Title

Modern endodontic retreatment: A systematic review, meta-analyses, and comparisons to alternative treatment options

Author

seyed sadrkhani, seyed moein

Publication Date

2020

Peer reviewed|Thesis/dissertation

UNIVERSITY OF CALIFORNIA

Los Angeles

Modern endodontic retreatment: A systematic review, meta-analyses, and comparisons to alternative treatment options

A thesis for submission of the

requirements for the degree Master of Science

in Oral Biology

by

Seyed Moein Seyed Sadrkhani

ABSTRACT OF THE THESIS

Modern endodontic retreatment: A systematic review, meta-analyses, and comparisons to alternative treatment options

by

Seyed Moein Seyed Sadrkhani

Master of Science in Oral Biology

University of California, Los Angeles, 2020

Professor Shane White, Chair

Statement of problem. Clinicians are regularly confronted with difficult choices. Should a tooth that has not healed through non-surgical root canal treatment be treated through traditional non-surgical retreatment, modern retreatment, or modern apical microsurgery? Acquiring complete, unbiased current information to help clinicians and their patients make these choices requires a systematic review of the literature on treatment outcomes, meta analyses and statistical comparisons.

Purpose. The purpose of this paper was to answer the following questions: What are the success rates of modern endodontic retreatment in teeth that had previously received NSRCT, where periradicular pathosis had not healed? Does modern endodontic retreatment result in increased

healing rates over time? Does modern endodontic retreatment result in improved outcomes to those previously established for traditional retreatment? Does modern endodontic retreatment result in improved outcomes to those previously established for modern apical surgery?

Materials and methods. Searches were performed in Pubmed, Cochrane Library, and EMBASE databases on modern endodontic retreatment. Previously established datasets describing traditional endodontic retreatment and modern apical microsurgery were identified. Datasets were analyzed using funnel plots to examine bias, Forest plots to calculate weighted mean success rates and their associated confidence limits, and regression analysis to identify the simple linear equations relating percentage success rate to years of follow-up time.

Results. The quality of the papers reporting on modern endodontic retreatment was high and bias was low. The success rate for modern endodontic retreatment was largely unchanged through a period from 1 to 5 years of follow-up, a steady state was approximated. The success rate of modern endodontic retreatment was approximately 86% through 1 to 5 years after treatment. The success rate of modern endodontic retreatment was significantly higher than of traditional retreatment, 81%. The success rate of modern endodontic retreatment was equivalent to that of modern apical microsurgery, 85%.

Conclusions. Modern non-surgical endodontic retreatment should generally be the first-line treatment option after failure of initial non-surgical root canal treatment. Prospective, long-term modern retreatment studies of comprehensively described patient populations using a broad range of outcome measures are needed.

The thesis of Seyed Moein Seyed Sadrkhani is approved.

Mo Kang

Reuben Kim

Wei Chen

Shane White, Committee Chair

University of California, Los Angeles

2020

TABLE OF CONTENTS

LIST OF FIGURES

INTRODUCTION

Teeth affected by disease of pulpal origin may be predictably retained through non-surgical root canal treatment (NSRCT) and restoration. NSRCT is efficacious, valued by patients, and cost effective (Torabinejad et al. 2007; Hamedy et al. 2013). Systematic reviews of longitudinal studies on NSRCT show extremely high success and survival rates; nonetheless, some cases fail to demonstrate healing (Torabinejad et al. 2007; Iqbal et al. 2008; Ng et al. 2011). Moreover, cross-sectional data demonstrates a surprisingly high prevalence of apical pathology related to teeth that have received NSRCT (Pak). The first-line treatment option after failure of initial NSRCT is considered to be nonsurgical retreatment (Torabinejad et al. 2016).

Nonsurgical retreatment was validated by Strindberg in the 1950s, but was found to have lower healing rates than for initial NSRCT (Strindberg 1956). Likewise, 2009, 2011, and 2015 systematic reviews of nonsurgical retreatment outcomes by Torabinejad et al, Ng et al, and Kang et al estimated lower healing rates than those generally reported for initial NSRCT, but all included a mixture of data on modern and traditional retreatment (Torabinejad et al. 2009, Ng et al 2011, Kang et al 2015). Torabinejad et al reported that healing rates for retreatment significantly increased over time; whereas, apical surgery resulted in more failures over time. Torabinejad et al concluded that nonsurgical retreatment offers a more favorable long-term outcome to apical surgery (Torabinejad et al. 2009). Kang et al did not find a clear trend for nonsurgical retreatment success rates over time, but they reported that apical surgery success rates decreased over time, and that overall pooled success rates for apical surgery were superior to those for retreatment (Kang et al, 2015).

Over the past couple of decades considerable advances have been made in the conduct of both initial NSRCT and retreatment. Advances include the use of magnification, microscopes,

loupes, and endoscopes; ultrasonic instruments for the precise removal of dentin to identify canals and ramifications, and remove posts; and the use of adhesive materials for perforation repair (Farzaneh et al. 2004; Gorni and Gagliani. 2004; Ercan et al. 2007; de Chevigny et al. 2008; Hsiao et al. 2009; Salehrabi et al. 2010; Metska et al. 2013; Davies et al. 2016; Mente et al. 2015; Orhan et al. 2017; He et al. 2017; Eyuboglu et al. 2017; Al Nuaimi et al. 2017; Pirani et al. 2018; Chybowski et al. 2018; Alghofaily et al. 2018; Alharmoodi et al. 2019; Olcay et al. 2019; Zandi et al. 2019). Such modern technical advances were recently shown to improve the outcomes of endodontic microsurgery in comparison to traditional endodontic surgery (Torabinejad et al. 2015, Kohli et al 2018; Setzer et al 2012; von Arx & White, 2017). The extant literature on modern endodontic microsurgery appears to be exclusively based upon care provided by endodontic specialists (Torabinejad et al. 2015, Setzer et al, 2012; von Arx & White, 2017).

Critical examination of newly available evidence on modern endodontic nonsurgical retreatment through systematic review and meta-analysis could enable comparisons with other techniques, providing objective data to assist dentists and patients, in making decisions about the efficacy of contemporary retreatment in retaining teeth that have not healed after initial NSRCT.

Research questions were formulated (Torabinejad et al. 2007; Bader et al, 2004). What are the success rates of modern endodontic nonsurgical retreatment in teeth that had previously received NSRCT, where periradicular pathosis had not healed? Does modern endodontic nonsurgical retreatment result in increased healing rates over time? Does modern endodontic retreatment result in superior outcomes to traditional retreatment? Does modern endodontic nonsurgical retreatment result in superior outcomes to modern apical surgery?

MATERIALS AND METHODS

Inclusion Criteria

Inclusion criteria included comparative or non-comparative, prospective or retrospective, longitudinal data related to clinical outcomes of modern endodontic retreatment from January 1, 1990 through February 5, 2020. Articles reviewed were published in English, in the refereed indexed literature, and studied subjects were 10 or more teeth. The minimum follow up time was 6 months, starting from the procedure.

The units of study were the teeth that underwent modern endodontic retreatment, not the patient or root. Clear and defined outcome measures, criteria for success or survival, detailed descriptions of the sample size, treatments provided, and follow-up time were required.

Literature on modern endodontic retreatment was defined as being non-surgical root canal retreatment using magnification including microscopes, loupes, and oroscopes; ultrasonic instrumentation; and provided in the context of specialty care, including specialists, specialty trainees, and practices limited to endodontic care. Of course, a non-specialist can use modern techniques, but the extant literature is limited, and care provided by endodontic specialists has been reported to more closely align to best practice (Balto et al, 2004; Bigras et al. 2008; Madarati et al, 2008b, 2008a; Molen et al, 1998; Pagonis et al, 2000; Parashos et al, 2005). Where papers were not clear on clinical methodology, authors were contacted to determine if the inclusion criteria were met. Hence, some papers were excluded; for example, one author indicated that

rubber dam isolation was not always used and another indicated that magnification was only used occasionally (Nešković et al. 2016; Ashraf et al, 2007).

Exclusion Criteria

Exclusion criteria consisted of studies that failed to meet the above inclusion criteria.

Search Methodology

Electronic searches were performed in Pubmed, the Cochrane Library, Web of Science and EMBASE databases. Hand searching was extensively performed by two individuals with subject matter expertise, through citation mining of selected studies and prior systematic reviews. Guidance was provided by a reference librarian, and subject matter experts. Tables of contents of the *Journal of Endodontics* were hand searched.

Databases were searched in the following sequence: PubMed, Cochrane Library, Web of Science and EMBASE. The primary PubMed search strategy was developed through an iterative process to best represent the sentinel articles; it was adapted for use in EMBASE. Both MeSH (Medical Subject Headings) and free key word searches were performed (Figs. 2 & 3).

Study selection

After title review and abstract selection, full-text articles were used to verify that the inclusion criteria were met. Reasons for exclusion were recorded; these included: outcomes not being specifically assessed; outcomes criteria not being well-defined or described; less than 6

months of follow-up; or secondary data, meta-analyses, not original data. Accepted papers were reviewed by all authors and analyzed.

Study quality rating

Study quality, methodology, design, and data analysis were assessed by using the Wong Scale–Revised (Chiappeli et al, 2006). Studies were assessed by reviewer responses to 9 questions; a score of 1 (inappropriate), 2 (mediocre), or 3 (appropriate) was assigned to each question. The ‘‘what,’’ ‘‘who,’’ and ‘‘how’’ of each study received 3 questions apiece. Bias was principally addressed by the ‘‘how’’ questions. Out of a comprehensive total score of 9 to 27, a score under 19 would indicate that the methodology, design, and analysis of the study failed to support the reliability of the authors' conclusions, necessitating exclusion from the meta-analysis.

Data analysis

Data was extracted and an evidence tables was created. Data was reviewed and verified. Meta-analysis was conducted using Origin pro 2019b (OriginLab, Northampton, MA) (Agresti and Coull 1998). Pooled estimates with 95 % confidence interval of success and survival rates were calculated using the DerSimonian-Laird random effects pooling method, because assumptions of heterogeneity were not uniformly met (Cochrane Q test, $\alpha = 0.05$). Forest Plots were used to visually display the data from included studies and the overall pooled estimate with their 95% confidence intervals (CIs). Publication bias and heterogeneity was assessed using funnel plots. Regression analysis was used to identify the simple linear equations relating percentage success rate to years of follow-up time, and correlation coefficients, R^2, were calculated.

Treatment Comparisons

Papers included by prior authoritative systematic reviews on alternative treatments were used as comparators for the data on modern retreatment. Traditional retreatment study-sets were derived from Torabinejad et al, 2009; 5 papers which described traditional retreatment were used. Modern apical microsurgery study-sets were derived from Torabinejad et al, 2015. Distinct from the extractions and analyses in their parent publications, the comparator datasets were extracted and analyzed as described above, using Forest plots, funnel plots and regression analyses.

RESULTS

The modern retreatment literature

Electronic searches identified 711 distinct titles from Medline, Pubmed 47 from the Cochrane Library, 236 from EMBASE, and 208 from the Web of Science; hand searching did not identify any additional titles. From these 1201 titles, 256 abstracts were selected, 191 from Medline, 15 from the Cochrane Library, 23 from Embase, and 27 from the Web of Science. From these 256 abstracts, 83 papers were selected full text review, resulting in inclusion of 19 studies which included 20 datasets, all of which were initially located in Medline (Figs 3 & 4).

Quality of the modern retreatment literature

The quality of all the included studies were rated as high (Fig 5). No studies were rejected on the basis of insufficient quality. The commonest limitations were short recall times and low sample sizes (Fig 5). Most of the studies were recent; 10 of the papers were published within the last 3 years, and 17 out of 19 were published within the past 12 years (Fig 4). Recent publication on modern retreatment made this systematic review practicable.

Bias within the modern retreatment literature

Funnel plots of the 20 modern retreatment datasets indicated low overall bias; most studies with high precision were plotted close to the average, the spread was largely symmetrical, and few studies fell outside the funnel, and those that did were still close (Fig. 6). One data sub-set was not included in the analyses because it represented cases described by the authors as 'Root Canal Morphology Altered' during initial treatment, which may have manifested extracanal infection and been inherently unsuited to non-surgical retreatment alone (Gorni & Gagliani, 2004; Ricucci et al, 2015; Signoretti et al 2011); funnel plotting of that datum had shown it to be a most pronounced outlier. Potential sources of heterogeneity comprised of differences in: the lengths of follow-up time, and its reporting, exact or mean; treatment year; patient population and tooth type; sample size; technical procedures, instruments, files, sealers, anti-microbial irrigants and intracanal medications; study purpose, design and outcome measures.

Outcome measures in the modern retreatment literature

Retreatment outcomes were generally described in terms of success rather than by tooth survival. Orstavik's periapical index (Ørstavik et al, 1986) was the most widely used outcomes instrument, being used by 8 of the 19 included papers (Alharmoodi et al, 2019; Farzaneh et al, 2004; Alghofaily et al. 2018; Pirani et al. 2018; de Chevigny et al. 2008; Zandi et al. 2019; Olcay et al, 2019; Eyuboglu et al, 2017). Five papers used a system describing cases as Healed, Healing or Not-healed (Chybowski et al. 2018; Orhan et al, 2017; He et al. 2017; Hsiao et al, 2009; Al Nuaimi et al. 2017); another used a similar system, rating cases as undergoing Complete healing, Incomplete healing, or Unsatisfactory healing (Gorni & Gagliani. 2004). A criteria based upon those of Strindberg (1956) and Rud et al (1972) criteria was used in one study (Ercan et al. 2007), and the Molven, Halse and Grung (1987) classification was used by another (Mente et al. 2015).

Others used their own systems (Ng et al, 2011). One study followed insurance billing codes to track retreated teeth, until they underwent additional endodontic interventions or extraction (Salehrabi et al, 2010). One study used both cone beam tomographic images as well as periapical images for assessment; another used volumetric changes in lesion size as determined by cone beam imaging (Davies et al. 2016; Metska et al. 2013). Only one study reported patient-centered quality of life outcome data (He et al, 2017).

Success rate of modern retreatment

Modern retreatment success had a weighted mean success rate of 86%, with 95% confidence limits of 85% to 87%, and a range from 65% to 93%, for 20 datasets, from 19 papers (Fig. 8).

Regression Plots of modern retreatment success against time

Plotting and regression analysis of the 20 datasets (Fig. 11) revealed that:

Success rate = 0.002 x the number of years followed + 85 % (Eqn. 2);

the negligible slope, 0.002, indicating that a steady state was approached throughout the period described by the included data, from by one through 5 years after treatment, implying that healing had generally occurred by 1 year, and that through 5 years the numbers of additional healed cases approximated the number of new failures. Hence, retreatment data from throughout the time-period described, 1 to 5 years, could be pooled.

Comparison with traditional retreatment

Data describing traditional retreatment from papers defined by a prior systematic review, was extracted and plotted (Torabinejad et al. 2009) (Figs. 12-14). A funnel plot was suggestive of bias given a lack of symmetry, and 3 out of 5 studies having low precision. A Forest plot provided a weighted mean for the 5 traditional retreatment datasets of 81%, with 95% confidence limits of 79% to 84% (Fig. 13). This differed from modern retreatment ($p < 0.05$). Plotting and regression analysis revealed that:

Success rate = - 0.001 x the number of years followed + 76 % (Eqn. 3),

indicating that a steady state was approached throughout the period described by the included data, from 3 to 5 years after treatment (Fig. 14). Because, the slope was negligible, data from throughout the time-period described, 3 to 5 years, could be pooled.

Comparison with modern microsurgery

Data describing modern microsurgery success from papers defined a prior systematic review was extracted and plotted (Torabinejad et al. 2015) (Figs. 15-17). A funnel plot was suggestive of some bias given a lack of symmetry, and all studies having moderate or low precision (Fig. 15). A Forest plot provided a weighted mean success rate for the 6 modern microsurgery datasets of 85%, with 95% confidence limits of 81% to 88% (Fig. 16). Modern microsurgery success rates did not differ from modern retreatment ($p > 0.05$). Plotting and regression analysis revealed that:

Success rate = - 0.008 x the number of years followed + 91 % (Eqn. 4),

indicating that for traditional retreatment a steady state was approached throughout the period described by the included data, from 2 to 7 years after treatment (Fig. 17). Because, the slope was negligible, data from throughout the time-period described, 2 to 7 years, could be pooled.

The same 6 modern microsurgery datasets were analyzed for survival, rather than success (Figs. 18–20). A funnel plot was suggestive of some bias given a lack of symmetry and most studies having only moderate precision (Fig. 18). A Forest plot provided a weighted mean survival rate for the 6 modern microsurgery datasets of 91%, with 95% confidence limits of 88% to 93% (Fig. 19). This differed significantly from the success rate for modern apical microsurgery ($p < 0.05$). Plotting and regression analysis revealed that:

Success rate = - 0.008 x the number of years followed + 95 % (Eqn. 5),

indicating that for traditional retreatment a steady state was approached throughout the period described by the included data, from 2 to 7 years after treatment (Fig. 20). Because, the slope was negligible, data from throughout the time-period described, 2 to 7 years, could be pooled.

DISCUSSION

The success rate for modern retreatment was high, 86%. Healing of successful cases had generally been accomplished by one-year post-treatment, and little if any change occurred as far as 5 years post-treatment. By one-year post treatment, a steady state was approximated. It is possible that some additional cases healed during this period; if so, an equal number of failures occurred. A direct comparison indicated that the success rate for modern retreatment was superior to traditional retreatment, which approximated a steady state with an 81% success rate from 3 to 5 years post-treatment. Another direct comparison indicated that the success rate for modern retreatment indicated was equal to modern apical microsurgery, which approximated a steady state with an 85% success rate from 2 to 7 years post-treatment. Even if the data sub-set described by the authors as 'Root Canal Morphology Altered" been included (Gorni & Gagliani, 2004), the results of the above comparisons would not have been altered.

Comparison of independent systematic reviews allows for multiple interpretations of data (Low et al. 2017). Use of indirect comparison can provide estimates for use in decision making (Edwards et al. 2009). In this paper, data from prior study-sets was reanalyzed, allowing the same statistical methodology to be applied throughout and direct comparisons to be made.

For modern retreatment, 1-year follow up data was predictive of success through 5 years post treatment. In contrast, the prior systematic review by Torabinejad et al, which included both modern and traditional retreatment studies, suggested a trend for increased success rates of retreatment over time (Torabinejad et al. 2009). They attributed the apparent trend to the number slow-healing cases outweighing the numbers of failures. Whereas, this current study suggests that the apparent trend was due to disproportionally more modern cases than traditional cases being included in Torabinejad et al's longer term follow-up groups. Likewise, the results of this current

study focusing on modern techniques produced results that contrasted with a prior systematic review by Kang et al that pooled data on modern and traditional techniques (Kang et al, 2015). Although the slopes were negligabe, their signs, positive or negative were consistent with trends suggested by Torabinejad et al (Eqns &). The approach used in this current study, new analyses of established study-sets, allowed novel insights and conclusions to be made.

Even if success rates for modern retreatment and modern apical microsurgery did not differ over the 2 to 5 year post-treatment timeframe for which comparisons can be made, the first-line treatment option after failure of initial root canal treatment should generally be modern nonsurgical retreatment (Torabinejad & White 2016). Modern retreatment preserves root length, avoids a surgical procedure, and retains the possibility of modern apical microsurgery as a second-line option (Torabinejad and White 2016; Von Arx & White 2017; White & Torabinejad 2017).

Both modern retreatment and modern apical surgery success rates overlapped with long-term success rates previously reported for initial NSRCT, ~84% (Torabinejad et al. 2007; Iqbal et al, 2007). However, the data describing modern retreatment and modern apical surgery derived from specialty care; whereas, the data on initial NSRCT primarily derived from care provided by generalists and dental students. Moreover, great attention must be paid to best practice during initial treatment so that additional treatments as well as their risks and costs are avoided. Much cross-sectional data indicates that many initial NSRCT is of poor quality (Pak).

The extant modern retreatment literature generally focused on success rates, most using similar types of prognostic instrument; unfortunately, survival rates were generally not reported. As described above, the survival rate for modern microsurgery, 91% was found to be higher than its success rate, 85%. As previously described in the literature, initial NCRCT, long-term survival rates, 97%, are much higher than success rates 84% (Torabinejad et al. 2007; Iqbal et al, 2007).

Instruments such as the Strindberg Criteria and the Orstavik Criteria were intended for use in identifying prognostic factors, not for measuring patient-based outcomes. Success rates derived from such instruments may have little relevance to patients or dentists. It is recommended that new more relevant patient-based outcomes criteria be developed and validated. These might be based upon the concept of function without additional intervention (Lazaraski et al, 2001). In the meantime survival rates should be reported.

Scoping studies indicated that the modern retreatment literature does not yet allow rigorous measurement or comparison of other relevant outcomes, e.g. psychosocial, economic, complications, and need for additional interventions, etc. These factors need to be considered, along with success data, when individual patient decisions are being made. However, clinicians tend not to use current evidence when making decisions and to disagree amongst themselves (Zitzmann et al. 2011; Junges et al. 2014). The dentist's own expertise and patient preference may dominate (Junges et al. 2014). Therefore, specific guidelines and protocols are needed (White et al. 2006; Junges et al. 2014).

Few of the included modern retreatment studies provided complete descriptions of the included populations, medication usage, or other factors that might influence healing. The included studies generally did not describe the specific reasons for retreatment e.g. missed canals, perforations, length issues, absence of coronal restorations, etc. Nonetheless, the included modern retreatment studies generally were of high quality (Fig. 5) and had low levels of bias (Figs. 6 & 7). The generally short duration of follow up and the overall lack of serial follow-ups over time limit the utility of the extant data. The studysets from the previously defined comparators were of lower quality and higher bias, but were sufficient for statistical comparisons to be made.

CONCLUSIONS

The overall quality of the included papers reporting on modern endodontic retreatment was high and bias was low.

The success rate for modern endodontic retreatment was largely unchanged through a period from 1 to 5 years of follow-up, a steady state was approximated.

The success rate of modern endodontic retreatment was approximately 86% through 1 to 5 years after treatment.

The success rate of modern endodontic retreatment was significantly higher than that of traditional retreatment, approximately 81%.

The success rate of modern endodontic retreatment was equivalent to that of modern apical microsurgery, approximately 85%.

Prospective, long-term modern retreatment studies of comprehensively described patient populations using relevant outcome measures are needed.

Figure 1. Search strategy.

Current search string: ("Periapical Diseases"[Mesh] OR "Periapical Periodontitides"[tw] OR "Periapical Periodontitis"[tw] OR "apical periodontitides"[tw] OR "apical periodontitis"[tw] OR endontic*[tw] OR "root canal"[tw] OR "root filling"[tw] OR "Periapical pathoses"[tw] OR "Periapical complications"[tw] OR "Periapical Abscess"[tw] OR "periapical abscesses"[tw]) AND ("Retreatment"[Mesh] OR Retreat*[tw] OR "secondary treatment"[tw]) AND ("Root Canal Irrigants"[Mesh] OR "Root Canal Therapy"[Mesh] OR "Root Canal Filling Materials"[Mesh] OR Non-surgical*[tw] OR Orthograde*[tw] OR "Root Canal Irrigants"[tw] OR "root canal irrigant"[tw] OR "Root Canal Medicaments"[tw] OR "Root Canal Therapy"[tw] OR "Root Canal Therapies"[tw] OR "Root Canal treatment"[tw] OR "Root Canal Treatments"[tw] OR "Root Canal filling"[tw] OR "Root Canal fillings"[tw] OR "Root Canal sealant"[tw] OR "Root Canal sealants"[tw] OR "Endodontic therapy"[tw] OR "Endodontic therapies"[tw] OR "Endodontic treatment"[tw] OR "Endodontic treatments"[tw])) AND ("Treatment Outcome"[Mesh] OR "Prognosis"[Mesh] OR "Follow-Up Studies"[Mesh] OR "Epidemiology"[Mesh] OR "Survival"[Mesh] OR "Survival Analysis"[Mesh] OR "Survival Rate"[Mesh] OR "Quality of Life"[Mesh] OR "Patient Outcome Assessment"[Mesh] OR "Retrospective Studies"[Mesh] OR "Success*"[tw] OR "Failure*"[tw] OR "Rate*"[tw] OR "Outcome*"[tw] OR "PAI score"[tw] OR "PAI scores"[tw] OR "Surviv*"[tw] OR "Retention"[tw] OR "prognosis"[tw] OR "Prognostic*"[tw] OR "Follow up"[tw] OR "Quality of life"[tw] OR "Life quality"[tw] OR "Healing"[tw] OR "Healed"[tw] OR "Heal"[tw] OR "Non-healed"[tw] OR "Effectiveness"[tw] OR "Efficac*"[tw] OR "Retrospective*"[tw]) AND ("1990/01/01"[PDAT] : "3000/12/31"[PDAT]

Figure 2. Table relating clinical terms to MESH terms and keywords.

	MESH	Keywords	
Root canal	"Periapical Diseases"[Mesh] Includes: Periapical Periodontitis and Periapical abscess	"Periapical Periodontitides"[tw] OR "Periapical Periodontitis"[tw] OR "apical periodontitides"[tw] OR "apical periodontitis"[tw] OR endontic*[tw] OR "root canal"[tw] OR "root filling"[tw] OR "Periapical pathoses"[tw] OR "Periapical complications"[tw] OR "Periapical Abscess"[tw] OR "periapical abscesses"[tw]	MESH or TW = 34938
Retreatment	Retreatment	Retreat*[tw] OR "secondary treatment"[tw]	Mesh OR TW = 20715
Non-surgical intervention	("Root Canal Irrigants"[Mesh]) OR "Root Canal	Non-surgical*[tw] OR Orthograde*[tw] OR	Mesh OR TW = 42138 citations

	Therapy"[Mesh] OR "Root Canal Filling Materials"[Mesh] *Root canal preparation	"Root Canal Irrigants"[tw] OR "root canal irrigant"[tw] OR "Root Canal Medicaments"[tw] OR "Root Canal Therapy"[tw] OR "Root Canal Therapies"[tw] OR "Root Canal treatment"[tw] OR "Root Canal Treatments"[tw] OR "Root Canal filling"[tw] OR "Root Canal fillings"[tw] OR "Root Canal sealant"[tw] OR "Root Canal sealants"[tw] OR "Endodontic therapy"[tw] OR "Endodontic therapies"[tw] OR "Endodontic	

		treatment"[tw] OR "Endodontic treatments"[tw]	
Outcomes	"Treatment Outcome"[Mesh] OR "Prognosis"[Mesh] OR "Follow-Up Studies"[Mesh] OR "Epidemiology"[Mesh] OR "Survival"[Mesh] OR "Survival Analysis"[Mesh] OR "Survival Rate"[Mesh] OR "Quality of Life"[Mesh] OR "Patient Outcome Assessment"[Mesh] OR	"Success*"[tw] OR "Failure*"[tw] OR "Rate*"[tw] OR "Outcome*"[tw] OR "PAI score"[tw] OR "PAI scores"[tw] OR "Surviv*"[tw] OR "Retention"[tw] OR "prognosis"[tw] OR "Prognostic*"[tw] OR "Follow up"[tw] OR "Quality of life"[tw] OR "Life quality"[tw] OR "Healing"[tw] OR	Mesh OR TW = 6612115

	"Retrospective Studies"[Mesh]	"Healed"[tw] OR "Heal"[tw] OR "Non-healed"[tw] OR "Effectiveness"[tw] OR "Efficac*"[tw] OR "Retrospective*"[tw]	

Figure 4. Evidence Table summarizing modern retreatment success rates. Moein, ADD

THE OVERALL WONG SCORE IN A 5th COLUMN

Article	Sample Size	Recall Years	Success Rate	Wong Score
Farzaneh 2004	99	5	83.84%	24
Gorni 2004	250	2	87%	27
Gorni 2004	202	2	47%	27
Ercan 2007	40	1.2	82.5%	21
Chevingy 2008	126	5	83%	26
Hsiao 2009	5	1	80%	22
Salehrabi 2010	4744	5	86%	27
Metska 2013	27	1	86%	22
Davies 2015	98	1	93%	23
Mente 2015	27	1	87%	22
Orhan 2017	16	1	87.5%	20
He 2017	63	2	90%	24
Eyuboglue 2017	110	2.5	90%	27
Al- Nuaimi 2017	137	1	88%	22
Pirani 2017	132	5	83%	27
Chybowski2018	72	2.5	91.7%	25

Alghofaily2018	16	3.5*	87%	23
Alharmoodi 2019	109	0.8*	81%	27
Olcay 2019	101	2.8	85.1%	27
Zandi 2019	52	4	81%	24
Zandi 2019	52	1	65%	24

*: Average time of recall

Figure 5. Study quality ratings, Wong Scores.

Articles	Wong 1	Wong 2	Wong 3	Total
Farzaneh 2004	A 3 B 3	A 2 B 2	A 3 B 2	24
Gorni 2004	A 3 B 3	A 3 B 3	A 3 B 3	27
Ercan 2007	A 3 B 3	A 1 B 1	A 3 B 3	21
Chevingy 2008	A 3 B 3	A 3 B 3	A 3 B 2	26
Hsiao 2009	A 3 B 3	A 1 B 1	A 3 B 3	22
Salehrabi 2010	A 3 B 3	A 3 B 3	A 3 B 3	27
Metska 2013	A 3 B 3	A 1 B 1	A 3 B 3	22
Davies 2015	A 3 B 3	A 1 B 2	A 3 B 3	23
Mente 2015	A 3 B 3	A 1 B 1	A 3 B 3	22
Orhan 2017	A 2 B 3	A 1 B 1	A 3 B 2	20
He 2017	A 3 B 3	A 2 B 2	A 3 B 3	24
Eyuboglue 2017	A 3 B 3	A 3 B 3	A 3 B 3	27

Al- Nuaimi 2017	A 2 B 2	A 2 B 2	A 3 B 3	22
Pirani 2017	A 3 B 3	A 3 B 3	A 3 B 3	27
Chybowski2018	A 3 B 3	A 2 B 3	A 2 B 3	25
Alghofaily2018	A 3 B 3	A 1 B 2	A 3 B 3	23
Alharmoodi 2019	A 3 B 3	A 3 B 3	A 3 B 3	27
Olcay 2019	A 3 B 3	A 3 B 3	A 3 B 3	27
Zandi 2019	A 3 B 3	A 2 B 3	A 3 B 2	24

Figure 7. Funnel plot for modern endodontic retreatment, 20 datasets.

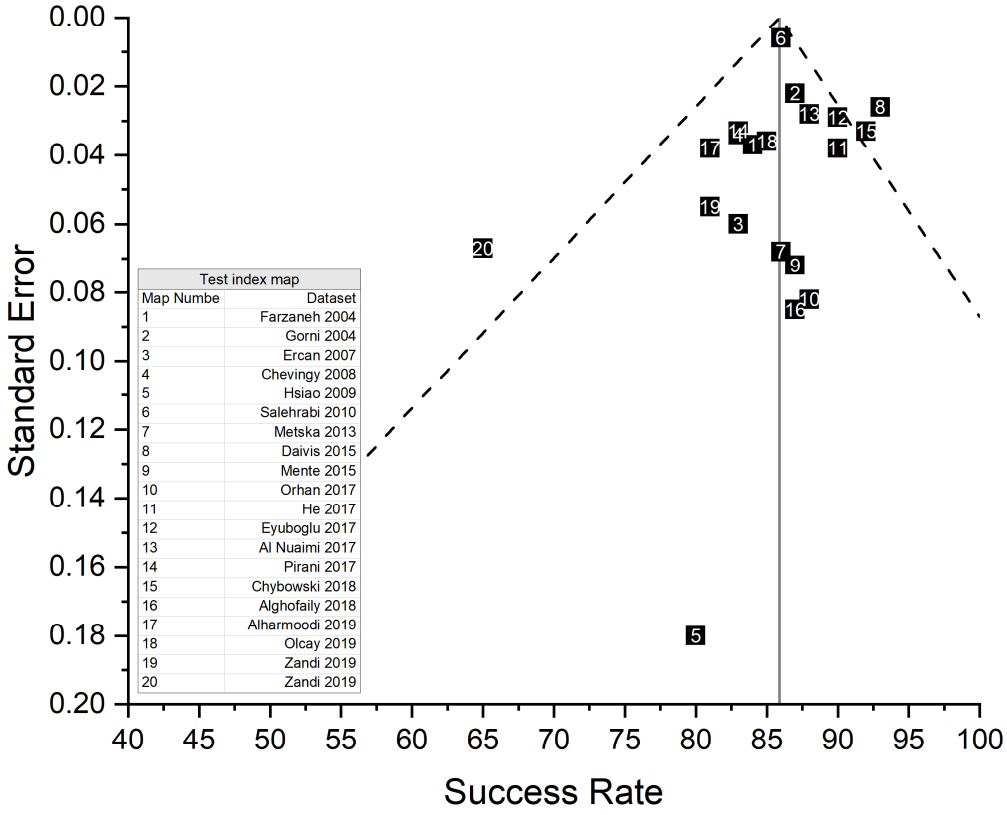

Standard Error
Success Rate
0.00
0.02
0.04
0.06
0.08
0.10
0.12
0.14
0.16
0.18
0.20
40
45
50
55
60
65
70
75
80
85
90
95
100
Test index map
Map Numbe Dataset
1 Farzaneh 2004
2 Gorni 2004
3 Ercan 2007
4 Chevingy 2008
5 Hsiao 2009
6 Salehrabi 2010
7 Metska 2013
8 Daivis 2015
9 Mente 2015
10 Orhan 2017
11 He 2017
12 Eyuboglu 2017
13 Al Nuaimi 2017
14 Pirani 2017
15 Chybowski 2018
16 Alghofaily 2018
17 Alharmoodi 2019
18 Olcay 2019
19 Zandi 2019
20 Zandi 2019

Figure 8. Forest plot for modern endodontic retreatment, 20 datasets. The random effects model was used to report point estimates and 95% confidence limits. The mean weighted success rate was 85.89%, with 95% confidence limits from 85.03% to 86.75%.

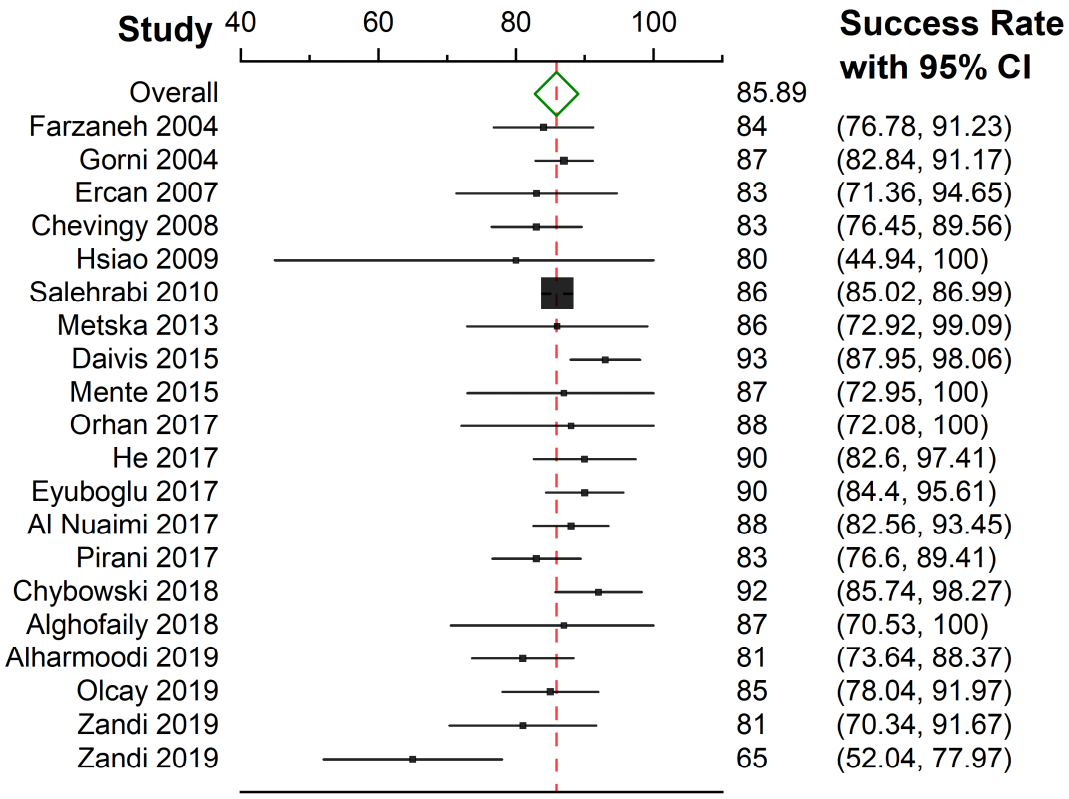


Figure 9. Plot of weighted mean success rate against years of follow-up for 20 modern endodontic retreatment datasets.

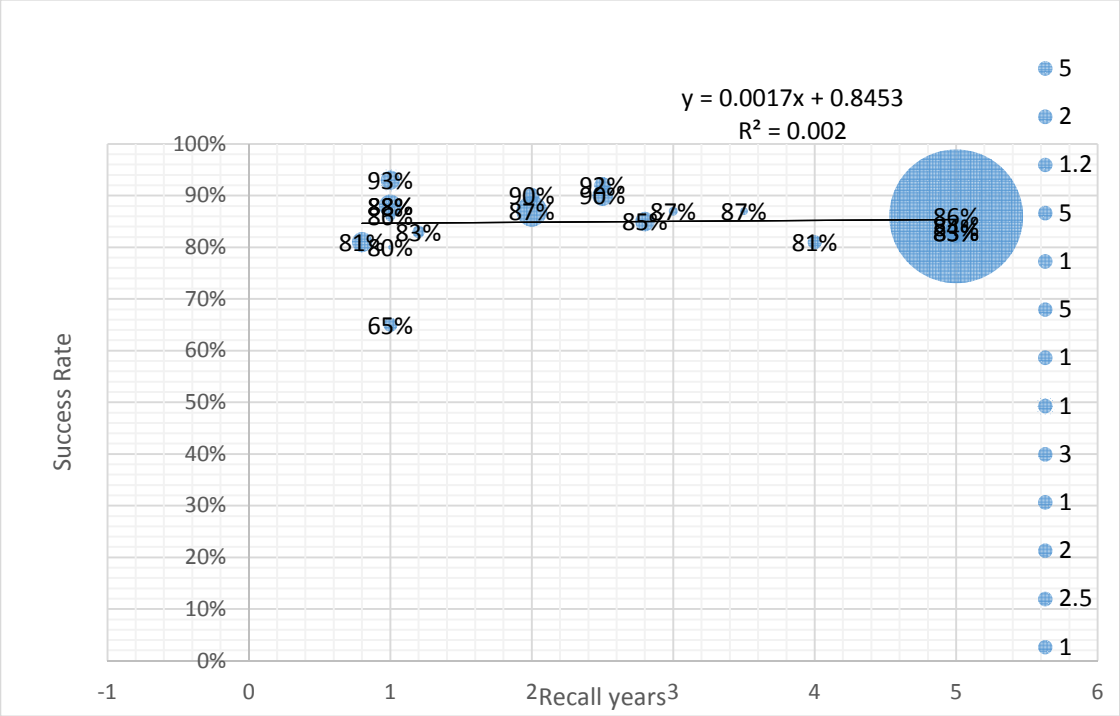


Figure 10. Funnel plot for traditional endodontic retreatment, 5 datasets.

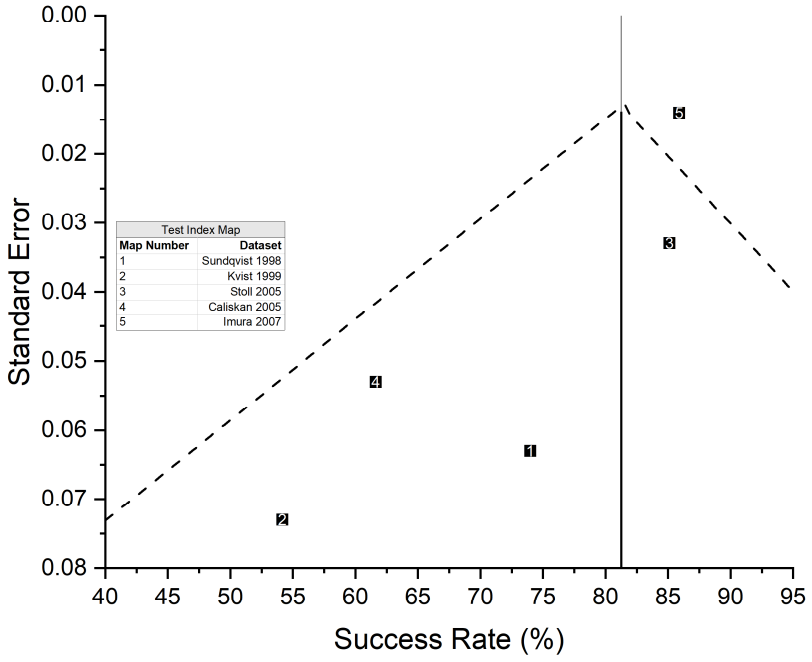


Figure 11. Forest plot for traditional endodontic retreatment, 5 datasets. The random effects model was used to report point estimates and 95% confidence limits. The mean weighted success rate was 81.27%, with 95% confidence limits from 78.77% to 83.79%.

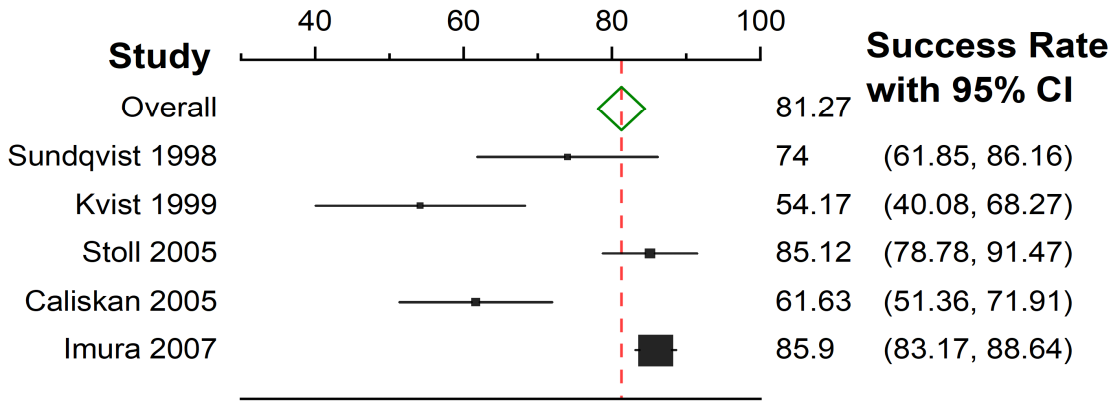


Figure 12. Plot of mean weighted success rates against years of follow-up for traditional endodontic retreatment, 5 datasets.

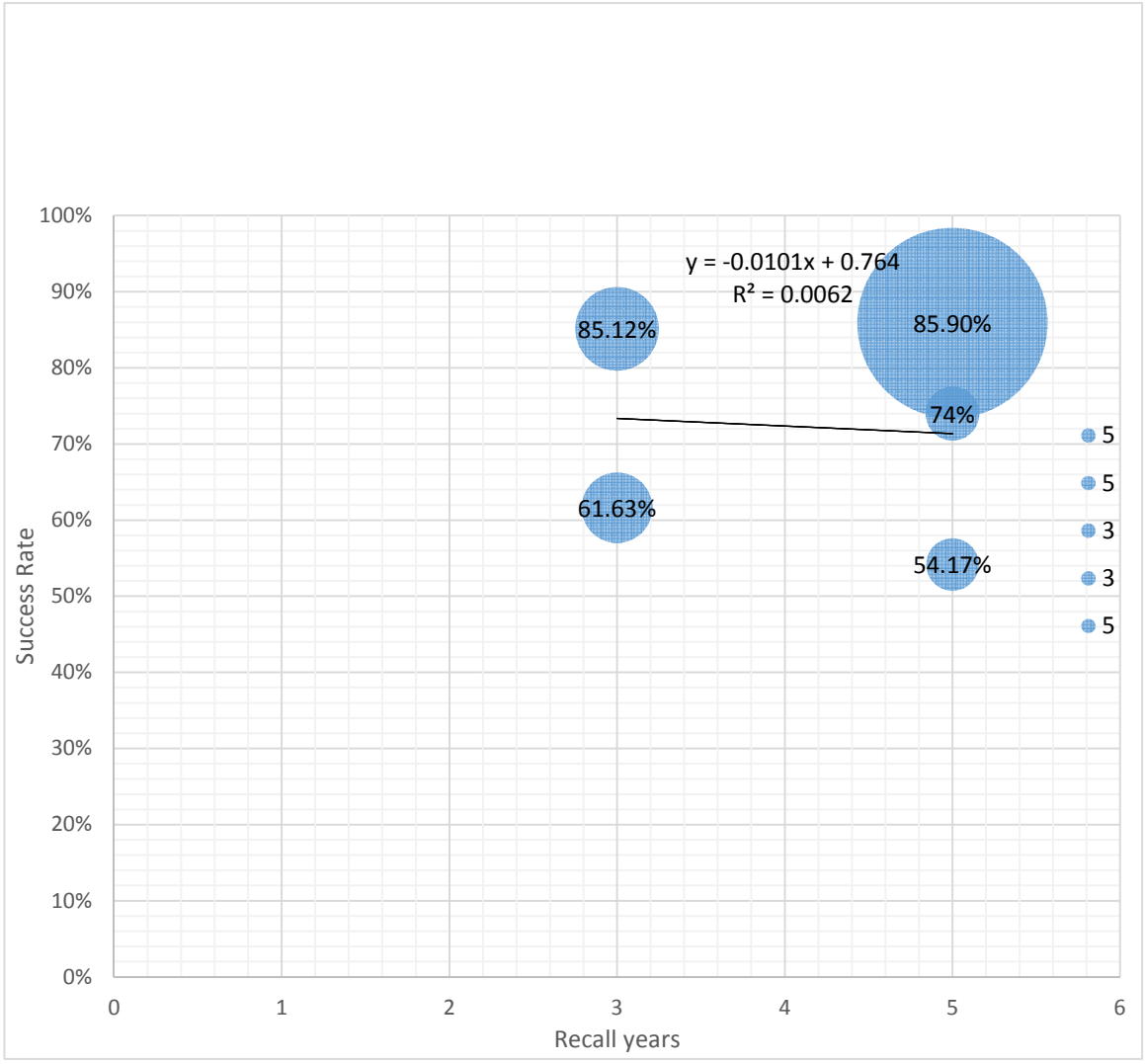


Figure 13. Funnel plot for success rates of modern endodontic microsurgery.

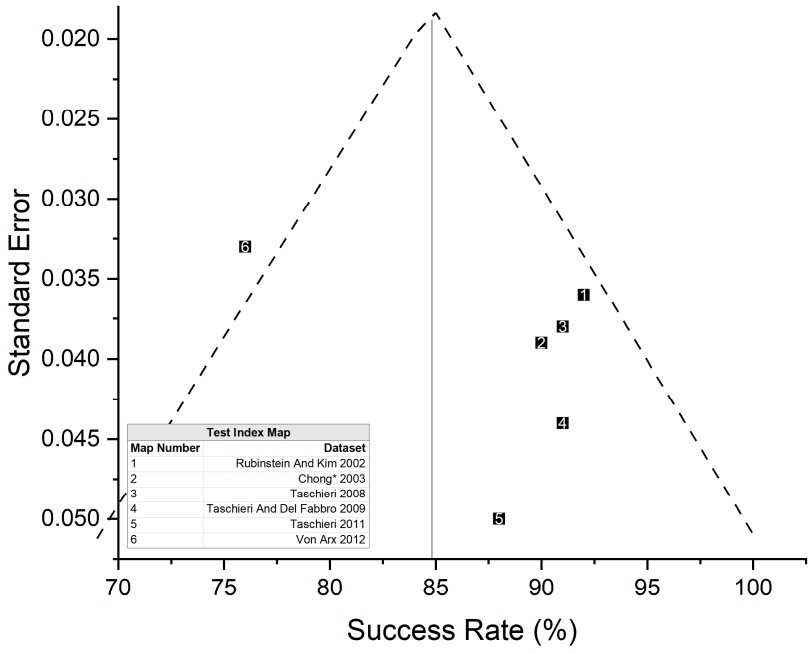


Figure 14. Forest plot for success rates of modern endodontic microsurgery, 6 datasets. The random effects model was used to report point estimates and 95% confidence limits. The mean weighted success rate was 84.84 %, with 95% confidence limits from 81.47% to 88.21%.

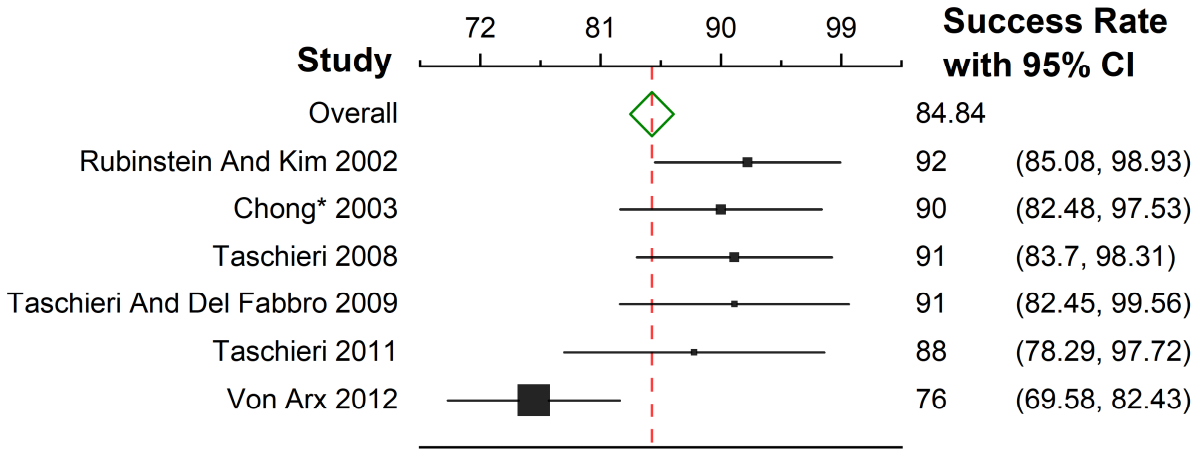


Figure 15. Plot of mean weighted success rate against years of follow-up for modern apical microsurgery, 6 datasets.

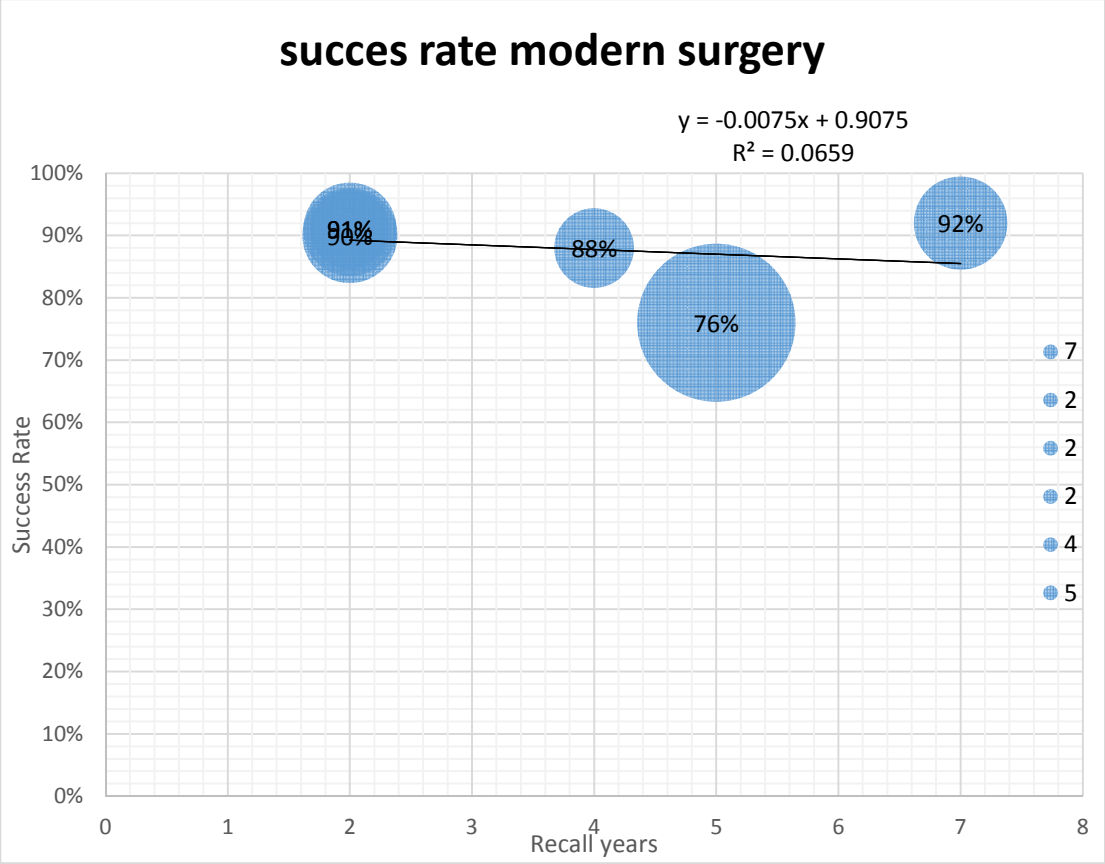


Figure 16. Funnel plot for survival rates of modern endodontic microsurgery, 6 datasets from.

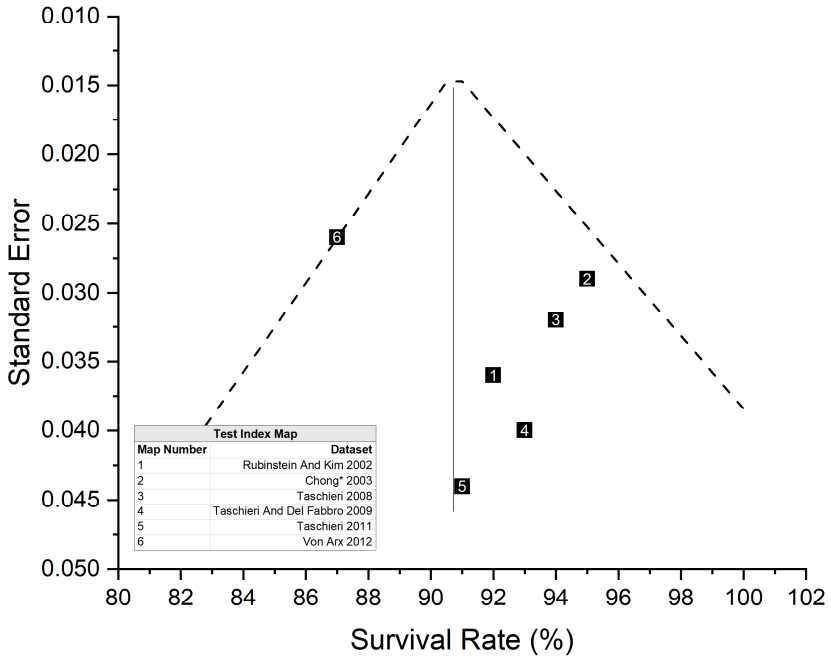


Figure 17. Forest plot for survival rates of modern endodontic microsurgery, 6. The random effects model was used to report point estimates and 95% confidence limits. The mean weighted success rate was 90.74 %, with 95% confidence limits from 88.02% to 93.47%.

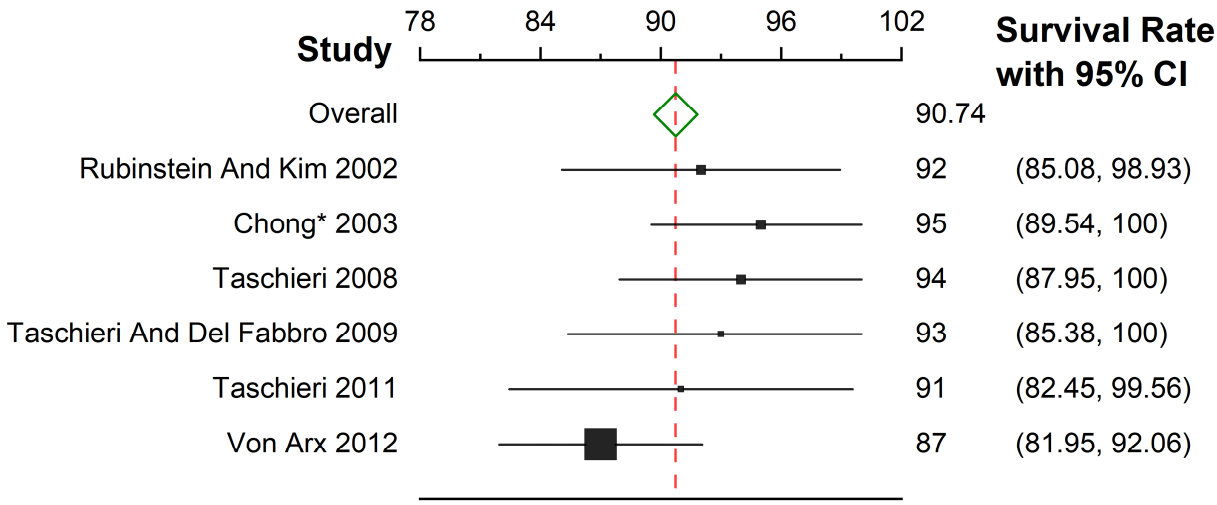
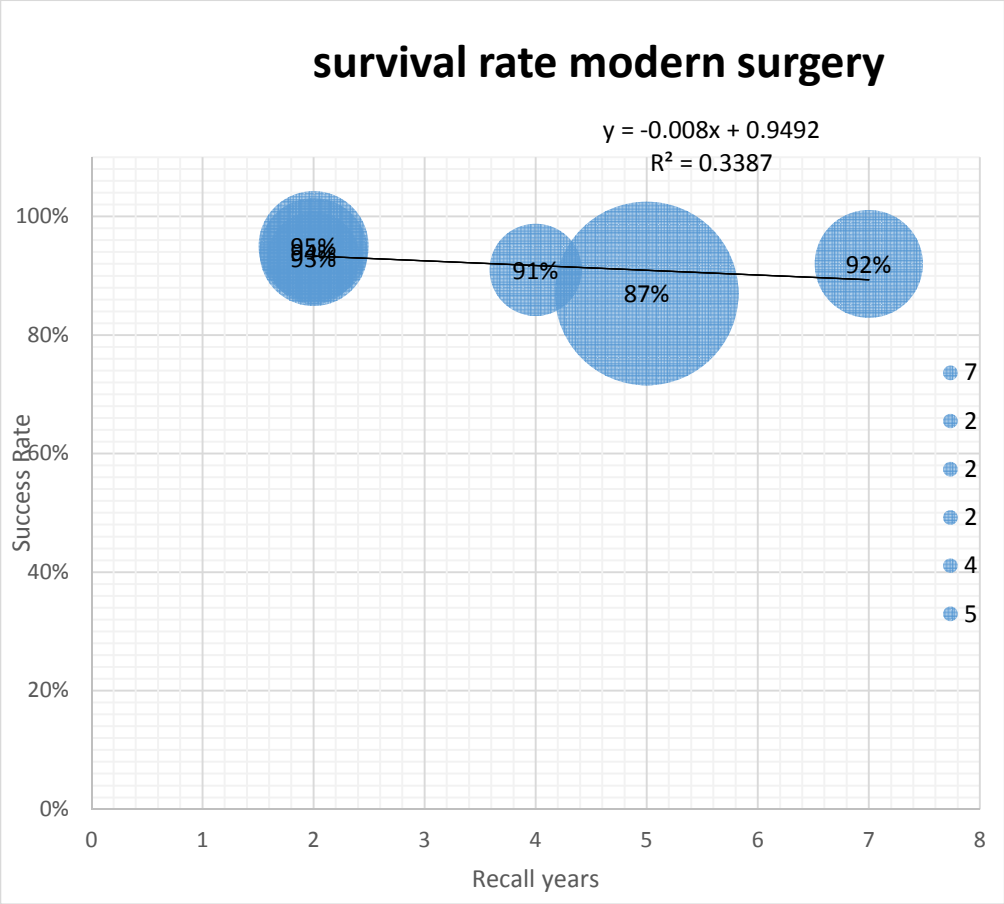


Figure 18. Plot of mean weighted survival rate against years of follow-up for modern apical microsurgery, 6 datasets.


survival rate modern surgery
y = -0.008x + 0.9492
R² = 0.3387
100%
80%
60%
40%
20%
0%
Success Rate
0
1
2
3
4
5
6
7
8
Recall years
95%
94%
93%
91%
87%
92%
7
2
2
2
4
5

REFERENCES

Agresti A, Coull BA. Approximate is better than “exact” for interval estimation of binomial proportions. Am Stat 1998; 52:119-26.

Al□Nuaimi L, Patel NS, Austin RS, Mannocci F. A prospective study assessing the effect of coronal tooth structure loss on the outcome of root canal retreatment. Int Endod J 2017 50:1143-57.

Alghofaily M, Tordik P, Romberg E, Martinho F, Fouad AF. Healing of apical periodontitis after nonsurgical root canal treatment: the role of statin intake. J. Endod, 44: 1355-60

Alharmoodi R, Al-Salehi S. Assessment of the quality of endodontic re-treatment and changes in periapical status on a postgraduate endodontic clinic, J Dent. 2019 92: 103261.

Ashraf H, Milani AS, Shakeri Asadi S. Evaluation of the success rate of nonsurgical single visit retreatment. Iran Endod J. 2007;2(2):69-72.

Avila G, Galindo-Moreno P, Soehren S, Misch CE, Morelli T, Wang HL. A novel decision-making process for tooth retention or extraction. J Periodontol. 2009;80(3):476-491.

Bader J, Ismail A; ADA Council on Scientific Affairs; Division of Science; Journal of the American Dental Association. Survey of systematic reviews in dentistry. J Am Dent Assoc. 2004;135(4):464-473.

Balto HA, Al-Madi EM. A comparison of retreatment decisions among general dental practitioners and endodontists. J Dent Educ. 2004;68(8):872-879.

Bigras BR, Johnson BR, BeGole EA, Wenckus CS. Differences in clinical decision making: a comparison between specialists and general dentists. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2008;106(1):139-144.

Chiappelli F, Navarro AM, Moradi DR, Manfrini E, Prolo P. Evidence-Based Research in Complementary and Alternative Medicine III: Treatment of Patients with Alzheimer's Disease. Evid Based Complement Alternat Med. 2006;3(4):411-424.

Chybowski EA, Glickman GN, Patel Y, Fleury A, Solomon E, He J. Clinical Outcome of Non-Surgical Root Canal Treatment Using a Single-cone Technique with Endosequence Bioceramic Sealer: A Retrospective Analysis [published correction appears in J Endod. 2018 Jul;44(7):1199]. J Endod. 2018;44(6):941-945.

Davies A, Patel S, Foschi F, Andiappan M, Mitchell PJ, Mannocci F. The detection of periapical pathoses using digital periapical radiography and cone beam computed tomography in endodontically retreated teeth - part 2: a 1 year post-treatment follow-up. Int Endod J. 2016;49(7):623-635.

de Chevigny C, Dao TT, Basrani BR, et al. Treatment outcome in endodontics: the Toronto study--phases 3 and 4: orthograde retreatment. J Endod. 2008;34(2):131-137.

Edwards SJ, Clarke MJ, Wordsworth S, Borrill J. Indirect comparisons of treatments based on systematic reviews of randomised controlled trials. Int J Clin Pract. 2009;63(6):841-854.

Ercan E, Dalli M, Duülgergil CT, Yaman F. Effect of intracanal medication with calcium hydroxide and 1% chlorhexidine in endodontic retreatment cases with periapical lesions: an in vivo study. J Formos Med Assoc. 2007;106(3):217-224.

Eyuboglu TF, Olcay K, Özcan M. A clinical study on single-visit root canal retreatments on consecutive 173 patients: frequency of periapical complications and clinical success rate. Clin Oral Investig. 2017;21(5):1761-1768.

Farzaneh M, Abitbol S, Friedman S. Treatment outcome in endodontics: the Toronto study. Phases I and II: Orthograde retreatment. J Endod. 2004;30(9):627-633.

Gerritsen AE, Allen PF, Witter DJ, Bronkhorst EM, Creugers NH. Tooth loss and oral health-related quality of life: a systematic review and meta-analysis. Health Qual Life Outcomes. 2010;8:126. Published 2010 Nov 5.

Gorni FG, Gagliani MM. The outcome of endodontic retreatment: a 2-yr follow-up. J Endod. 2004;30(1):1-4.

Greenstein G, Cavallaro J, Tarnow D. When to save or extract a tooth in the esthetic zone: a commentary. Compend Contin Educ Dent. 2008;29(3):136-158.

Hamedy R, Shakiba B, Fayazi S, Pak JG, White SN. Patient-centered endodontic outcomes: a narrative review. Iran Endod J. 2013;8(4):197-204.

Hansson P, Sunnegårdh-Grönberg K, Bergdahl J, Bergdahl M, Nyberg L, Nilsson LG. Relationship between natural teeth and memory in a healthy elderly population. Eur J Oral Sci. 2013;121(4):333-340.

He J, White RK, White CA, Schweitzer JL, Woodmansey KF. Clinical and Patient-centered Outcomes of Nonsurgical Root Canal Retreatment in First Molars Using Contemporary Techniques. J Endod. 2017;43(2):231-237.

Hsiao A, Glickman G, He J. A retrospective clinical and radiographic study on healing of periradicular lesions in patients taking oral bisphosphonates. J Endod. 2009;35(11):1525-1528.

Iqbal MK, Kim S. For teeth requiring endodontic treatment, what are the differences in outcomes of restored endodontically treated teeth compared to implant-supported restorations? [published correction appears in Int J Oral Maxillofac Implants. 2008 Jan-Feb;23(1):56]. Int J Oral Maxillofac Implants. 2007;22 Suppl:96-116.

John V, Chen S, Parashos P. Implant or the natural tooth--a contemporary treatment planning dilemma?. Aust Dent J. 2007;52(1 Suppl):S138-S150.

Junges R, Zitzmann NU, Walter C, Rösing CK. Dental care providers' decision making regarding maintenance of compromised teeth and implant therapy indication: an analysis of gender and enrollment in teaching positions. Clin Oral Implants Res. 2014;25(9):1027-1033.

Kang M, In Jung H, Song M, Kim SY, Kim HC, Kim E. Outcome of nonsurgical retreatment and endodontic microsurgery: a meta-analysis. Clin Oral Investig. 2015;19(3):569-582

Kohli MR, Berenji H, Setzer FC, Lee SM, Karabucak B. Outcome of Endodontic Surgery: A Meta-analysis of the Literature-Part 3: Comparison of Endodontic Microsurgical Techniques with 2 Different Root-end Filling Materials. J Endod. 2018;44(6):923-931.

Lazarski MP, Walker WA 3rd, Flores CM, Schindler WG, Hargreaves KM. Epidemiological evaluation of the outcomes of nonsurgical root canal treatment in a large cohort of insured dental patients. J Endod. 2001;27(12):791-796.

Levin L, Halperin-Sternfeld M. Tooth preservation or implant placement: a systematic review of long-term tooth and implant survival rates. J Am Dent Assoc. 2013;144(10):1119-1133.

Low J, Ross JS, Ritchie JD, et al. Comparison of two independent systematic reviews of trials of recombinant human bone morphogenetic protein-2 (rhBMP-2): the Yale Open Data Access Medtronic Project. Syst Rev. 2017;6(1):28.

Madarati AA, Watts DC, Qualtrough AJ. Opinions and attitudes of endodontists and general dental practitioners in the UK towards the intra-canal fracture of endodontic instruments. Part 2. Int Endod J. 2008;41(12):1079-1087.

Madarati AA, Watts DC, Qualtrough AJ. Opinions and attitudes of endodontists and general dental practitioners in the UK towards the intracanal fracture of endodontic instruments: part 1. Int Endod J. 2008;41(8):693-701.

Mente J, Leo M, Michel A, Gehrig H, Saure D, Pfefferle T. Outcome of orthograde retreatment after failed apicoectomy: use of a mineral trioxide aggregate apical plug. J Endod. 2015;41(5):613-620.

Metska ME, Parsa A, Aartman IH, Wesselink PR, Ozok AR. Volumetric changes in apical radiolucencies of endodontically treated teeth assessed by cone-beam computed tomography 1 year after orthograde retreatment. J Endod. 2013;39(12):1504-1509.

Molven O, Halse A, Grung B. Observer strategy and the radiographic classification of healing after endodontic surgery. Int J Oral Maxillofac Surg. 1987;16(4):432-439.

Molen CK, BeGole EA, Jacobsen EL. Endodontic patient recall procedures: a national survey of endodontic practices. Journal of Endodontics. 1998 Dec;24(12):829-832.

Nesković J, Zivković S, Medojević M, Maksimović M. Outcome of orthograde endodontic retreatment--A two-year follow-up. Srp Arh Celok Lek. 2016;144(3-4):174-180.

Ng YL, Mann V, Gulabivala K. A prospective study of the factors affecting outcomes of nonsurgical root canal treatment: part 1: periapical health. Int Endod J. 2011;44(7):583-609.

Okoje VN, Dosumu OO, Alonge TO, Onyeaso C. Tooth loss: are the patients prepared?. Niger J Clin Pract. 2012;15(2):172-175.

Olcay K, Eyüboglu TF, Özcan M. Clinical outcomes of non-surgical multiple-visit root canal retreatment: a retrospective cohort study. Odontology. 2019;107(4):536-545.

Orhan EO, Dereci Ö, Irmak Ö. Endodontic Outcomes in Mandibular Second Premolars with Complex Apical Branching. J Endod. 2017;43(1):46-51.

Orstavik D, Kerekes K, Eriksen HM. The periapical index: a scoring system for radiographic assessment of apical periodontitis. Endod Dent Traumatol. 1986;2(1):20-34.

Pagonis TC, Fong CD, Hasselgren G. Retreatment decisions--a comparison between general practitioners and endodontic postgraduates. J Endod. 2000;26(4):240-241.

Pak JG, Fayazi S, White SN. Prevalence of periapical radiolucency and root canal treatment: a systematic review of cross-sectional studies. J Endod. 2012;38(9):1170-1176.

Parashos P, Messer HH. Uptake of rotary NiTi technology within Australia. Aust Dent J. 2005;50(4):251-257.

Pirani C, Iacono F, Gatto MR, et al. Outcome of secondary root canal treatment filled with Thermafil: a 5-year follow-up of retrospective cohort study. Clin Oral Investig. 2018;22(3):1363-1373.

Ricucci D, Siqueira JF Jr, Lopes WS, Vieira AR, Rôças IN. Extraradicular infection as the cause of persistent symptoms: a case series. J Endod. 2015;41(2):265-273.

Rud J, Andreasen JO, Jensen JF. A multivariate analysis of the influence of various factors upon healing after endodontic surgery. Int J Oral Surg. 1972;1(5):258-271.

Saintrain MV, de Souza EH. Impact of tooth loss on the quality of life. Gerodontology. 2012;29(2):e632-e636.

Salehrabi R, Rotstein I. Epidemiologic evaluation of the outcomes of orthograde endodontic retreatment. J Endod. 2010;36(5):790-792.

Setzer FC, Kohli MR, Shah SB, Karabucak B, Kim S. Outcome of endodontic surgery: a meta-analysis of the literature--Part 2: Comparison of endodontic microsurgical techniques with and without the use of higher magnification. J Endod. 2012;38(1):1-10.

Signoretti FG, Endo MS, Gomes BP, Montagner F, Tosello FB, Jacinto RC. Persistent extraradicular infection in root-filled asymptomatic human tooth: scanning electron microscopic analysis and microbial investigation after apical microsurgery. J Endod. 2011;37(12):1696-1700.

Strindberg LZ. .The dependence of the results of pulp therapy on certain factors-an analytica study based on radiographic and clinical follow-up examination, Acta Odontol Scand, 1956; 14: 1-175.

Torabinejad M, Anderson P, Bader J, et al. Outcomes of root canal treatment and restoration, implant-supported single crowns, fixed partial dentures, and extraction without replacement: a systematic review. J Prosthet Dent. 2007;98(4):285-311.

Torabinejad M, Corr R, Handysides R, Shabahang S. Outcomes of nonsurgical retreatment and endodontic surgery: a systematic review. J Endod. 2009;35(7):930-937.

Torabinejad M, Landaez M, Milan M, et al. Tooth retention through endodontic microsurgery or tooth replacement using single implants: a systematic review of treatment outcomes. J Endod. 2015;41(1):1-10.

Torabinejad M, White SN. Endodontic treatment options after unsuccessful initial root canal treatment: Alternatives to single-tooth implants. J Am Dent Assoc. 2016;147(3):214-220.

Von Arx T & White SN. In Modern Endodontic Surgery, Ed Torabinejad. The art and science of contemporary surgical endoddontics. Hanover Park: Quintessence; 2017.

White SN, Miklus VG, Potter KS, Cho J, Ngan AY. Endodontics and implants, a catalog of therapeutic contrasts. J Evid Based Dent Pract. 2006;6(1):101-109.

White SN & Torabinejad M. Chapter 13 Endodontic outcomes. In Eds Chugal and Lin. Endodontic prognosis. Gewerbestrasse: Springer international;2017.

Zandi H, Petronijevic N, Mdala I, et al. Outcome of Endodontic Retreatment Using 2 Root Canal Irrigants and Influence of Infection on Healing as Determined by a Molecular Method: A Randomized Clinical Trial. J Endod. 2019;45(9):1089-1098.e5.

Zitzmann NU, Scherrer SS, Weiger R, Lang NP, Walter C. Preferences of dental care providers in maintaining compromised teeth in relation to their professional status: implants instead of periodontally involved maxillary molars?. Clin Oral Implants Res. 2011;22(2):143-150.

Zitzmann NU, Krastl G, Hecker H, Walter C, Weiger R. Endodontics or implants? A review of decisive criteria and guidelines for single tooth restorations and full arch reconstructions. Int Endod J. 2009;42(9):757-774.