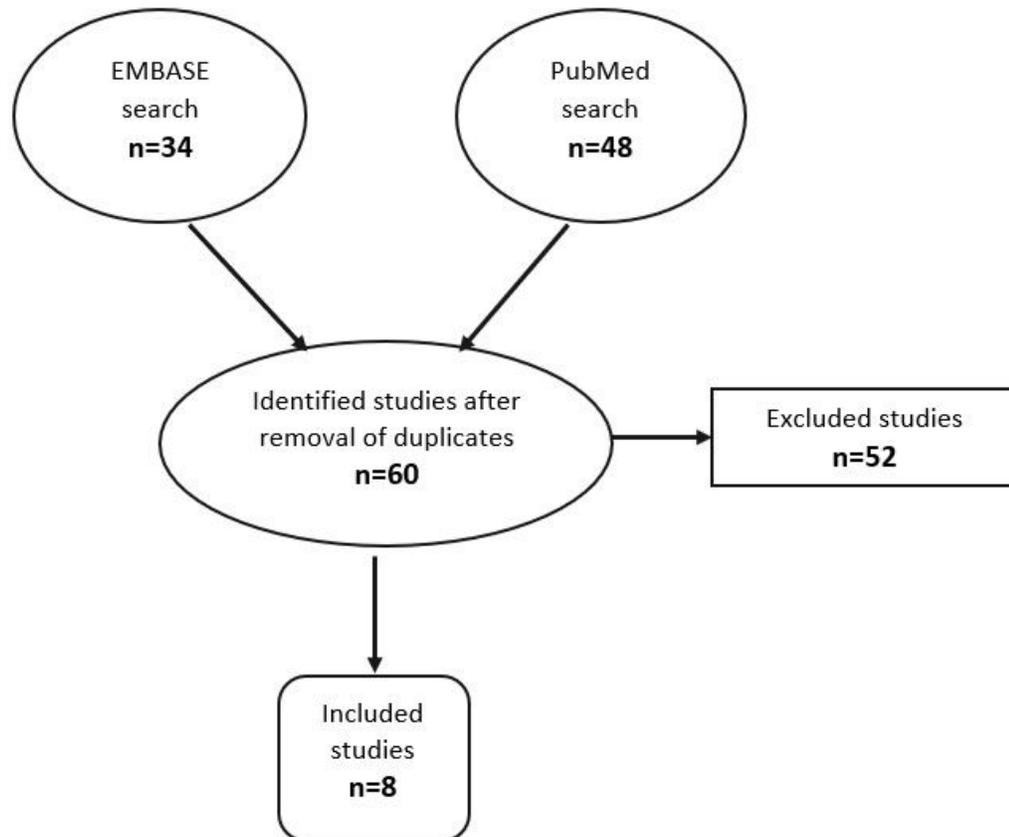


Figure 1

Flow diagram of literature search and final sample of included papers.

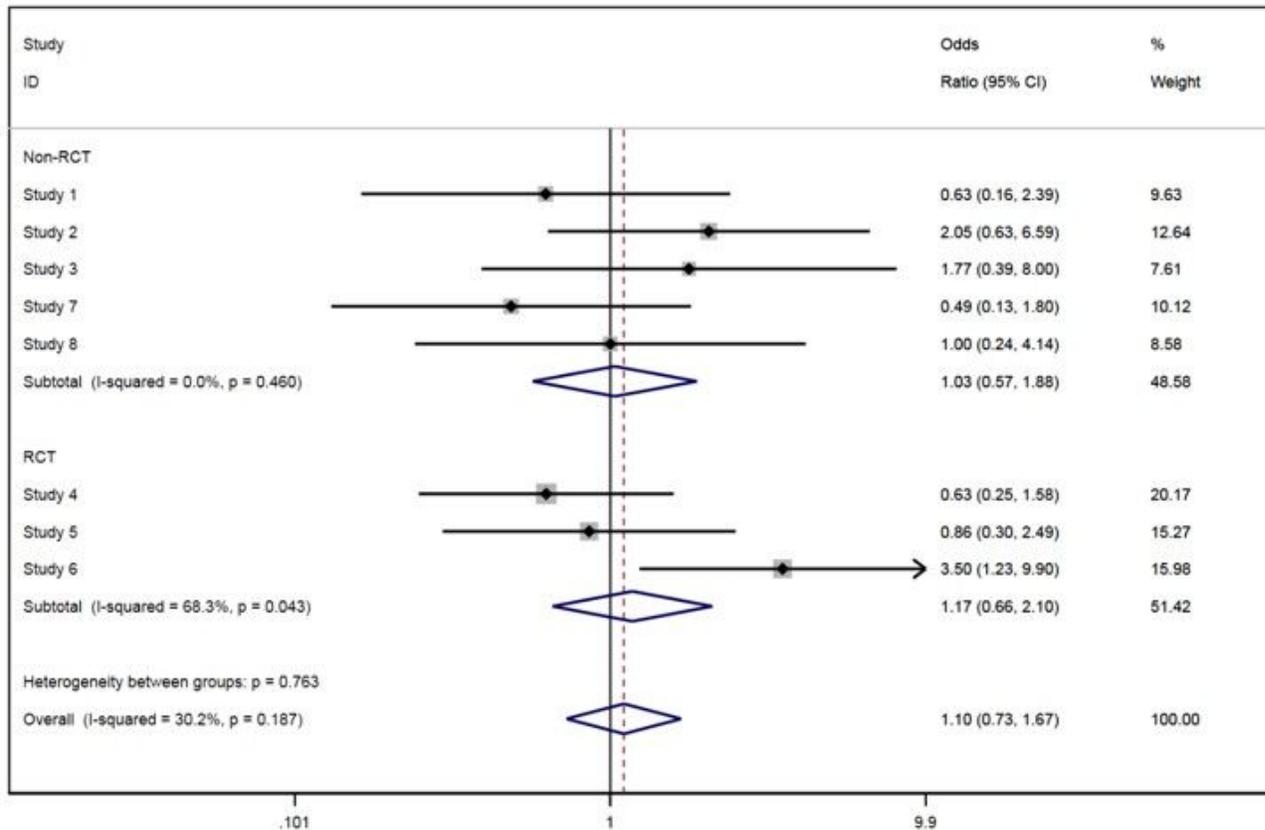


Figure 2

Forest plot of the pooled data. Eight odds ratios, squares, proportional to weights used in meta-analysis are presented, with the summary measure (centre line of diamond) and associated confidence intervals (lateral tips of diamond), and solid vertical line of effect. The ID number relates to the included studies given in Table 5. Odds ratios and confidence intervals are given for the separate study and the overall. Horizontal line shows the 95 % confidence interval. The transparent diamonds are the pooled result with horizontal tips demonstrating 95 % confidence interval and vertical tips illustrating pooled risk difference. The first diamond sums up the OR for the non-randomized controlled studies (OR 1.03). The second diamond summarize the overall OR for the randomized controlled trials (OR 1.17). The final diamond summarize the total of all eight studies (OR 1.10).

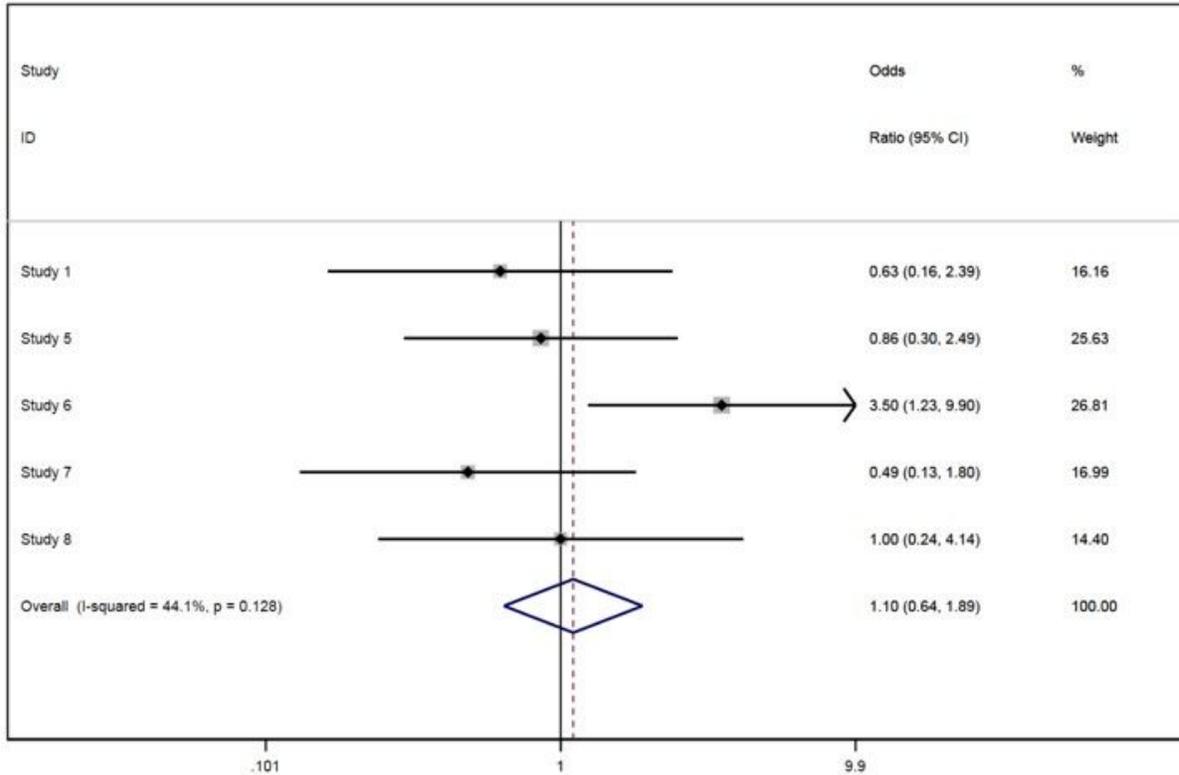


Figure 3

Forest plot of the pooled data for the studies using PAI-index for radiographic evaluation of apical healing. The ID number relates to the included studies given in Table 5. Odds ratios and confidence intervals are given for the separate studies and the overall. Horizontal line shows the 95 % confidence interval. The transparent diamond is the pooled result with horizontal tips demonstrating 95% confidence interval and vertical tips illustrating pooled risk difference (OR 1.10).

Supplementary Files

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